Acute Lung Injury and ARDS
10:30 AM - 12:00 PM

ALVEOLAR FLUID REABSORPTION IS IMPAIRED BY HYPERCAPNIA INDEPENDENTLY OF EXTRACELLULAR AND INTRACELLULAR PH

Arturo Briva MD* Lynn Welch BS Jiwang Chen PhD Pavlos Myrianthefs MD Zaher Azzam MD Emilia Lecuona PhD Vidas Dumasius BS Daniel Batlle MD Yosef Gruenbaum PhD Jacob I. Sznajder MD Northwestern University, Chicago, IL

PURPOSE: Alveolar epithelium is exposed to high CO2 tensions (hypercapnia) in patients with COPD and during permissive hypercapnia in mechanically ventilated subjects. Recently, some reports propose that hypercapnia could be beneficial in the treatment of ALI/ARDS. However, more recently new data has been presented suggesting that hypercapnia may have deleterious effects on the pulmonary epithelium. The objective of our investigation was to determine the effects of hypercapnia on alveolar epithelial function.

METHODS: Alveolar fluid reabsorption (AFR) was assessed during hypercapnia with normal and acid pH as compared to metabolic acidosis in the isolated rat lung model. In parallel, Na,K-ATPase activity and protein abundance in alveolar type II cell cultures was evaluated.

RESULTS: Hypercapnia decreased AFR by ~ 60% (pCO2 ~ 80 mmHg, pH = 7.15). With high pCO2 even at normal pH (7.40) alveolar fluid reabsorption was decreased but not during metabolic acidosis (pH 7.2 and normal PCO2). The deleterious effect of hypercapnia on AFR was not associated with changes of intracellular pH and reversed when pCO2 was normalized. The Na,K-ATPase activity and protein abundance was decreased in alveolar epithelial cells exposed to hypercapnia but not metabolic acidosis.

CONCLUSION: Our data suggest that hypercapnia but not metabolic acidosis impairs alveolar fluid reabsorption via an endocytosis-mediated process of the Na,K-ATPase in alveolar epithelial cells leading to decreased Na,K-ATPase activity.

CLINICAL IMPLICATIONS: We reason that permissive hypercapnia may have deleterious effects on alveolar epithelial function and the ability of the lungs to clear edema in mechanically ventilated patients.

DISCLOSURE: Arturo Briva, None.

INTRAOPERATIVE TIDAL VOLUME AS A RISK FACTOR FOR REPIRATORY FAILURE AFTER PNEUMONECTOMY

Evans R. Fernández MD* Mark T. Keegan MD Daniel R. Brown MD Francis C. Nichols MD Rolf D. Hubmayr MD Ognjen Gajic MD Mayo Clinic, Rochester, MN

PURPOSE: Clinical and experimental studies identified large tidal volume (Vt) as an important risk factor for development of acute respiratory failure and acute lung injury (ALI). Patients undergoing pneumonectomy may be at particular risk for adverse ventilator settings during surgery. We hypothesized that larger intraoperative Vt may be associated with postoperative respiratory failure in patients undergoing pneumonectomy.

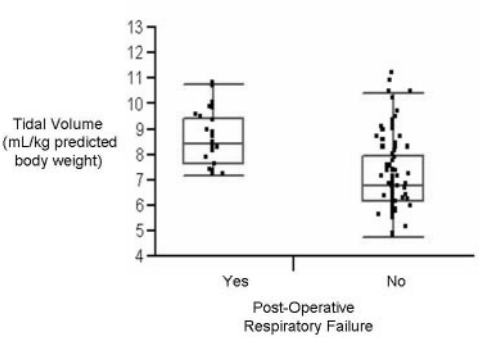
METHODS: We reviewed the electronic medical records of all patients having elective pneumonectomy at our institution from January 1999 to January 2003. In addition to intraoperative Vt, we collected data on demographics, comorbities, neoadjuvant chemotherapy and radiotherapy, pulmonary function tests, operative procedures, duration of surgery and intraoperative fluid administration. Respiratory failure was defined as the need for mechanical ventilation for greater than 48 hours postoperatively or the need for reinstitution of mechanical ventilation after extubation.

RESULTS: Of 170 consecutive pneumonectomy patients, 30 (18%) developed post-operative respiratory failure. Causes of respiratory failure were ALI in 15 patients (50%), cardiogenic edema in 5 (17%), pneumonia in 7 (23%), bronchopleural fistula in 2 (7%) and pulmonary thromboembolism in 1 (3%). Patients who developed respiratory failure were ventilated with larger intraoperative Vt than those who did not (median 8.3 vs 6.7 mL/kg predicted body weight, $p<0.001$, Figure). In a multvariate logistic regression analysis, larger intraoperative Vt (odds ratio 1.45 for each mL/Kg of predicted body weight, 95% CI 1.12-1.92,) and larger volumes of intraoperative fluid (odds ratio 1.47 per liter of fluid infused, 95% CI=1.00-2.18), were identified as risk factors of postoperative respiratory failure. The 60-day mortality rate after pneumonectomy was 7.6% (13 of 170 patients), with respiratory failure accounting for 46% of the deaths. Patients who developed post-operative respiratory failure had longer hospital length of stay (31.5 ± 10.4 days vs. 7.8 ± 1.3 days; $p<0.001$).

CONCLUSION: Large intraoperative Vt and larger volumes of intravenous fluids during pneumonectomy are associated with an increased risk of post-operative respiratory failure.

CLINICAL IMPLICATIONS: Potentially harmful intraoperative ventilatory settings, in particular large tidal volumes, should be avoided during pneumonectomy.

DISCLOSURE: Evans Fernández, None.



METHYLPREDNISOLONE INFUSION IN PATIENTS WITH EARLY ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) SIGNIFICANTLY IMPROVES LUNG FUNCTION: RESULTS OF A RANDOMIZED CONTROLLED TRIAL (RCT)

Gianfranco U. Meduri MD* Emmel Golden MD Amado X. Freire MD Edwin Taylor MD Mohamad Zaman MD Stephanie J. Carson MD Mary Gibson MD Reba Umberger MD University of Tennessee Health Science Center, Memphis, TN

PURPOSE: To determine the effects of prolonged methylprednisolone infusion (PMPI) in patients with early ARDS.

METHODS: Patients were stratified by medical and surgical ARDS. Treatment: methylprednisolone (MP) loading 1 mg/kg I.V. was followed by PMPI at 1 mg/kg/day (days 1-14), 0.5 mg/kg/day (days 15-21), 0.25 mg/kg/day (days 22-25), and 0.125 mg/kg/day (days 26-28). Patients failing to improve lung injury score (LIS) by study day 7-9(unresolving ARDS) received open label MP (2mg/kg/day) treatment as previously reported (JAMA 1998; 280: 159). Infection surveillance and avoidance of paralysis were integral components of the protocol. The primary end-point to terminate the study was a 1-point reduction in lung injury score (LIS) by study day 7.

RESULTS: 91 patients entered the study (intention to treat - ITT)and 79 were eligible for analysis (55 treated and 24 control) on study day 7.The two groups had similar characteristics at study entry (Table 1). By day 7 (Table 2), the response of the two groups clearly diverged with almost twice the proportion of treated patients achieving a1-point reduction in LIS (69.8% vs. 37.5%; P = 0.002)and about 50%more treated patients breathing without assistance (53.9% vs. 25.0%; P = 0.01). Treated patients had a significant reduction in C-reactive protein levels and by day 7 had significantly lower LIS and multiple organ dysfunction syndrome (MODS) score. Treatment was associated with a reduction in the duration of MV, ICU staynd ICU mortality. The treatment group developed more frequently hyperglycemia (52.5% vs. 28.6%; P = 0.06), and polyneuropathy (2 vs. 0). Among treated patients, infection surveillance identified most nosocomial infections (65%) in the absence of fever.

CONCLUSION: PMPI was associated with significantly improved lung function and reduced duration of mechanical ventilation. These findings are consistent with the effects of prolonged glucocorticoid treatment previously reported in patients with unresolving ARDS (2 RCTs)and severe community-acquired pneumonia (AJRCCM 2005; 171; 242-248).

CLINICAL IMPLICATIONS: The findings of this study support the use of PMPI in association with infection surveillance and avoidance of paralysis in patients with ARDS.

Table 1—*Baseline Characteristics*

Variable	Methylpr.	Placebo	P value
No. of Patients	55	24	
Age, years *	49.6	53.3	0.34
Male gender (%) #	30 (54.6)	11 (45.8)	0.48
APACHE III score ICU entry	58.9	55.0	0.43
APACHE III score study entry	57.6	62.8	0.28
Direct cause of ARDS (%)	40 (72.7)	14 (58.3)	0.21
Sepsis-induced ARDS (%)	42 (76.4)	22 (91.7)	0.13
Presence of Shock (%)	11 (20.0)	8 (33.3)	0.20
Lung Injury Score	3.23	3.14	0.44
PaO_2:FiO_2	117.4	129.2	0.52
MODS score	1.91	1.92	0.96
C-reactive protein	27.4	25.9	0.33

DISCLOSURE: Gianfranco Meduri, None.

TRANSFUSION RELATED PULMONARY EDEMA IN THE INTENSIVE CARE UNIT (ICU)

Rimki Rana MD* Sameer Rana MD Evans R. Fernández MD Syed A. Khan MD Ognjen Gajic MD Mayo Clinic, Rochester, MN

PURPOSE: The reported incidence of transfusion related acute lung injury (TRALI) varies due to the lack of standardized definition. Using the Toronto Consensus Panel definition, we aimed to describe the incidence of TRALI, possible TRALI and transfusion associated circulatory overload (TACO) in critically ill patients not requiring respiratory support at the time of transfusion.

METHODS: Patients were identified using custom electronic surveillance system consisting of institutional transfusion database and respiratory information system which accurately chart time of transfusion and onset of respiratory support. Respiratory failure was defined as the onset of noninvasive or invasive ventilator support within 6 hours of transfusion. Electronic records of patients with respiratory failure were reviewed by experts and cases categorized as TRALI, possible TRALI and TACO, according to definition.

RESULTS: 8902 units were transfused in 1351 critically ill patients, not requiring respiratory support at the time of transfusion. 94 patients required new respiratory support within 6 hours of transfusion. Of 49 patients with confirmed acute pulmonary edema, experts identified 7 TRALIs, 17 possible TRALIs and 25 cases with TACO. The incidence of TRALI was 1/356 per unit transfused, possible TRALI was 1/193 per unit transfused and TACO was 1/120 per unit transfused. Acute pulmonary edema developed after 1 in 49 fresh frozen plasma units (FFP), 1 in 59 platelet units and 1 in 72 of red blood cell (RBC) units. Compared to patients who did not develop pulmonary edema the mean number of FFP units was significantly higher in the TRALI group (4.7 vs 1.9, $p=0.002$). There was no significant difference in mean and maximum storage age of RBC and donor gender between the patients who did and did not develop TRALI, possible TRALI or TACO after transfusion.

CONCLUSION: In the ICU, pulmonary edema is commonly temporally associated with blood product transfusion. The incidence of TRALI and TACO appears to be higher than previously reported and was highest after transfusion of FFP.

CLINICAL IMPLICATIONS: Both TRALI and TACO are important causes of respiratory failure after transfusion.

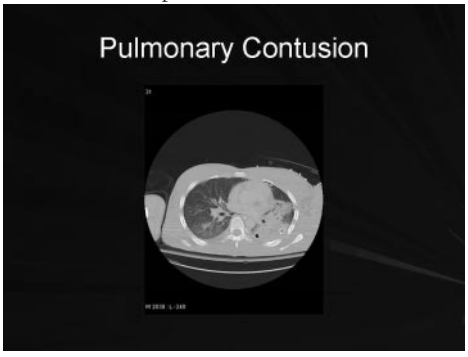
DISCLOSURE: Rimki Rana, None.

THORACIC MANIFESTATIONS OF BLAST INJURY: A WALTER REED EXPERIENCE

Binh T. Nguyen MD* Gary Riley MD Walter Reed Army Medical Center, Washington, D.D., DC

PURPOSE: Thoracic Manifestations of Blast Injury: A Walter Reed Experience.

METHODS: Retrospective review of radiologic studies, between Jan 04-Jan 05, of war injuries at WRAMC identifying those patients with hitory of blast injury. The CT studies were reviewed by two staff radiologists and characterized as well as graded into the following categories: pulmonary contusion, pneumothorax, consolidation, atelectasis, effusions, ARDS, and injuries of the chest wall, cardiac, vascular, airway or extrathoracic compartments.



RESULTS: Of 196 war patients identified, 83 documented blast injury patients were selected. Thirty seven patients had pulmonary contusions; associated findings from this group include 23 patients with chest wall/musculoskeletal injuries, 21 with pneumothorax and 20 with effusions. The most common manifestations of 86 patients were effusions (58) and atelectasis (46). Of the 58 patients with effusions, 55 had associated extrathoracic injuries including extremities (32), abdomen/pelvis (27), head (18) and others (3). Other pulmonary manifestations include consolidation/airspace disease (24), ARDS (9), PE (6), documented infections (4) and presumed fat emboli (2). Non-pulmonary manifestations include pericardial effusions (9), direct vascular injuries (2), lung resection (1), major airway laceration (1), and mediastinal hematoma (1).

CONCLUSION: While effusions and atelectasis are the most common intrathoracic findings, they are most closely associated with extrathoracic injuries. The most common clinically relevant pulmonary manifestation is pulmonary contusion which is strongly associated with pneumothoraces and chest wall/musculoskeletal injuries, i.e. direct blast lung injury. In patients with predominantly pulmonary injuries and less commonly associated cardiovascular or intra/extrathoracic musculoskeletal injuries, there is reduced morbidity/mortality.

CLINICAL IMPLICATIONS: Further understanding of the mechanisms of direct blast lung injury and associated intra/extrathoracic manifestations will enhance prediction of long-term prognosis of these conditions. In addition, recognizing the patterns of pulmonary manifestations of blast injuries may provide an optimal work-up algorithm for efficient and accurate triage and treatment of blast victims in military or civilian armed crises.

DISCLOSURE: Binh Nguyen, None.

Acute Lung Injury and ARDS, continued

CONTINUOUS LATERAL ROTATION THERAPY FOR ACUTE LUNG INJURY: TIMING MATTERS

Cindy Grimes RN Rhonda Anderson MS* Bruce M. Fleegler MD Sarasota Memorial Healthcare System, Sarasota, FL

PURPOSE: Continuous Lateral Rotation Therapy has been shown to reduce nosocomial pneumonia, intensive care unit (ICU) length of stay (LOS) and the number of ventilator days. No study has addressed the effect of this therapy specifically on the course of acute lung injury (ALI) or the effect of timing of institution of Continuous Lateral Rotation Therapy (CLRT). This study was designed to determine whether use of a CLRT protocol would decrease morbidity and mortality, ventilator days and/or ICU LOS in ALI.

METHODS: The study was conducted in a 32 bed Medical/Surgical ICU in an 828 bed community owned acute care hospital. Twenty-three patients were selected over a three month period who met the protocol criteria of mechanical ventilation, FIO2 >0.5 and PaO2/FIO2 ratios <300. A randomized retrospective control group of 23 subjects (every other patient who met study criteria) was selected from a comparable time period during the previous year. A randomized subgroup of the treatment group was selected to evaluate the impact of therapy lag time on clinical outcomes. Twenty patients who were placed on CLRT <5 days after meeting study criteria were compared to 14 patients placed on CLRT > 5 days after meeting criteria.

RESULTS: The two groups had no significant difference in age. The CLRT group had a significantly higher Acute Physiology Score (APS), and predicted mortality based on the APACHE III database although these differences were not statistically significant. Comparisons between the CLRT initiation <5 days and CLRT >5 days are contained in Table 1. Mean ventilator days and ICU LOS were significantly reduced for patients placed on CLRT earlier in their course. Standardized mortality ratio (SMR- observed/predicted mortality) was decreased but the sample size was too small to permit statistical analysis.

CONCLUSION: Earlier institution of CLRT may improve ALI outcomes. Larger trials are necessary to confirm these results.

CLINICAL IMPLICATIONS: Early institution of CLRT should be considered for all patients with ALI. Delay in initiation may increase ventilator days and ICU length of stay.

	CLRT Lag time ≥ 5 days n = 14	CLRT Lag time < 5 days n = 20	p Value
Acute Physioloy Score (APS)	66.98	65.17	0.233
Ventilator Days (avg)	23.43	11.5	0.008
ICU LOS (avg)	27.86	14.65	0.003
Hospital LOS (avg)	31.5	22.5	0.202
Standardized Mortality Ratio (SMR)	1.71	1.0	N/A

DISCLOSURE: Rhonda Anderson, Other Statistical support and partial analysis was provided by Hill-Rom

Assessing Function in COPD
10:30 AM - 12:00 PM

LIPID PEROXIDATION AND GLUTATHIONE PEROXIDASE ACTIVITY IN PATIENTS WITH COPD: RELATIONSHIP TO DISEASE SEVERITY

Ruzena J. Tkacova MD* Darina Petrasova PhD Zuzana Kluchova MD Pavol Joppa MD Roman Klimcik MD Zuzana Dorkova MD Dept. Respirology and TB, L. Pasteur Teaching Hospital, Kosice, Slovak Republic

PURPOSE: An oxidant/antioxidant imbalance is thought to play an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). We hypothesized that antioxidant capacity reflected by erythrocyte glutathione peroxidase (GPx) activity will be lower, and serum levels of the lipid peroxidation product malondialdehyde (MDA) will be higher in patients with mild compared to those with severe COPD.

METHODS: Erythrocyte GPx activity and serum levels of MDA were measured in 103 consecutive patients with stable COPD. Pulmonary function tests were assessed using bodyplethysmography. Differences between the groups were assessed by one-way ANOVA.

RESULTS: Moderate COPD (FEV1 50-80%) was present in 31, severe (FEV1 30-50%) in 51, and very severe COPD (FEV1 < 30%) in 21 patients. Both, erythrocyte GPx activity and serum MDA levels differed significantly between the moderate, severe, and very severe COPD groups (GPx: 47.7±2.9 versus 45.2±1.8, and 37.4±2.3 u/gHb, respectively, $p<0.05$; MDA: 2.1±0.9 versus 2.3±0.1, and 2.5±0.1 nmol/ml, respectively, $p<0.05$).

CONCLUSION: Findings of the present study suggest that antioxidant capacity reflected by erythrocyte GPx activity and serum levels of the lipid peroxidation product MDA are linked to the severity of COPD. The lowest erythrocyte GPx activity and the highest serum MDA levels were seen in patients with very severe COPD.

CLINICAL IMPLICATIONS: In patients with stable COPD, erythrocyte GPx activity and serum MDA levels may serve as additional markers of disease severity.

DISCLOSURE: Ruzena Tkacova, None.

COMPREHENSIVE MEASUREMENT OF BREATHLESSNESS USING THE SELF-ADMINISTERED COMPUTERIZED VERSIONS OF THE BASELINE AND TRANSITION DYSPNEA INDEXES

Donald A. Mahler MD* Laurie Waterman BA Joseph Ward John C. Baird PhD Dartmouth-Hitchcock Medical Center, Lebanon, NH

PURPOSE: To examine and compare the component and total scores of the self-administered computerized (SAC) versions of the Baseline (BDI) and the Transition (TDI) Dyspnea Indexes with scores from the interviewer-administered (IA) original versions.

METHODS: Observational study of 56 patients with respiratory disease who had a chief complaint of dyspnea on exertion at an initial visit and at a follow-up (~ 4 weeks) visit after treatment. Order of administration of the SAC and IA dyspnea instruments was random. Spirometry and inspiratory capacity (IC) were measured at each visit.

RESULTS: Age was 67 ± 11 years. There were 29 females and 27 males. Diagnoses were: COPD (n=40); asthma (n=7); ILD (n=7); and other (n=2). BDI total scores (mean/SD)were 5.4/2.2 (IA) and 6.4/2.0 (SAC); TDI total scores were + 2.1/3.1 (IA) and + 1.9/3.0 (SAC). Pearson's correlation coefficients between IA and SAC versions were: 0.76 for functional impairment, 0.58 for magnitude of task, 0.64 for magnitude of effort, and 0.84 for total scores for the BDI; and 0.74 for change in functional impairment, 0.80 for change in magnitude of task; 0.82 for change in magnitude of effort, and 0.79 for the total scores of the TDI. Both IA TDI total score (r=0.85, 0.55, 0.53) and SAC TDI total score (r=0.77, 0.54, 0.53) were significantly related to the changes in total health score reported by the patient, forced vital capacity (% predicted), and IC (% predicted), respectively ($p < 0.001$).

CONCLUSION: Component and total scores of the IA and the SAC versions of the BDI/TDI were similar in patients with symptomatic respiratory disease. The TDI total scores from the IA and SAC versions had similar correlations with changes in overall health and with changes in lung function.

CLINICAL IMPLICATIONS: The SAC versions of the BDI/TDI are recommended to measure dyspnea rather than the original IA method becasue the SAC instruments use standardized methodology, are patient-reported, and provide a continuous measure of any change in dyspnea.

DISCLOSURE: Donald Mahler, None.

Assessing Function in COPD, continued

HEALTHCARE AND ECONOMIC BURDEN IN UNDIAGNOSED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS

Aylin Riedel PhD Benjamin Chastek MS Rohit D. Borker PhD* Glaxo-Smithkline, Research Triangle Park, NC

PURPOSE: To quantify the resource utilization and cost burden in patients in the year prior to their diagnosis with COPD.

METHODS: This retrospective administrative claims analysis compared healthcare utilization and cost in patients with COPD to their counterparts with no COPD for the 12 months prior to the date of COPD diagnosis. COPD patients (identified using ICD9-CM codes) were matched to their counterparts with no COPD based on age, gender, eligibility, geographic region, and index date. Multivariate analysis was employed to determine the incremental impact of undiagnosed COPD on resource utilization and costs. Logistic and negative binomial regressions were used to model the occurrence of all-cause and respiratory-related inpatient and emergency department (ED) visits, and physician office visits. A two part model was employed to assess costs.

RESULTS: A total of 28,968 and 81,322 patients were identified in the COPD and control cohorts, yielding a match ratio of approximately 1:3. The cohorts had similar age, regional and gender distribution as a result of matching. Logistic models produced odds ratios of 5.6 (95 % CI: 5.4 – 5.9) and 17.1 (95% CI: 15.4 – 19.9) for COPD subjects vs. controls for all-cause and respiratory-related inpatient/ED visits, respectively, indicating a greater likelihood of events in the COPD cohort. Similarly, incidence rate ratios for all-cause and respiratory-related physician office visits were 4.1 (95% CI: 4.0 – 4.2) and 7.4 (95% CI: 7.2 – 7.7) for COPD patients vs. controls. Based on the two-part model for cost, the predicted total medical cost in the COPD cohort was $6.539.6 compared to $809.9 for non-COPD cohort. Predicted respiratory related medical costs were also substantially higher for COPD cohort compared to non-COPD cohort ($1,703.8 in COPD cohort vs. $64.6 in non-COPD cohort).

CONCLUSION: Undiagnosed COPD patients consume a significant amount of healthcare resources and cost in the 12 months prior to their diagnosis with the condition.

CLINICAL IMPLICATIONS: Early identification of these patients and early intervention may help mitigate some of this healthcare use and cost.

DISCLOSURE: Rohit Borker, Employee GlaxoSmithKline

THE ROLE OF SCREENING SPIROMETRY IN THE EARLY IDENTIFICATION OF OBSTRUCTIVE LUNG DISEASE IN AN INNER CITY ADULT POPULATION

E. R. Malone MS * George Car PhD J. M. FitzGerald MD Vancouver Coastal Health Authority, Vancouver, BC, Canada

PURPOSE: To determine the role of screening spirometry in a high-risk inner city population for early identification of obstructive lung disease (OLD). We hypothesized that inner city adult smokers may have a high prevalence of undiagnosed OLD and have irreversible airflow obstruction before 40 years of age as a possible result of health risk factors associated with low socio-economic status and multi-inhaled substance use.

METHODS: Cross-sectional survey of an incidental sample of 300 adult cigarette smokers recruited through community gathering places in Vancouver's inner city. Spirometry and an interviewer administered questionnaire.

RESULTS: Participants ranged in age from 30 to 74 years (mean 45.7 years; SD 7.8) and had a mean smoking history of 33 pack/years (range 2.5-110.0). Participants reported a high prevalence of respiratory symptoms: chronic cough (64%), chronic sputum (62%), wheezing (59%) and shortness of breath with activity (69%). A past or current history of smoking another inhaled substance was common (marijuana 45%, cocaine 36%). The prevalence of OLD was 10.7% based on the CTS criteria and 31% based on the GOLD or ATS/ERS criteria. Mild obstruction was found in 7.7% or 21.1% of all participants and severe obstruction in 1.8% or 1.1% based on the CTS and the GOLD or ERS/ATS criteria respectively. The prevalence rate of airflow obstruction (30.2%), defined by a FEV1/FVC ratio < 70%, in participants 34 to 39 years of age was not significantly different from the rate (32.9%) in participants 40 years of age or older (p=0.70). Surprisingly, only 22% of participants with objective irreversible OLD reported a physician diagnosis of chronic bronchitis-,COPD or emphysema.

CONCLUSION: We found a high prevalence of undiagnosed OLD among a highly symptomatic inner city population.

CLINICAL IMPLICATIONS: Screening spirometry should be performed in inner city smokers who are 35 years of age or older to promote early detection of OLD.

DISCLOSURE: E. Malone, None.

INSPIRATORY CAPACITY, 6 MINUTES WALK TEST AND COPD SEVERITY

Clarice G. Freitas-Santos MD* Carlos Alberto d. Pereira MD Carlos Alberto d. Viegas MD Hospital Universitário de Brasília (UNB), Hospital de Base , Brasilia DF, Brasilia, Brazil

PURPOSE: To evaluate the correlation of the post bronchodilator IC (% predicted), with other prognostic and severity variables in COPD .

METHODS: 60 stable COPD patients (41 men, 19 women, age= 69 ± 7 years, FEV1/FVC= 48 ± 10%,) were submitted to spirometry with FVC and SVC maneuvers and 6 minutes walk test (6MWT) before and after albuterol spray (400 mcg). The IC% and other variables were correlated by univariate and multivariate analysis with the 6-minute walk distance post BD, percent predicted (6MWD%). The IC% was correlated with the BODE index and the GOLD staging severity of COPD.

RESULTS: The 6MWD% did not differ between genders and didn't correlate with age. Patients on long-term oxygen therapy had shorter 6MWD% (46±21% vs 95±17% patients without oxygen, p=0,001). The number of exacerbations per year correlates with the 6MWD% (p=0,05). The number of drugs and co-morbidities didn't correlate with the 6MWD%. The 6MWD% was linearly correlated with the FVC% after BD (r=0,46 p<0,001), FEV1% (r=0,57, p< 0,001), CI% (r=0,68, p<0,001), Borg after 6 minutes (r=-0,62, p= <0,001), SpO2 (r=0,36, p= 0,005) and FEV1/FVC% (r=0,56, p<0,001). In a stepwise forward logistic regression analysis, the strongest association with the 6MWD% was: IC % (r2=0,44), long term oxygen use (r2 = 0,62) and Borg 6 min (r2 = 0,65). IC ≤ 70% was observed in 11/23 patients (47%) in GOLD stages 3 or 4 vs. 6/37 patients (16%) in GOLD stages 1 or 2 (x2=6,98, p=0,008). IC ≤ 70% was observed in 8/17 patients (47%) with BODE index 3 or 4 compared to 9/43 patients in BODE 1 or 2 (20%) (x2=4,096, p=0,043).

CONCLUSION: The IC % postBD is the better functional predictor of the 6-minute walk distance and has a strong association with other severity variables in COPD.

CLINICAL IMPLICATIONS: In COPD the Inspiratory Capacity (IC) reflects the lung hyperinflation and correlates with the 6MWD%, BODE index and GOLD. This study considered the IC% measured by spirometry, a simple and usual method.

DISCLOSURE: Clarice Freitas-Santos, None.

PREVALENCE OF HYPERINFLATION IN COPD AND CORRELATION WITH FLOW-VOLUME INDICES

Pieter Zanen PhD* Frans Rutten MD Arno W. Hoes PhD Jan-Willem J. Lammmers RRT UMCU, Utrecht, Netherlands

PURPOSE: Identification of hyperinflation in COPD is important, because it causes dyspnea and limitation of exercise, and it is a predictor of mortality. Detection of hyperinflation in primary care, however, is difficult because only hand-held spirometers are used.

METHODS: 441 patients, classified as COPD by their general practitioner, visited our out-patient clinic for further pulmonary investigations. Diagnosis of COPD was based on the GOLD criteria (postbronchodilator FEV1/FVC <0.70). The RV/TLC ratio was used to chart hyperinflation, and a value ≥1.64 SD from the predicted value was used to indicate hyperinflation. Prevalence of hyperinflation, and correlation with pre-bronchodilator spirometry indices were calculated. The latter was done to assess whether spirometry indices could be used as surrogate marker of hyperinflation.

RESULTS: In COPD patients with GOLD stage 0, 13% of the subjects showed hyperinflation. 22.4% of the patients in GOLD stage 1 were hyperinflated, in GOLD stage 2 55.1%, and patients in GOLD stage 3 87.2%. Non-parametric correlation showed that of the spirometry indices, FEV1 (as percent of predicted) correlated best with RV/TLC ratio (r= -0.682; p<0.001). Second and third best were the MEF75 and PEF with r = -0.656, and r= -0.649 (both p<0.001). The FEV1-reversibility had a low correlation (r= 0.217; p<0.001).Linear regression showed that with

Assessing Function in COPD, continued

each percent of FEV1 lost, the RV/TLC ratio increased by 0.044 SD points. The optimal cut off value for the baseline FEV1 ap-peared to be 70% of the predicted value (<70% indicates hyperinflation). Receiver Op-erating Characteristics (ROC) curve analysis showed that a high FEV1 correctly diag-nosed an absence of hyperinflation in 85.6% of all cases. The sensitivity/specificity of excluding hyperinflation at this 70% cut off level was 78.0% and 76.7%.

CONCLUSION: Hyperinflation is often present in COPD and when FEV1 <70% of predicted hyperinflation is very probable.

CLINICAL IMPLICATIONS: FEV1 may be used as a surrogate marker for detect hyperinflation when helium dilution and/or bodyplethysmography are unavailable.

DISCLOSURE: Pieter Zanen, None.

Diagnosis and Evaluation of Adult Sleep Disorders
10:30 AM - 12:00 PM

THE NSF 2005 SLEEP IN AMERICAN POLL AND THOSE AT RISK FOR RLS

Barbara A. Phillips MD* Pat Britz BA Wayne Hening MD University of KY College of Medicine, Lexington, KY

PURPOSE: The purpose of this analysis was to investigate the prevalence and correlates of Restless Legs Syndrome (RLS) symptoms in the 2005 National Sleep Foundation (NSF) Sleep in America 2005 Poll.

METHODS: The NSF poll is an annual telephone interview of a random sample of United States adults 18 years of age and older who are representative of the US population. Respondents are queried about many aspects of sleep, sleep disorders and daily living.

RESULTS: The NSF 2005 poll included 1506 adults. Their mean age was 49 years, and 775 were women. Symptoms of RLS that included unpleasant feelings in the legs for at least a few nights a week and which were worse at night were reported by 9.7 % of individuals in this poll, including 8% of men and 11% of women. Those from the South and West were more likely to be at risk for RLS than those from the Northeast ($p < 0.05$). Those who were unemployed or smoked daily were more likely to be at risk for RLS, as were those with hypertension, arthritis, gastroesophageal reflux disease, depression, anxiety, and diabetes. Adults who were at risk for RLS appeared to also be at increased risk for sleep apnea and insomnia, and were more likely to stay up longer than they planned, to take longer than 30 minutes to fall asleep, to drive when drowsy, and to report daytime fatigue than those who were not at risk. They were also more likely to report being late to work, missing work, making errors at work, and missing social events because of sleepiness than other respondents in the poll.

CONCLUSION: RLS is significantly associated with medical and psychiatric conditions, with other sleep disorders, with unfavorable lifestyle behaviors, and with adverse effects on daytime function.

CLINICAL IMPLICATIONS: Chest physicians who practice Sleep Medicine need to be able to manage RLS, which is prevalent and is associated with considerable morbidity.

DISCLOSURE: Barbara Phillips, Consultant fee, speaker bureau, advisory committee, etc. Astra ZenecaBoehringer-IngelheimGSKNIH Data Safety and Monitoring Board, COPD CCRNNHLBI Observational Study Monitoring Board (OSMB) for the CARDIA studyNIH Patient Oriented Research Career Development Awards PanelResMedSanofi-AventisAmerican College of Ca

PREVALENCE OF RISK FACTORS FOR OBSTRUCTIVE SLEEP APNEA IN THE US: RESULTS FROM THE 2005 SLEEP IN AMERICA POLE

David M. Hiestand MD* Pat Britz Barbara Phillips MD University of Kentucky, Lexington, KY

PURPOSE: Obstructive sleep apnea (OSA) is a common medical condition with serious adverse consequences including car accidents, hypertension, and cardiovascular disease. There are few studies assessing the risk of OSA in the general population.

METHODS: The National Sleep Foundation's (NSF) 2005 Sleep in America Poll included the Berlin Questionnaire, a previously validated instrument for estimating risk of OSA. The Berlin Questionnaire has three components, and those scoring high on at least two sections are considered at risk for OSA. The 2005 NSF poll surveyed 1506 adults aged 18 and over via telephone. This data was analyzed for the characteristics of respondents identified as being at risk for OSA.

RESULTS: Overall, 26% of adults were found to be at risk for OSA, including 31% of males and 21% of females. The risk of OSA increased with age to age 65: age 18-29 - 19%, 30-49 - 25%, and 50-64 - 33%. Only 21% of individuals 65 and over were at risk. 57% of obese individuals were at risk. Those at risk for OSA were more likely to report sleep problems (44% vs. 9%). Those respondents reporting an impact of sleep on quality of life were at increased risk for OSA (41 vs 11 %). The presence of a chronic medical increased the likelihood of OSA (35% vs. 11%).

CONCLUSION: The NSF 2005 poll indicates a strikingly high risk of OSA in the U.S. population. Risk is higher in men and higher in the obese. Risk as defined by the Berlin Questionnaire increases with age up to age 65. Individuals at risk for OSA are more likely to have a sleep problem and to believe this problem impacts quality of life. Finally, having other chronic medical problems is associated with increased risk of OSA.

CLINICAL IMPLICATIONS: The prevalence of risk for OSA in the population is significant. Further emphasis on screening and evaluation is warranted.

DISCLOSURE: David Hiestand, None.

OBSTRUCTIVE SLEEP APNEA SYNDROME: ARE WE MISSING AN AT-RISK POPULATION?

Christopher J. Lettieri MD* Arn H. Eliasson MD Teotimo Andrada MS Andrei Khramtsov MD Marc Raphaelson MD David A. Kristo MD Walter Reed Army Medical Center, Washington DC, DC

PURPOSE: While age and body-mass index (BMI) are well-established risk factors for obstructive sleep apnea syndrome (OSAS), this disorder occurs across a wide spectrum of ages and weights. Preconceptions regarding "classic" patients with OSAS may lead to an under diagnosis in at-risk populations, particularly women or younger, non-overweight individuals. We hypothesized that disease severity is independent of age and BMI. We compared military service members to civilians to determine if disease severity was equivalent in a younger, less obese population.

METHODS: Prospective study of consecutive patients diagnosed with OSAS. Active duty military, National Guardsmen and civilians were compared to determine if age and BMI correlated with disease severity.

RESULTS: 270 subjects (120 active duty military, 80 National Guardsmen and 70 civilians) were included. Active duty military were significantly younger and less overweight than National Guardsmen and civilians. 64.3% of civilians and 48.8% of National Guardsmen were obese, while only 19.2% of active-duty had BMI $\geq$30 Kg/m2 ($p<0.001$ for both). However, prevalence of severe disease did not differ between groups. 37.5% of active duty had severe disease, compared with 42.5% of National Guard and 45.7% of civilians ($p=0.18$ and 0.09, respectively). BMI did not differ between active duty with severe disease and those with mild or moderate OSAS (26.7 Kg/m2 versus 26.9 Kg/m2, $p=0.40$) and disease severity did not correlate with BMI ($R=0.09$, $p=0.33$). There was a low correlation between age and AHI ($R=0.21$, $p=0.02$).

CONCLUSION: OSAS occurs in young, non-obese individuals. While obesity and age are risk factors for OSAS, they did not correlate with disease severity. Obesity is not a diagnostic criterion for OSAS and should not be required for evaluation.

CLINICAL IMPLICATIONS: OSAS should be considered in symptomatic patients regardless of age or BMI. Failing to consider this diagnosis in individuals who do not fit into the stereotypical image of OSAS patients may under diagnose an at-risk population.

DISCLOSURE: Christopher Lettieri, None.

Diagnosis and Evaluation of Adult Sleep Disorders, continued

DAYTIME SLEEPINESS AND SLEEP DISORDERS AFTER TRAUMATIC BRAIN INJURY

Richard J. Castriotta MD* Mark C. Wilde MS Jenny M. Lai MD Strahil Atanasov MD Brent E. Masel MD Samuel T. Kuna MD Univ of Texas Health Science Center at Houston, Houston, TX

PURPOSE: This study was designed to evaluate the prevalence and consequences of sleepiness and sleep disorders after traumatic brain injury (TBI).

METHODS: Subjects over 18 years old with TBI, at least 3 months post brain injury, were prospectively recruited and underwent physical examination, nocturnal polysomnography (NPSG), multiple sleep latency test (MSLT) and neuropsychological testing. The latter was done on all patients at the same time of day (after the 2nd MSLT nap) and consisted of Psychomotor Vigilance Test (PVT), Profile of Mood States (POMS) and Functional Outcome of Sleep Questionnaire (FOSQ).

RESULTS: Of the 87 patients who completed the protocol, there were 24 women (28%) and 63 men (72%) with an average age of 38.3 ± 15.2 (SD) years. Forty one subjects (47%) had abnormal sleep studies. Nineteen patients (22%) were diagnosed with obstructive sleep apnea (OSA), 10 (15%) had posttraumatic hypersomnia (PTH), 6 (7%) had narcolepsy and 6 (7%) had periodic limb moovements in sleep (PLM). Twenty three subjects (23.4%) were categorized as objectively sleepy on the basis of MSLT score < 10 minutes. There were no differences between the sleepy and non-sleepy subjects in age, race, gender, education, GCS scores, cause of injury, CT findings, injury severity or months post injury. Sleepy patients had a greater body mass index (BMI) than the non-sleepy ($p = 0.01$). Obese patients (BMI ≥ 30) were more likely to have OSA ($p < 0.0001$). Sleepy subjects had slower fastest reaction times ($p < 0.05$), slower slow reaction times ($p < 0.05$)and more lapses ($p < 0.05$)on PVT. PMS did not differ significantly. Sleepy patients had higher FOSQ scores ($p < 0.05$), indicating better quality of life.

CONCLUSION: Almost half (47%) of an unselected TBI population can be expected to have a sleep disorder with OSA being the most common (22%), followed by PTH (15%). Sleepy TBI patients have impaired cognitive functioning and PVT performance, but may be unaware of problems.

CLINICAL IMPLICATIONS: All TBI patients should be evaluated for sleep disorders with NPSG and MSLT.

DISCLOSURE: Richard Castriotta, Grant monies (from industry related sources) Cephalon, Inc. contributed to the funding of this research.; Consultant fee, speaker bureau, advisory committee, etc. I have spoken at conferences sponsored by Cephalon

MAINTENANCE OF WAKEFULNESS TEST IN ACTIVE DUTY SOLDIERS WITH UPPER AIRWAY RESISTANCE SYNDROME AND MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA

Christopher R. Powers MD* William C. Frey MD Brooke Army Medical Center, Fort Sam Houston, TX

PURPOSE: Sleep Disordered Breathing(SBD) is a common disorder that is becoming more recognized in the active duty military population. A major consequence of SDB is excessive daytime sleepiness(EDS). The maintenance of wakefulness test(MWT) is a daytime polysomnography(PSG) performed after nighttime PSG that has been used to evaluate EDS. It can assess an individual's tendency to fall asleep which has important military relevance for those soldiers whose duties include guard duty as well as operating heavy machinery and driving military vehicles. We conducted consecutive MWTs on active duty soldiers diagnosed with mild to moderate Obstructive Sleep Apnea(OSA) and Upper Airway Resistance Syndrome(UARS) to evaluate their tendency to fall asleep.

METHODS: Active duty soldiers referred to the BAMC Sleep Disorders Center between February 2004 and March 2005 who were evaluated with an overnight PSG and had an apnea-hypopnea index(AHI) greater than 5/hr and less than 30/hr were defined as having OSA in the mild or moderate range. Soldiers with EDS and an AHI less than 5/hr but a respiratory disturbance index(RDI) of >5/hr were defined as UARS. After overnight PSG, soldiers with mild to moderate OSA and UARS were evaluated with a 40 minute protocol MWT. Sleep during the MWT was defined as three consecutive epochs of stage one or one epoch of any other stage of sleep. Abnormal MWT was defined as a sleep onset latency mean of the 4 sessions below 35 minutes.

RESULTS: Sixty-nine soldiers met entry criteria. Thirty-nine percent(39%) were diagnosed with UARS and 61% of soldiers with OSA. This subjective excessive sleepiness was confirmed with a mean MWT sleep onset latency of 27 minutes. Fifty-two percent of soldiers had abnormal MWTs.

CONCLUSION: Patients with untreated SDB who have excessive daytime sleepiness could pose a problem in the military work environment where wakefulness and attentiveness are essential for both job performance and mission accomplishment.

CLINICAL IMPLICATIONS: Soldiers with UARS and mild to moderate OSA should not be deployed into situations where alertness is required for personal and unit safety.

DISCLOSURE: Christopher Powers, None.

PREVALENCE OF MODERATE OR SEVERE LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN OBESE PERSONS WITH OBSTRUCTIVE SLEEP APNEA

Jasdeep Sidana MD* Wilbert S. Aronow MD Gautham Ravipati MD Brian Di Stante MD John A. McClung MD Robert N. Belkin MD Stuart G. Lehrman MD New York Medical College, Valhalla, NY

PURPOSE: To investigate the prevalence of moderate or severe left ventricular diastolic dysfunction (LVDD) in obese persons with moderate or severe obstructive sleep apnea (OSA).

METHODS: We investigated prior to gastric bypass surgery the prevalence of LVDD by Doppler and tissue Doppler echocardiography in 14 obese women and in 6 obese men, mean age 45 years, who had nocturnal polysomnography for OSA. OSA was considered mild if the respiratory disturbance index (RDI) was 5-15, moderate if the RDI was 15-30, and severe if the RDI was >30. The Doppler echocardiographic data were analyzed blindly without knowledge of the clinical characteristics or whether OSA was present or absent.

RESULTS: Of the 20 persons, 8 (40%) had no OSA, 4 (20%) had mild OSA, and 8 (40%) had moderate or severe OSA. The mean age, body mass index, and prevalence of smoking, hypertension, diabetes mellitus, and hypercholesterolemia were not significantly different between 8 persons with moderate or severe OSA and 12 persons with no or mild OSA. Five of 8 persons (63%) with moderate or severe OSA and 1 of 12 persons (8%) with no or mild OSA were men ($p<0.01$). Moderate or severe LVDD was present in 4 of 8 persons (50%) with moderate or severe OSA and in none of 12 persons (0%) with no or mild OSA ($p<0.01$).

CONCLUSION: Obese persons with moderate or severe OSA have a significantly higher prevalence of moderate or severe LVDD than obese persons with no or mild OSA ($p<0.01$).

CLINICAL IMPLICATIONS: The higher prevalence of moderate or severe LVDD in obese persons with moderate or severe OSA predisposes them to develop congestive heart failure with a normal left ventricular ejection fraction.

DISCLOSURE: Jasdeep Sidana, None.

Non-Respiratory Critical Care Infections 10:30 AM - 12:00 PM

INCREASED SYSTEMIC CANDIDIASIS IN ICU PATIENTS WITH PROLONGED ANTIFUNGAL TREATMENT OF CANDIDURIA

Matthew P. Chambers PharmD* David A. Kuhl PharmD G. C. Wood PharmD Bradley A. Boucher PharmD Amado X. Freire MD The Regional Medical Center at Memphis, Memphis, TN

PURPOSE: The incidence of candiduria in ICU patients and risk factors associated with its development have been described; However, links with developing systemic candidiasis following candiduria are lacking. This study identifies incidence and predictive factors for systemic candidiasis in ICU patients with candiduria.

METHODS: Patients admitted to a University-affiliated teaching hospital ICU from Jan–Dec 2004 were evaluated. All patients with their first candiduria isolate in the ICU were included. Patients with candiduria <48h from admission were excluded. Twelve variables (Table 1) were evaluated by univariate analysis. Variables with $p<0.1$ were entered into a logistic regression model for identification of independent predictors of systemic candiasis. Mortality and fungal species isolated (both urine and systemic) were also examined.

RESULTS: Of 89 patients screened, 82 met criteria. 21 (25.6%) patients developed systemic candidiasis subsequent to candiduria. Pa-

Non-Respiratory Critical Care Infections, continued

tients were similar with respect to age, prior antibiotic and antifungal exposure, prior positive bacterial and fungal cultures, blood and steroid exposure, and glucose and serum creatinine (Table 1). Mortality was higher in the systemic candidiasis group (42.9% versus 27.9%, p=0.2), but not statistically different. Patients with systemic candidiasis were more likely to be male (63% versus 37%; p=0.08), have a longer duration of initial candiduria treatment (7.4 versus 4.5 days; p=0.004), and a higher incidence of recurrent candiduria (61.9% versus 32.3%; p=0.02) compared to those with candiduria only. Logistic regression analysis identified duration of treatment as an independent predictor of systemic candidiasis (Table 2). Although 80% of urine isolates were not speciated, 49% of systemic infections were C. albicans with 28% being C. glabrata.

CONCLUSION: Systemic candidiasis occurs frequently in ICU patients following candiduria. Patients receiving a longer duration of antifungal therapy for candiduria were at highest risk with males and those with recurrent candiduria having a trend for increased risk. Over one fourth of systemic infections were C. glabrata.

CLINICAL IMPLICATIONS: Strategies should be investigated to identify or prevent systemic infection following candiduria including shortening candiduria antifungal treatment duration.

Table 1—*Univariate comparison of patient factors Increased Systemic Candidiasis with Prolonged Antifungal Treatment in Patients with Candiduria in the ICU.*

Factor	Urine Only	Systemic	p-Value
Age – years[1]	49.8±17.4	46.8±19.7	0.57
Males – n(%)	19 (30.6)	11 (52.4)	0.08
LOS prior to candiduria – days[2]	13 (3-109)	14 (5-121)	0.55
Steroid Treatment – n(%)	18 (29.5)	9 (42.9)	0.26
Blood products given – n(%)	27 (44.3)	9 (42.9)	0.91
Serum glucose > 180 mg/dl – n(%)	30 (49.2)	8 (38.1)	0.38
Serum Creatinine > 1.5 mg/dl – n(%)	22 (36.1)	5 (23.8)	0.42
Prior antibiotic exposure – n(%)	57 (93.4)	19 (90.5)	0.64
Prior positive bacterial cultures – n(%)	42 (68.9)	15 (71.4)	0.82
Prior systemic candidiasis – n(%)	19 (31.1)	8 (38.1)	0.82
Prior systemic antifungals – n(%)	6 (9.8)	3 (14.3)	0.69
Recurrent candiduria – n(%)	20 (32.8)	13 (61.9)	0.02
Treatment of first candiduria – n(%)	49 (80.3)	14 (66.7)	0.2
Candiduria treatment duration – days[1]	4.5±2.8	7.4±4.6	0.004
Mortality – n(%)	17 (27.9)	9 (42.9)	0.2

1 – Mean + standard deviation; 2 – Median (range)

DISCLOSURE: Matthew Chambers, None.

CLINICAL CHARACTERISTICS AND RISK FACTORS OF MORTALITY AMONG SEVERE BURN PATIENTS WITH ISOLATES OF VANCOMYCIN-RESISTANT ENTEROCOCCI

Heung J. Woo MD* Cheol H. Kim MD Jin K. Kim MD Young I. Park MD In G. Hyun MD Young M. Ahn MD Department of Internal Medicine, Hallym University College of Medicine, Seoul, South Korea

PURPOSE: Vancomycin-resistant enterococci (VRE) are multi-drug resistant organisms that have emerged as important nosocomial pathogens in recent years. VRE emergence has been blamed mainly on the increased and inappropriate use of antibiotics, in particular, the cephalosporins and the glycopeptide, vancomycin. Burn patients are highly vulnerable to acquiring VRE infection. This study was focused on the clinical characteristics and risk factors of mortality among severe burn patients with VRE isolation during recent 4 years.

METHODS: 104 cases (M:F=69:35) that had VRE isolation from January 1, 2000 to December, 2003, were reviewed. We analyzed clinical characteristics and the risk factors that contribute to death by using univariate and multivariate analyses, retrospectively.

RESULTS: Mean percent total body surface area (%TBSA) of survivors (n=80) and non-survivors (n=24) were 41.64±20.68% and 58.08±22.64% (p=0.003). Total 144 strains of VRE were isolated from 104 patients. Most of VRE colonization or infection were caused by Enterococcus faecium (82.6%) and E. casseliflavus (14.6%). There were no significant difference in VRE species distribution between survivors and non-survivors (p> 0.05). The risk factors for mortality were %TBSA burn, APACHE II scores, mechanical ventilation, nasogastric tube, previous use of cefepime and ticarcillin/clavulanate, rectal VRE colonization and initial VRE bacteremia in univariate analysis. However, independent risk factor of death were APACHE II score, mechanical ventilation and initial VRE bacteremia in multivariate analyses.

CONCLUSION: Severe burn patients with VRE isolation should be reassessed carefully, especially in those who had high APACHE II scores at ICU admission, mechanical ventilation and initial VRE bacteremia.

CLINICAL IMPLICATIONS: More strict infection control and efforts to eradicate VRE may be needed among severe burn patients with VRE isolation.

DISCLOSURE: Heung Woo, None.

ACINETOBACTER BUMANNII BACTEREMIA IN CRITICALLY ILL PATIENTS: EPIDEMIOLOGY, OUTCOMES, AND THE IMPACT OF OPERATION IRAQI FREEDOM

Andrew F. Shorr MD* Alex G. Truesdell MD Laura A. Pacha MD Dennis M. Sarmiento MD John D. Betteridge MD Allesa J. Ewell PhD Washington Hospital Center, Washington, DC

PURPOSE: Acinetobacter bumannii (AB) is a highly-resistant pathogen & is an important cause of nosocomial infection. We noted an outbreak of AB bacteremia at our institution following the onset of Operation Iraqi Freedom (OIF). We sought to describe the epidemiology of AB bacteremia and its differential impact on trauma and non-trauma patients.

METHODS: We retrospectively identified all patients with AB bacteremia seen at our facility from Jan 2001 thru Aug 2004. Mortality represented our primary endpoint. We compared outcomes in injured service members to those seen in non-trauma patients and explored the effect of initially inappropriate antibiotic treatment on survival (defined as prescription of an anti-infective to which the pathogen was resistant based on sensitivity testing).

RESULTS: During the study period, there were 47 cases of AB bacteremia. From 2001 to 2004 the prevalence of AB bacteremia increased from 0.7 cases to 14.0 cases per 100,000 patient-days (p<0.001). Seventy-five percent of subjects were in the ICU when their blood cultures became positive, and 40% of cases represented nosocomial spread to non-active duty patients. Nearly 20% of isolates were carbepenem resistant. Colistin was given in 2 cases. Non-OIF subjects were older, more often immunosuppressed, and more severely ill. Although the overall case fatality rate was 17%, mortality was 15.8 times (95% CI: 1.8-144.2) more likely in non-OIF patients than in injured service members. The one death in a soldier was not infection-related. This differential in survival was present despite the fact that OIF subjects more often received initially inappropriate antimicrobial therapy (50.0% vs. 22.2%).

CONCLUSION: Nosocomial spread of AB bacteremia poses a major threat to non-trauma patients. Despite the extent of their injuries and severity of illness, AB has less of an impact on critically ill trauma patients.

CLINICAL IMPLICATIONS: Infection control must remain a central aspect of any approach to addressing AB. That inappropriate antimicrobial therapy did not correlate with mortality in previously healthy trauma patients suggests that the importance of this factor on outcomes relates to the specific population studied.

DISCLOSURE: Andrew Shorr, None.

Non-Respiratory Critical Care Infections, continued

EXTENDED-SPECTRUM BETA-LACTAMASES PRODUCING KLEBSIELLA PNEUMONIAE (ESBL-KP) INFECTION, RISK FACTORS, ANTIBIOTIC USE AND BACKGROUND

Frew H. Gebreab MD* Nasser Saad RPh Liziamma George MD Teena Abraham PharmD Imran Aurangzeb MD Elias Ashame MD Kelly Marion RN Suhail Raoof MD New York Methodist Hospital, Brooklyn, NY

PURPOSE: The development of multi-drug resistant bacterial infections is a serious problem in many hospitals. This study was conducted to identify the risk factors and antibiotic usage in medical intensive care and pulmonary step down patients who developed ESBL-KP infections at New York Methodist Hospital.

METHODS: Medical records of 47 patients who developed 50 ESBL-KP infections between January to December 2004 were reviewed. Data collection included demographics,admission diagnosis,and risk factors for development of ESBL-KP infections.

RESULTS: Of 47 patients; 74.5% (n=35)were females, and 25.5% (n= 12) were males in which 59.6% of them were admitted from home while the remaining 40.4% came from nursing facilities. Patients were admitted for sepsis (27.6%),acute respiratory failure (14.8%),pneumonia (17%),urinary tract infections (12.8%),acute renal failure (12.8 %), acute abdomen (8.5%), hepatic encephalopathy (4.3%) and malignancy (2.1%). All patients were treated with at least one broad spectrum antibiotic (Figure 1) for a mean duration of 14.5 days prior to the development of ESBL-KP infections. Ninety-eight percent of patients had at least 1 invasive procedure (Figure 2). The study identified that out of fifty ESBL-KP isolates; 52% (n=26) resulted in urinary tract, 24% (n=12) respiratory tract, 22% (n=11) blood stream, and 2% (n=1) surgical wound infection. Eighty four percent of isolates were sensitive to aminoglycosides whereas only 46% were sensitive to a carbapenem (Figure 3). The mean length of stay of ESBL-KP infections 46 days and all cause mortality was 32%.

CONCLUSION: 1. There was no community acquired ESBL-KP infections. 2. Majority of ESBL-KP infections were sensitive to aminoglycosides. 3. Urinary tract was the most common site of infection 4. Majority of patients had invasive procedures and all were treated with broad spectrum antibiotics prior to ESBL-KP isolation.

CLINICAL IMPLICATIONS: Identification of possible risk factors for development infection with multi-drug resistant pathogen like ESBL-KP will be helpful in prevention ,early detection and treatment of such infection.

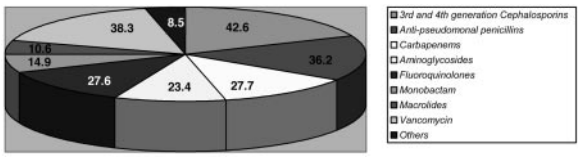


FIGURE 1. Antibiotic use in patients with ESBL-KP infection between January to December 2004 at New York Methodist Hospital

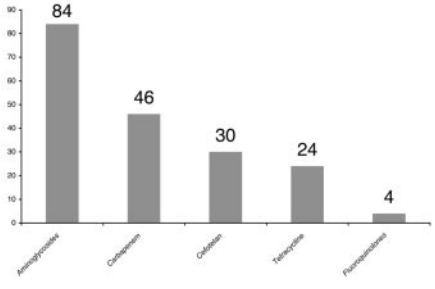


FIGURE 2. Number and type of invasive procedure performed prior to the development of ESBL-KP infections between January to December 2004 at New York Methodist Hospital.

DISCLOSURE: Frew Gebreab, None.

CLINICAL MANIFESTATIONS AND CAUSATIVE PATHOGENS OF INFECTIOUS COMPLICATIONS AMONG TSUNAMI VICTIMS FROM SOUTH SEA THAILAND: CASES SERIES OF SAMITIVEJ SRINAKARIN HOSPITAL BANGKOK THAILAND

Theerasuk Kawamatawong MD* Patarapong Kamalaporn MD Mastorn Shaipanich MD Suchart Wiratkapan MD Vikrom Jarusdhirakul MD Charoen Chotigavanichaya MD Ubolrat Pitasawad MD Anupan Tantachun MD Teerachai Chantarojanasiri MD Samitivej Srinakarin Hospital, Bangkok, Thailand

PURPOSE: According to disaster from tsunami on December 26, 2004. The victims who were suffered from the submersion injuries developed infectious complications that were related to aspiration and exposure of seawater or sewage. Clinical presentations and causative pathogens were summarized for recognition and appropriate management.

METHODS: The series of cases were collected from medical records including clinical and microbiological data during hospitalization in medical and surgical service after evacuation from southern Thailand.

RESULTS: Thirty cases were hospitalized. Mean age was 44 years (12 to 77 years) .Soft tissue and musculoskeletal infections (infected wound and opened fracture) were diagnosed in 27 cases (90 %). Respiratory tract infections (pneumonia associated with near drowning and sinusitis) were diagnosed in 10 cases (33%). Six cases (20%) had multiple sites of infection. The most common pathogens isolated from clinical specimens (wound swab in operating room, sputum, and lavage fluid) were Aeromonas sobria (20 %).One third of cases had polymicrobial gram negative infection. Commonly used antibiotics before obtaining microbiological result were amoxicillin-clavulanate (40 %), fluoroqiunolones (21%) and third generation cephalosporins (14%) respectively. Combination antibiotics were used in one third of patients. Pneumonia patient with lobar atelectasis underwent flexible bronchoscopy for removal of foreign material. All of patients with infected wound and opened fracture were treated by immediate surgical debridement and tetanus immunization. Nasal endoscopies and irrigations were performed in sinusitis patients. Average total length of stay was 4 days (1 to14 days). There was no mortality of our cases.

CONCLUSION: The incidence of soft tissue and musculoskeletal infections is more common than respiratory tract infections among survivors from tsunami. Enteric gram negative bacilli were common pathogens encountered in infectious complications.

CLINICAL IMPLICATIONS: The effective antimicrobial treatment of infectious complication related to submersion injuries from seawater are either beta lactam antibiotics or fluoroquinolones. Surgical debridement and endoscopy with lavage for removal of foreign material are necessary part of treatments.

DISCLOSURE: Theerasuk Kawamatawong, None.

Pulmonary Hypertension Evaluation
10:30 AM - 12:00 PM

OBESITY, HYPERTENSION, AND SLEEP APNEA CONFOUND THE DIAGNOSIS OF PULMONARY ARTERIAL HYPERTENSION

Terry A. Fortin MD* C. W. Hargett MD Victor F. Tapson MD Duke University Medical Center, Durham, NC

PURPOSE: Obese patients with elevated right ventricular systolic pressure (RVSP) by echocardiography (ECHO) are often diagnosed with pulmonary arterial hypertension (PAH) but may not actually have it. We sought to better characterize such patients.

METHODS: A review of our catheterization data in obese patients presenting with suspected PAH based upon an abnormal ECHO, suggested that diastolic dysfunction and not PAH was frequently the etiology of the elevated RVSP. We further evaluated these obese patients with normal left ventricular (LV) systolic function, an elevated pulmonary capillary wedge pressure (PCWP) and normal to mildly elevated pulmonary vascular resistance (PVR) (<3 Wood units).

RESULTS: 29 individuals had a mean pulmonary arterial pressure (mPAP) > 25 mm Hg , normal LV systolic function and PCWP > 15 mm Hg and a PVR < 3 Wood units (likely diastolic dysfunction). Thirteen of

Pulmonary Hypertension Evaluation, continued

this cohort had conditions expected to contribute to PAH including congenital heart disease (3), connective tissue disease (4), high cardiac output syndromes (2). Four patients had left-sided or valvular heart disease. The remaining 16 patients as well as 7 with PVR 3 to 5 Wood units had some combination of obesity, a sleep disorder or hypertension as contributing factors. All 23 had poorly controlled hypertension and obesity with body mass index (BMI) > 30, with mean BMI of 43.9 (range 30.9 to 65). Fourteen (66.7%) had morbid obesity (BMI >40). Seventeen (74%) had known obstructive sleep apnea. Twelve had normal right ventricular (RV) size on ECHO, while nine had mildly enlarged right ventricles. Two patients had initial ECHO with moderately enlarged right ventricles but all had normal RV function.

CONCLUSION: The combination of hypertension, sleep apnea, and obesity in these patients is likely contributing to the apparent diastolic dysfunction and resulting mild PH.

CLINICAL IMPLICATIONS: It should not be assumed that patients with an elevated RVSP by ECHO have PAH. PCWP and diastolic dysfunction may be causative. Complete evaluation including cardiac catheterization prior to therapy for PH is essential. This population merits further study.

DISCLOSURE: Terry Fortin, None.

MEASURES OF PULMONARY HYPERTENSION (PAH) SEVERITY DO NOT IDENTIFY PATIENTS AT RISK FOR SIGNIFICANT NOCTURNAL HYPOXEMIA (NH)

Chirag M. Pandya MD* Omar A. Minai MD J. A. Golish MD K. McCarthy RRT J. Avecillas MD A. C. Arroliga MD Cleveland Clinic Foundation, Cleveland, OH

PURPOSE: NH not related to sleep-disordered breathing has been reported in patients with PAH. We describe the incidence of NH in PAH patients without parenchymal lung disease, and evaluate associated factors.

METHODS: Patients who spent >10% of the total sleep time with an SpO2 <90% were considered nocturnal desaturators (Desat). Variables analyzed included: demographics, spirometry, hemodynamics, and 6-minute walk test (6MW). Unpaired Student's t-test and Mann-Whitney rank sum test were used to compare variables between Desat and nondesat (ND).

RESULTS: Of the 38 patients (33 F/5 M; mean age: 47, range 18-71 yrs), 26 (68%) were Desat and 12 (32%) were ND. Patients in the Desat group spent 46±27% (mean±SD) of sleep time with SpO2 <90%. Desats were older (50±12 vs 40±14; p=0.02), had higher BMI (30±5 vs 27±3; p=0.07, had lower resting SpO2 (94±3.5 vs 97±2.4; p=0.01), lower FEV1% pred. (75±12 vs 85±13; p=0.03), and higher Hb level (14.4±1.7 vs 13±1.2; p=0.02) than ND. There was no statistically significant difference in terms of hemodynamics, 6MW distance, BNP, Borg, or TSH. In the Desat group 65% (17/26) did not require supplemental oxygen during their 6MW. Patients in the Desat group undergoing sleep studies were not found to have significant OSA.

CONCLUSION: A high prevalence of NH was seen among our group of patients with PAH. The severity of NH was significant given the time spent <90% and the elevated Hb levels. NH did not correlate with accepted indices of PAH severity or with O2 need during 6MW. The inclusion of overnight oximetry in the routine work-up of patients with PAH is warranted since other indices of PAH severity or oxygen need during 6MW may not accurately identify these patients.

CLINICAL IMPLICATIONS: Overnight oximetry should be a part of the routine work-up of patients with PAH since other indices of PAH severity or oxygen need during 6MW may not accurately identify patients with nocturnal hypoxia.

DISCLOSURE: Chirag Pandya, None.

PERFORMANCE OF PULMONARY CAPILLARY WEDGE PRESSURE (PCWP) VS. LEFT VENTRICULAR END DIASTOLIC PRESSURE (LVEDP) IN THE DIAGNOSIS/CLASSIFICATION OF PATIENTS WITH SUSPECT PULMONARY ARTERIAL HYPERTENSION (PAH)

Francisco J. Soto MD* Ronald Siegel MD David Marks MD James Kleczka MD Timothy Woods MD James P. Maloney MD Amina Syed MD Amjad Syed MD Sonika Gupta MD Kenneth Presberg MD Medical College of Wisconsin, Milwaukee, WI

PURPOSE: Some therapies - e.g. bosentan or prostacyclin- are only indicated and approved for PAH but not for pulmonary venous hypertension (PVH). A diagnosis of PAH implies a mean pulmonary arterial pressure (mPAP) >25 mmHg at rest and a normal left ventricular (LV) filling pressure (<15 mmHg) to exclude PVH. A PCWP <15 mmHg is generally assumed to exclude PVH but a rigorous comparison of PCWP with the "gold standard" LVEDP < 15 mmHg in patients with PAH is lacking. We hypothesized that sole reliance on PCWP might erroneously misclassify a significant number of patients with PVH as PAH.

METHODS: We reviewed the records and raw catheterization data from 131 patients who underwent simultaneous right and left catheterization as part of their evaluation for suspected pulmonary hypertension (PH) and in whom PH was confirmed. The diagnostic performance of PCWP vs. LVEDP was evaluated using a 2 x 2 contingency table. A chi-square test was used to compare those results. Linear regression analysis was used for comparison of continuous variables.

RESULTS: Our patients were 60 years of age, mostly women (76%) and predominantly white (75%). The most common etiologies of PH were collagen vascular disease (24%), LV diastolic dysfunction (20%) and idiopathic PAH (18%). LVEDP suggested PVH in 59% of patients vs. 37% by PCWP (p= <0.0001). Up to 37% of patients with PVH would have been misclassified as PAH by PCWP measurement alone.

CONCLUSION: We report limitations to the use of PCWP as the only method of assessing LV filling pressures in patients with suspected PAH, especially when PCWP is >10. We found that LVEDP measurement was important to accurately differentiate between PAH and PVH.

CLINICAL IMPLICATIONS: Since the current data support the benefit of certain therapies in PAH only, careful assessment of LV filling pressures is indicated before such therapies are initiated. PAH-specific therapies are not only expensive but can lead to higher morbidity and mortality when used in PVH.

Table. Classification of PH by LV filling pressures: LVEDP vs. PCWP

	LVEDP ≤15	LVEDP >15		PAH Diagnosis by PCWP				
	PAH	PVH	Total		Sens	Spec	PPV	NPV
PCWP ≤15 PAH	48	34	82	≤15 mmHg	.89	.56	.59	.88
				≤14 mmHg	.82	.62	.60	.83
				≤13 mmHg	.76	.70	.64	.81
				≤12 mmHg	.70	.71	.63	.78
PCWP >15 PVH	6	43	49	≤11 mmHg	.69	.77	.67	.78
				≤10 mmHg	.67	.83	.74	.78
				≤9 mmHg	.59	.91	.82	.76
	54	77	131	≤8 mmHg	.50	.94	.84	.73

DISCLOSURE: Francisco Soto, None.

CHARACTERISTICS OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH ELEVATED PULMONARY CAPILLARY WEDGE PRESSURE

Terry A. Fortin MD* Abigail Krichman RRT C. W. Hargett MD Victor F. Tapson MD Duke University Medical Center, Durham, NC

PURPOSE: While randomized trials of pulmonary arterial hypertension (PAH) therapy exclude patients with an elevated pulmonary capillary wedge pressure (PCWP), 25 percent of our referred pulmonary hypertension (PH) population has a PCWP > 15 mmHg. These patients often otherwise meet WHO criteria for PAH. We sought to better characterize these patients.

METHODS: We reviewed PH patients referred to our center from 2001 to 2005 to determine the characteristics of those patients with an elevated PCWP. We included those with a mPAP > 25 mmHg, and PCWP > 15 mmHg. Those with PH and abnormal LV systolic function, or pulmonary vascular resistance (PVR) < 3 were excluded. Baseline characteristics, diagnosis, disease severity, and therapy were analyzed.

RESULTS: 114 patients had normal LV function, mPAP > 25 and PCWP > 15; 29 with PVR < 3 were excluded. The remaining 85 patients had multiple comorbidities; 73.8% had hypertension, 54.1% had LV hypertrophy, and 57.6% were obese. Approximately 1/3 had one or more of the following: atrial fibrillation, coronary disease, chronic obstructive pulmonary disease or diabetes. Mean hemodynamics were as follows: mPAP 52.9 mmHg (29-138), PCWP 21.5 mmHg (16-40), PVR 7.9 Wood Units (WU) (3.1-32.9), and cardiac index (CI) 2.4 L/min/m2 (1.3-4.34). The mPAP was >55 mmHg in 36.4%, right atrial pressure >20 mmHg in 25%, and CI <2.0 L/min/m2 in 20%. Mild PH (PVR 3 to 5 WU)was present in 40%. Specific PAH therapy (e.g., prostacyclins or endothelin antagonist)was safely administered in 39/51 patients with more severe PH. Major diagnoses included PAH, (8 idiopathic, 7 connective tissue disease,

Pulmonary Hypertension Evaluation, continued

1 portopulmonary, 6 congenital heart) while left-heart / valvular disease, or primary lung or sleep disorders appeared to contribute in 30 and 23 patients respectively. The remainder had chronic thromboembolism, sarcoidosis, sickle cell, and high output disorders.

CONCLUSION: Patients with PH and an elevated PCWP but with normal LV systolic function have significant comorbidities complicating their management.

CLINICAL IMPLICATIONS: Future controlled clinical trials should study specific PAH therapy in this population.

DISCLOSURE: Terry Fortin, None.

NITROPRUSSIDE (NTP) IN THE ASSESSMENT OF PULMONARY HYPERTENSION (PH) ASSOCIATED WITH ELEVATED LEFT VENTRICULAR (LV) FILLING PRESSURES DUE TO DIASTOLIC DYSFUNCTION

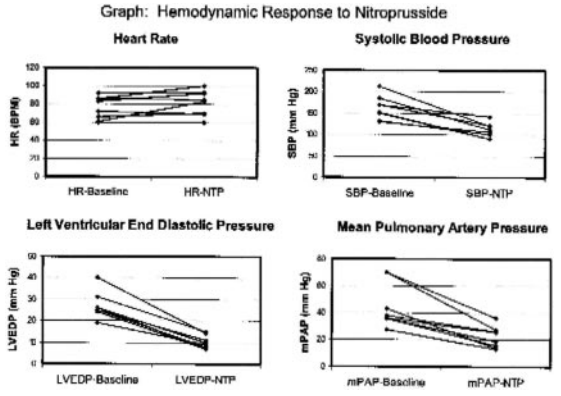
Zouras K. Wendy MD* James Kleczka MD David Marks MD Ronald Siegel MD Kenneth Presberg MD Timothy Woods MD Michael Cinquegrani MD Amjad Syed MD Amina Syed MD Francisco J. Soto MD Medical College of Wisconsin, Milwaukee, WI

PURPOSE: A diagnosis of pulmonary arterial hypertension (PAH) implies a mean pulmonary artery pressure (mPAP) >25 mm Hg and normal LV filling pressures (<15 mmHg). Higher LV pressures suggest pulmonary venous hypertension (PVH) and preclude the use of PAH-specific therapies. However, some patients with PVH present with severe PH that seems "out-of-proportion" to the elevation in LV pressures, suggesting the presence of both PVH and PAH. We hypothesize that a trial of NTP - administered in an attempt to normalize left ventricular end-diastolic pressure (LVEDP) and assess the degree of residual PH- can help in differentiating those with predominant PVH from those with an additional component of PAH.

METHODS: We reviewed the cardiac catheterization records and tracings of eight patients with PH in whom it was questioned whether PVH alone could be causative. All patients underwent a right heart catheterization that included an intravenous (IV) NTP trial. Hemodynamic measurements at baseline and while receiving NTP were compared and analyzed. In two patients the NTP trial was conducted after a trial of prostacyclin and nitric oxide failed to show a significant reduction in pulmonary pressures. LV ejection fraction was >50% in all patients but one (45%). Average NTP dose and time to response was 1.8 mcg/kg/min and 6.8 minutes, respectively.

RESULTS: IV NTP resulted in a significant decrease in LV filling pressures and mPAP, without deleterious changes in blood pressure or heart rate. LVEDP was normalized (<15 mmHg) in all patients and in 7/8 patients the mPAP became <30 mmHg.

CONCLUSION: This preliminary study demonstrates that use of NTP



during a diagnostic catheterization provides valuable information for differentiating between PH due to PVH alone and that due to a combination of PVH and PAH. This occurs predominantly by decreasing LVEDP.

CLINICAL IMPLICATIONS: Near normalization of pulmonary arterial pressures after reduction of LV filling pressures during a trial of NTP suggests a predominant component of PVH and thus guides treatment decisions.

DISCLOSURE: Zouras Wendy, None.

CIRCULATING PROSTAGLANDIN D2 SYNTHASE (PGDS)LEVELS IN PULMONARY HYPERTENSION

Terence K. Trow MD* Adam Hurewitz MD Gregory Ferreira MD Mary Bartlett RN Louis Ragolia PhD Winthrop-University Hospital, Mineola, NY

PURPOSE: Eicosanoids have been linked to the control of both pulmonary artery (PA)smooth muscle function and proliferation and are important in the contol of pulmonary hypertension (PH). One such prostaglandin, prostaglandin D2 (PGD2) has been shown to be a mediator of apoptosis and in many studies is antiproliferative to smooth muscle growth. The role of PGD2S, a circulating enzyme, has not been investigated in PH. We examined the circulating levels of PGDS in 20 PH patients and 20 age and sex matched controls without PH.

METHODS: Patients were >18, non-pregnant, and did not have renal failure, systemic hypertension, diabetes mellitus and were not using nonsteroidal anti-inflammatory agents, COX-2 inhibitors, or aspirin. Five milliliters of blood was drawn by venipuncture and centrifuged at 2000 X G, and the sera frozen at -80°C for later assay. Both lipocalin and hematopoeitic forms of PGDS were assayed by enzyme linked immunoabsorbant assay. Patient characterisics including systolic PA and mean PA pressures, age, sex, therapy at the time of assay, and New York Heart Association functional class were recorded.

RESULTS: Lipocalin PGDS was found in significantly higher levels in PH patients than in controls [mean=1030 ng/ml SEM=97.6 vs. 652 ng/ml SEM=42.5; p=0.003]. No significant differences were found between male and female patients [female mean=1017 ng/ml SEM=147 vs. male means=1109 ng/ml SEM=111; p=0.672]. Correlation with PGDS levels and degree of PH as reflected by systolic PA pressure was modest [R2=0.20].

CONCLUSION: Circulating levels of PGDS are elevated in PH and correlate modestly with systolic PA pressures. No apparent differences between male and female patients with PH were noted. A larger study of PH patients is warranted.

CLINICAL IMPLICATIONS: The significance of elevated PGDS levels remains to be clarified. Whether this is a primary anomaly in PH or an attempt to defend against other primary causes of smooth muscle overgrowth remains to be defined. Inverse correlation with mean PA pressures raises the possibility of using PGDS levels as a marker of disease severity or response to therapy.

DISCLOSURE: Terence Trow, None.

Surgical Management of Lung Cancer
10:30 AM - 12:00 PM

SURGICAL TREATMENT FOR METACHRONOUS LUNG CANCER

Makoto Takahama MD* Takashi Tojo MD Michitaka Kimura MD Keiji Kushibe MD Takeshi Kawaguchi MD Shigeki Taniguchi MD Nara Medical University School of Medicine, Kashihara, Japan

PURPOSE: The benefits of surgical treatment for metachronous lung cancer are not well described. The aim of this study was to evaluate the validity and efficacy of surgical treatment for metachronous lung cancers.

METHODS: From January 1995 to December 2004, a total of 37 patients underwent a second resection for a metachronous lung cancer. We reviewed the charts of these patients and analyzed type of resection, operative morbidity, mortality, and survival by stage. All tumors were classified postsurgically. Survival was calculated by the Kaplan-Meier method and the data were evaluated with the log rank's test.

RESULTS: The mean interval between the first and second resection was 39.7±31.0 months. Ninety-five percent of the patients presented stage I cancers, 2.7% with stage II, and 2.7% with stage III cancers. Lobectomy was performed in 16.2% of the patients, segmentectomy in 27.0%, and wedge resection in 56.8% for the metachronous cancers. Operative mortality for the second resection was 5.4% (2 out of 37 patients). These two patients died of acute respiratory distress syndrome during the early postoperative period. The mean follow-up after the second resection was 42.1 months. The 1-, 2-, 5-year actuarial survival for the entire group after the second resection was 86.5, 83.4, and 79.5% respectively.

CONCLUSION: Operations for metachronous lung cancers provided the improved prognosis of these patients. Surgical treatment should be

Surgical Management of Lung Cancer, continued

considered as a safe and effective strategy for resectable metachronous lung cancers in patients with adequate physiologic pulmonary reserve.

CLINICAL IMPLICATIONS: We found surgical resection of metachronous lung cancers could be performed in selected patients with meaningful long-term survival. This finding suggests that there might be benefit to systematic postoperative surveillance of patients after resection with the goal of detecting metachronous tumors at the earliest possible stage.

DISCLOSURE: Makoto Takahama, None.

EXTRAPLEURAL PNEUMONECTOMY OR VATS PLEURECTOMY / DECORTICATION FOR EARLY STAGE MALIGNANT MESOTHELIOMA? A CASE CONTROL STUDY

John G. Edwards PhD Antonio E. Martin-Ucar MD* Duncan J. Stewart MBBS David A. Waller Glenfield Hospital, Leicester, United Kingdom

PURPOSE: To examine whether radical surgery has benefits over debulking for malignant pleural mesothelioma (MM), we compared the results of extrapleural pneumonectomy (EPP) and VATS pleurectomy / decortication (P/D) in a case control study.

METHODS: We analysed the results of EPP or P/D in 145 consecutive patients with early stage MM over a seven year period. If deemed medically fit, patients received EPP. Those unfit underwent P/D (a subtotal parietal pleurectomy followed by visceral decortication to gain full lung expansion). The distribution of known prognostic factors between the groups was compared. Postoperative survival and time to progression (TTP) data were analysed.

RESULTS: EPP was performed in 95 and P/D in 50 patients. Those in the P/D group were older (median age 68 vs. 57 years, $p<0.001$), of poorer performance status ($p=0.001$) and were associated with poorer EORTC ($p=0.002$) and CALGB prognostic groups($p=0.03$). Pathological TNM stages in the EPP group were : 6 stage I, 8 stage II, 56 stage III and 25 stage IV. The P/D group had shorter hospital stay (median 6 vs. 13 days, $p=0.001$). In-hospital mortality was 7 (7.4%) and 3 (6%) in the EPP and P/D groups respectively. There was no difference in survival between the EPP and P/D groups ($p=0.48$). Compared to the P/D group, median survival was longer in the epithelioid node negative cases (29.8 months, $p=0.03$) but not in those with positive N2 nodes ($p=0.5$). P/D was associated with a shorter TTP (7.6 vs 12.0 months, $p=0.01$). There was no planned adjuvant chemotherapy or hemithorax irradiation in the P/D. In the EPP group, 20 received neoadjuvant and 17 adjuvant treatment.

CONCLUSION: Radical surgery (EPP) for mesothelioma may achieve better local control than debulking surgery but this has not been shown to influence distant disease progression or survival. However, survival following VATS P/D appears to be no better than for the N2 positive EPP group.

CLINICAL IMPLICATIONS: We conclude that the role of EPP should be subject to evaluation in a randomised trial.

DISCLOSURE: Antonio Martin-Ucar, None.

PARENCHYMA-SPARING SURGERY FOR PROXIMAL NSCLC: SLEEVE RESECTIONS RESULT IN EQUIVALENT SURVIVAL AND BETTER PERFORMANCE THAN PNEUMONECTOMIES

Gary M. Hochheiser MD* Maggie C. Oldham John R. Roberts MD Eastern Virginia Medical School, Norfolk, VA

PURPOSE: The perioperative risk after pneumonectomy is high (8-12%) and dramatically decreases a patient's quality of life, so that parenchyma-sparing procedures are needed. Airway sleeve resections have been described for several decades, but remain rarely done. Arterial sleeve resections are even rarer, and done in only a few centers. We have used airway and arterial sleeve resections commonly, and report a prospective comparison of perioperative complications and survival among airway sleeve resections, arterial sleeve resections, and pneumonectomies.

METHODS: All patients with NSCLC underwent surgical staging prior to resection. At resection patients underwent parenchymal sparing procedures if possible. All patients were resected with negative margins-.Survival was compared using nonparametric distribution analysis while differences among means were compared using Student's t test. Differences in proportions were compared using chi-square. p values <0.05 were considered significant.

RESULTS: Eighty-six patients underwent sleeve resections and 74 patients underwent pneumonectomy. The pneumonectomy patients were younger (58.4 vs 62.7 years) but were otherwise similar. Pneumonectomy patients spent more days in the ICU (3.5 vs. 1.2, $p=0.046$) but had similar lengths of stay. No difference in overall survival nor in comparisons between node-negative resections (see graph) were found.

CONCLUSION: Sleeve Resections give equivalent survival compared to pneumonectomies and allow preservation of pulmonary parenchyma. With postoperative chemotherapy becoming standard treatment after most hilar resections, preserving lung function, and thus ability to tolerate adjuvant chemotherapy, is more important.

CLINICAL IMPLICATIONS: Sleeve resections allow preservation of lung function and result in equivalent survival.

	1-year	2-years	3-years	4-years	5-years
Sleeves	85.70%	72.20%	57.10%	62.50%	50%
Pneumonectomies	93.80%	78.60%	76.90%	53.80%	50%

DISCLOSURE: Gary Hochheiser, None.

SURGICAL TREATMENT OF BRONCHIOLOALVEOLAR CARCINOMA

Pier Luigi Filosso MD* Giovanni Donati MD Davide Turello MD Fausto Pernazza MD Alberto Oliaro MD University of Torino Department of Thoracic Surgery, Castellamonte, Italy

PURPOSE: To assess prognostic factors in patients operated on for bronchiolalveolar carcinoma (BAC) of the lung.

METHODS: Between 1993 and 2000, 108 patients underwent pulmonary resection for BAC. There were 68 male (63%) and 40 female, mean age 63.8 years (range 29-77 years). Seventy-eight BACs (72.3%) were in the upper pulmonary lobes. Ninety-two lobectomies (85.2%) (69 upper), 7 pneumonectomies and 9 wedge-resections were carried out, and radical lymphadenectomy was always performed.

RESULTS: Fifty-one tumors were less than 3 cm and 57 (52.8%) more than 3 cm in size. BACs resulted well- or middle-differentiated in 98 cases (91%). Microvascular, perineural and visceral pleural invasion were evident in 38, 6 and 26 cases respectively. Seventy-four tumours (68.5%) were at stage I, 10 at stage II, 22 at stage IIIa and 2 at stage IIIb. Three, 5 and 10 year survival rates were 66% , 63% and 55%, respectively.No survival differences were observed for age, gender, tumor grading, tumor size and visceral pleural involvement. Significant prognostic factors were microvascular invasion ($p=0.01$), perineural invasion ($p=0.04$), nodal status ($p=0.007$) and pathological staging ($p=0.008$).

CONCLUSION: BACs show a better survival than others NSCLC, when radically resected. Microvascular and perineural invasions, nodal status and staging are significant factors in predicting long-term survival.

CLINICAL IMPLICATIONS: an early stage BAC has a favourable long-term survival. A solitary pulmonary nodule in high risk patient, should be considered as a possible BAC. Early diagnosis and surgical treatment are thus mandatory.

DISCLOSURE: Pier Luigi Filosso, None.

DOES MICROSCOPIC INVOLVEMENT OF RESECTION MARGINS AFFECT LONG-TERM SURVIVAL AFTER RESECTION OF STAGE I AND II LUNG CANCER?

Sherilyn K. Tay MB, ChB* Antonio E. Martin-Ucar MD Ed Black MD Lynda Beggs David Beggs MD John P. Duffy MD Ellis Morgan MD Thoracic Surgery. Nottingham City Hospital, Nottingham, United Kingdom

PURPOSE: To determine whether other pathological variables such as the degree of differentiation of the cancer cells and the presence of tumour cells on the resection margins on microscopy (R1 resection) did alter survival following resection for non-small-cell lung cancer (NSCLC).

METHODS: The clinical and pathological records of the 857 consecutive patients [586 male and 271 female, median age 66 (range 35 to 84) years] who underwent lobectomy/bilobectomy (n=558) or pneumonectomy (n=299) for Stage I (n=516) or II (n=341) NSCLC in our unit from 1991 to 2005 were reviewed. Survival was calculated according to the Kaplan-Meier method. The impact of multiple variables on survival was evaluated with univariate and multivariate tests.

Surgical Management of Lung Cancer, continued

RESULTS: Operative mortality was 4.1 % (35 cases) [2% (n=11) after lobectomy and 8% (n=24) after pneumonectomy]. In 47 cases (5.5%) the pathological report did not confirm excision to be complete microscopically (R0) due to: microscopic involvement of the bronchial margin in 34 cases, of the vascular margin in 8 cases and other resection margins in 5 cases. In addition, in a further 65 cases (8%) the shortest clear distance to the margin was less than 5 mm. Overall median survival was 59 months. The 5- and 10-year survivals were 55% and 36% for Stage I, and 41% and 22% for Stage II respectively. On univariate analysis staging, and degree of differentiation were predictors for long-term survival. R1 resection did approach significance (p=0.055), but not tumour being less than 5 mm from the clear margins (p=0.9).On multivariate analysis tumour staging was the only pathological variable affecting survival (Table 1).

CONCLUSION: Tumour stage is the pathological determinant for survival after anatomical resection of Stage I/II non-small-cell lung cancer. It does outweigh tumour cell differentiation, microscopic involvement of resection margins and close distance to clear resection margins as a predictor of long-term survival in these patients.

CLINICAL IMPLICATIONS: Demographic variables and tumour staging determine survival following surgery for lung cancer. Other pathological variables do not signifficantly alter outcomes.

Table 1—*Independent Predictors of Survival*

Variables	Hazard ratio (95% CI)	p
Gender	1.32 (1.04 to 1.66)	0.017
Age>75	1.42 (1.03 to 1.95)	0.028
Low BMI	1.72 (1.12 to 2.64)	0.012
Tumour Stage	2.49 (1.49 to 4.18)	0.005

DISCLOSURE: Sherilyn Tay, None.

OUTCOMES FOLLOWING LIMITED LUNG RESECTION FOR NON-SMALL CELL LUNG CANCER (NSCLC) IN HIGH RISK PATIENTS

Lisa M. Guirguis MD Eric C. C. Feliberti MD* Nicole Tsai MS Frederic W. Grannis MD City of Hope National Medical Center, Duarte, CA

PURPOSE: This study was undertaken to assess recurrence and survival outcomes among high risk patients treated with compromise limited lung resection for NSCLC. The impact of adjuvant therapy and co-morbid disease is also evaluated.

METHODS: A retrospective review of all NSCLC patients treated with limited resection between January 1987 and November 2004 at City of Hope National Medical Center was performed. Limited lung resections were performed when the extent of co-morbid disease made performance of standard resections hazardous. Medical records were reviewed for patient and tumor characteristics, type of operation, adjuvant treatment, disease recurrence and survival.

RESULTS: Sixty-two limited lung resections were performed for clinical stage I NSCLC. The median age was 68 years for this predominantly female (64.5%) patient population. All patients had at least one, and 53% had two or more co-morbid conditions. The 30-day operative mortality was 1.6%. Nineteen percent of the study population received post-operative radiation therapy and 4.8% received post-operative chemotherapy and radiation therapy. The five-year actuarial overall survival was 38%, with a median follow-up of 35 months (range 5.9 to 134.2). The local recurrence rate was 23%. No difference in time to recurrence among patients with or without adjuvant therapy was noted. All local recurrences received radiation therapy and/or chemotherapy with a median survival of 13 months (range 3.3 to 63.2) post-treatment. Time to death from lung cancer (21.9 months) was significantly shorter than time to death from co-morbid disease (42.4 months, p=<0.011). Histological subtype, angiolymphatic invasion, margin and lymph node status did not predict recurrence.

CONCLUSION: Lung cancer patients with prohibitive co-morbid disease can undergo compromise resections safely. Despite higher local recurrence, long-term survival is achieved in many patients. Adjuvant therapy did not appear to reduce local recurrence or improve survival.

CLINICAL IMPLICATIONS: Limited lung resection may be offered to clinical stage I NSCLC patients with severe co-morbid disease with the expectation that a substantial number obtain long-term survival.

Figure 1. Kaplan-Meier survival curve of the 61 high risk patients with non-small lung cancer treated with limited lung resection.

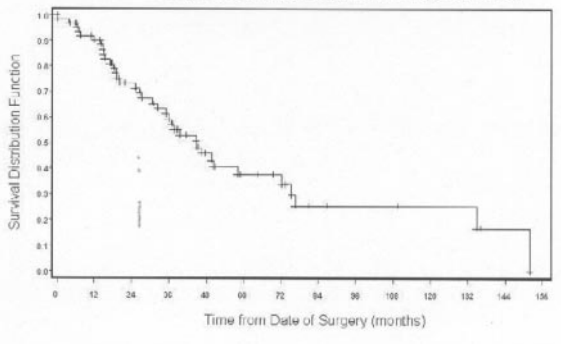
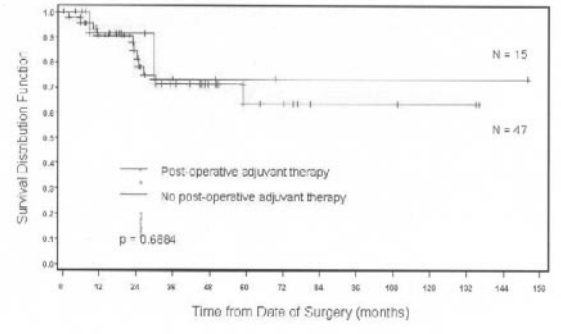


Figure 2. Time to local recurrence after limited lung resection among high risk patients who received post-operative adjuvant therapy versus those who did not.



DISCLOSURE: Eric C. Feliberti, None.

Tuberculosis Diagnosis and Evaluation 10:30 AM - 12:00 PM

WHAT IS THE MAGNITUDE AND COST BURDEN OF SUSPECTED TUBERCULOSIS?

Jessica A. Reading BS Thaddeus L. Miller MPH* Stephen E. Weis DO University of North Texas Health Science Center at Fort Worth, Fort Worth, TX

PURPOSE: There is little or no information in the literature regarding the numbers of patients who are suspected of but subsequently ruled out for TB infection before meeting reporting requirements. These patients represent an unmeasured cost of TB to the healthcare system. Without fully quantifying the burden of TB on U.S. healthcare, public TB prevention and control efforts are undervalued when considered on the basis of relative cost and benefits. This leads to reduced public and political support and resurgence of disease. We estimated the number of patients with suspected TB who are never reported using acid-fast bacillus (AFB) cultures completed as a proxy. Quantifying suspected tuberculosis in the community healthcare setting is one component of measuring the burden created by TB.

METHODS: We collected data on the number of AFB tests conducted in all hospitals in Tarrant County, Texas in calendar year 2002. Outcome measures were total number of AFBs, estimated cost incurred by testing, and number of individuals affected. Cost data is taken from the Texas

Tuberculosis Diagnosis and Evaluation, continued

Department of Health. The unit of analysis was the program and no patient identifiers or individual information was collected.

RESULTS: In Tarrant County, Texas hospitals 5,768 AFB cultures were completed in 1,920 patients over one calendar year. 181 of these cultures were positive for any AFB growth, and 43 were positive for M. tb. Each AFB culture completed cost approximately $96, creating a cost of $12,877 to confirm M. tb.

CONCLUSION: The suspicion of tuberculosis for many respiratory diseases incurs significant, previously unmeasured cost to the U.S. healthcare system. Over 134 AFB cultures are completed at a cost of $12,877 to confirm one tuberculosis case in our survey. It is vital to measure the full impact of tuberculosis on the healthcare system to accurately describe the value of elimination and control efforts.

CLINICAL IMPLICATIONS: Use of AFB culture to rule out tuberculosis in low-probability suspects is resource intensive and may be cost-inefficient.

DISCLOSURE: Thaddeus Miller, None.

IS CA-125 A RELIABLE SERUM MARKER FOR DIAGNOSIS OF TUBERCULOSIS?

Karthikeyan Kanagarajan MD* J. Williams MD V. Rupanagudi MD K. Julliard MS G. Gandev MD K. Gupta MD P. Krishnan MD Coney Island Hospital, Brooklyn, NY

PURPOSE: CA-125 levels have been shown to be elevated in patients with pelvic-peritoneal tuberculosis (TB) with ascites. There are few case reports of raised CA-125 levels in patients with pulmonary and extra pulmonary TB. The aim of our study was to determine the usefulness of CA-125 in the diagnosis of TB (both pulmonary and extra pulmonary) in the patients admitted with a clinical suspicion for TB.

METHODS: Prospective study of 50 patients who were admitted with a clinical suspicion for TB from July 2003 to March 2004. In all 50 patients CA-125 was done on admission. Patients who had other diseases that could cause high CA-125 such as benign or malignant gynecologic tumors, pelvic inflammatory disease, peritonitis and cirrhosis were excluded from the study. A positive culture for Mycobacterium Tuberculosis (MTB) was used to establish the diagnosis of TB.

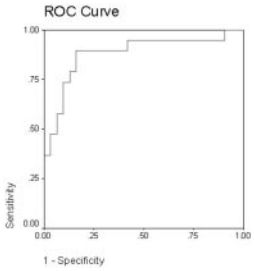
RESULTS: The following results obtained.

Patient Characteristics

Variables	Values (%)
Patients No.	50 (100%)
Gender Male Female	35 (70%) 15 (30%)
Culture MTB positive MTB negative	19 (38%) 31 (62%)
Tuberculosis Pulmonary Extra pulmonary	19 (38%) 14 (28%) 5 (10%)
Extra pulmonary Tuberculosis Lymph node Meningitis Pleural effusion	5 (10%) 2 (4%) 1 (2%) 2 (4%)

CONCLUSION: Raised levels of CA-125 are useful in the diagnosis of pulmonary and extra pulmonary TB with high sensitivity and specificity and a very high negative predictive value. The levels seems to correlate with the bacillary burden, being highest in miliary and cavitary pulmonary TB. In patients with TB lymphadenitis CA-125 was normal.

CLINICAL IMPLICATIONS: In patients suspected to have TB, a raised CA-125 greatly increases the likelihood of tuberculous infection. A normal CA-125 is strong evidence against tuberculous infection except in patients with lymphadenitis. A normal CA-125 level should prompt a search for an alternate diagnosis.



DISCLOSURE: Karthikeyan Kanagarajan, None.

PROSPECTIVE EVALUATION OF A NEW SEROLOGIC TEST (ASSURE TB RAPID TEST) FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS

Amartya Mukhopadhyay MBBS* Ming Guan PhD Ying H. Chen Lu Yang BSc Keang T. Lim MBBS National University Hospital, Singapore, Singapore

PURPOSE: Case detection and early treatment of positive patients are critical to the control of pulmonary tuberculosis (PTB). Traditionally, diagnosis of tuberculosis depends on smear-culture method which although considered "gold standard" leaves a lot to be desired. We prospectively compared ASSURE™ TB Rapid Test (Genelabs Diagnostics), which is a rapid tuberculosis serologic test, with traditional approaches for diagnosis of pulmonary tuberculosis.

METHODS: We enrolled all consecutive adult patients (≥18 years of age) suspected of having active PTB between June 2001 and March 2003.All patients were tested for 3 sputum samples (or tracheal aspirate in intubated patients) for smear and culture of Mycobacterium tuberculosis (MTB). ASSURE™ TB Rapid Test was done within 3 days of the sputum sampling.

RESULTS: A total number of 238 patients were included. Of these 171 patients were male and 67 female (2.5:1) with a mean age of 56.6 (18-96, ±18.4) years. Twenty-two patients were excluded because culture either showed Mycobacteria Other Than Tuberculosis (MOTT, 9), or were contaminated (7) or were not done (6). Final analysis therefore included 216 patients. The sensitivity and specificity of the new serological test were 60.2% (95% CI, 50.5 - 69.1%) and 82.3% (95% CI, 74.2-88.2%) respectively in relation to the final diagnosis in contrast to those of the smear test, which were 53.4%(95% CI, 43.8-62.7%) and 98.2% (95% CI, 93.8-99.5%). Combination of the sputum smear and serology provides an increased sensitivity of 74.8% (95% CI, 65.6-82.2%) but a relatively lower specificity of 80.5%(95% CI, 72.3-86.8%) with the tested cohort of high TB prevalence.

CONCLUSION: 1)A moderate increase in sensitivity but a decrease in specificity were observed with the new test in comparison with the direct smear examination, 2) Combination of the sputum smear and the new serology increased further the sensitivity while maintain a moderate specificity with the tested cohort.

CLINICAL IMPLICATIONS: ASSURE™TB Rapid Test is not beneficial if used alone as a tool for rapid diagnosis of PTB but can improve case-detection when combined with smear test.

	Final Diagnosis	PTB	Non-TB	Sensitivity	Specificity
Smear					
Positive (%)	57 (26.4)	55	2	53.4	98.2
Negative (%)	159 (73.6)	48	111		
Serology					
Positive (%)	82 (38)	62	20	60.2	82.3
Negative (%)	134 (62)	41	93		
Smear & Serology					
Positive (%)	99 (45.8)	77	22	74.8	80.5
Negative (%)	117 (54.2)	26	91		

DISCLOSURE: Amartya Mukhopadhyay, None.

Tuberculosis Diagnosis and Evaluation, continued

RELATIONSHIP BETWEEN TUBERCULIN HYPERSENSITIVITY AND SERUM ALBUMIN LEVELS IN PATIENTS WITH ACTIVE TUBERCULOSIS

Stylianos A. Michaelides MD* Dimitris Zachilas MD Olga Vartzioti MD Julia Vrioni MD Aimilia Tsarouha MD Georgios Diamantidis MD Ourania Anagnostopoulou MD Dpt of Thoracic Medicine, A. Fleming Gen. Hospital, Athens, Greece

PURPOSE: It has long ago been observed that the diameter of tuberculin skin response might be affected by a low dietary protein intake (Kardjito et al. Tubercle 1981;62: 31-35). In the present study we tried to investigate the possible relationship between intensity of tuberculin skin reaction and serum albumin levels in patients with active tuberculosis.

METHODS: We studied 42 patients (35 males and 7 females) aged 33.04 years (mean, 15.7 years (SD) all with established active pulmonary TB just before initiation of treatment by recording the tuberculin skin reaction (using 5TU of PPD RT23) and measuring their serum albumin levels. All patients had no evidence of any condition affecting serum albumin levels or immunological disorder.

RESULTS: The diameter of skin induration was 17.8 mm (mean), 6.01 mm (SD) and the mean serum albumin levels were 7.27 gr/dl(mean), 0.86 gr/dl (SD). Analysis showed a statistically significant positive correlation between intensity of tuberculin skin reaction and serum albumin levels ($R=0.528$, $p<0.001$).

CONCLUSION: The intensity of tuberculin skin response seems to be influenced by the levels of albumin in serum.

CLINICAL IMPLICATIONS: Factors affecting serum albumin concentration should be taken into account on interpreting the results of tuberculin skin testing.

DISCLOSURE: Stylianos Michaelides, None.

CT FINDINGS IMPLY THE BLEEDING SITE COMPARED WITH ANGIOGRAPHY IN TUBERCULOSIS PATIENTS WITH MASSIVE HEMOPTYSIS

Jin Hoon Cho MD* Ki Uk Kim MD Yon Seong Kim MD Min Ki Lee MD Yeong Dae Kim MD Yeon Joo Jeong MD Soon Kew Park MD Pusan National University Hospital, Internal Medicine, Pusan, South Korea

PURPOSE: Pulmonary Tuberculosis has been major cause of the massive hemoptysis in Korea. CT(Computed tomography) can provide useful informations about the cause of disease and the bleeding site as well. It allows more rapid and exact managements to know the bleeding site obviously from CT in emergent situation such as patients presented with massive hemoptysis. The aim of this study is to elucidate significant CT findings implying the bleeding site in pulmonary tuberculosis patients.

METHODS: From March 31, 2001 to June 30, 2004., 28 pulmonary tuberculosis patients of massive hemoptysis with chest CT of hemoptysis proctocol, bronchial angiography and embolization were reviewed retrospectively. To examine the CT findings implying the bleeding site, we determined bleeding lobe based on angiography and calculate the concordance rate of each CT findings. CT findings were classified to the air-meniscus sign, cavity, consolidation, fibrotic scar, bronchial dilatation, ground glass opacity. We analyzed the corresponding sites of CT and the angiographic findings of the foci lobe of bleeding. In other words, Numbers of lobes which each CT finding observed in bleeding lobe/ numbers of lobes which each CT finding observed in whole lung of overall patients was calculated. The hemoptysis proctocol is composed of two part. One is high resolution CT with 1mm thickness, 7-10 mm interval from apex to diaphragm. The other is contrast enhanced spiral CT with 1.25-2.5mm thickness and injection speed of dye 2.5ml/sec.

RESULTS: The concordance rate of air-meniscus sign is 90.9%, cavity 84%, consolidation 83.3%, fibrotic scar 75.7%, bronchial dilatation 67.5%, ground glass opacity 40.6%.

CONCLUSION: Air-meniscus sign, cavity, consolidation of chest CT suggest the bleeding site strongly in pulmonary tuberculosis patient presented with massive hemoptysis.

CLINICAL IMPLICATIONS: Air meniscus sign, cavity and consolidation suggest bleeding site could allow more rapid, precise management of massive hemoptysis patients of pulmonary tuberculosis.

DISCLOSURE: Jin Hoon Cho, None.

Ventilator Associated Infections 10:30 AM - 12:00 PM

CLINICAL AND TREATMENT PATTERNS AMONG 398 PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA: FINAL RESULTS OF THE ASSESSMENT OF LOCAL ANTIMICROBIAL RESISTANCE MEASURES (ALARM) STUDY

Marin H. Kollef MD* Kenneth V. Leeper MD Antonio Anzueto MD Lee E. Morrow MD Lisa Benz-Scott PhD Frank J. Rodino MS Michael S. Niederman MD Washington University School of Medicine, St. Louis, MO

PURPOSE: ALARM was a prospective, observational, cohort study designed to capture and analyze management and outcome variable patterns for ventilator-associated pneumonia (VAP).

METHODS: Investigators from 20 institutions within the United States identified 398 (60.8% male; mean age, 58.3 yrs) ICU patients with a diagnosis of VAP. Clinical, diagnostic, and treatment data were gathered on each patient for the duration of ICU stay. Escalation/de-escalation of therapy was defined as switching to or adding a drug class(es) with a broader/narrower spectrum, respectively, or additional/less coverage as defined by the following spectrum categories: carbapenem> cefepime> ureidopenicillin/monobactam> quinolone> other/none.

RESULTS: The mean duration of mechanical ventilation prior to VAP diagnosis was 7.3 + 6.9 days (range, 0-44 days). Tracheal aspirate cultures (58.3% of patients), bronchoalveolar lavage fluid cultures (33.7%), or both (1.8%) were used to identify major pathogens, which included methicillin-resistant Staphylococcus aureus (14.8%), Pseudomonas aeruginosa (14.3%), other Staphylococcus species (8.8%), Klebsiella pneumoniae (3.3%), Enterobacter (3.3%), E coli (3.0%), and Acinetobacter (2.0%). The most common initial treatment regimens consisted of (alone or with other agents): cefepime (30.4%), piperacillin/ tazobactam (27.9%), and vancomycin (17.8%). Mean duration of therapy was 11.8 days. Patterns of antibiotic therapy changes for VAP are shown in Table 1. Escalation of therapy occurred in 14.8% of patients and de-escalation in 22.4%. Overall mortality was 25.1%. Comparative mortality was lower among patients whose therapies were de-escalated (16.9%) compared to both patients undergoing escalation (42.4%) and those for whom therapy was neither escalated nor de-escalated (31.6%). Mean change in CPIS score at 72 hours was significantly less among patients who died (-0.10) compared with survivors (-2.35) ($p<.05$).

CONCLUSION: This multicenter study confirms that VAP in the ICU setting is associated with unacceptably high mortality rates.

CLINICAL IMPLICATIONS: Choices regarding initial antibiotic regimens and subsequent escalation/de-escalation of therapy have significant implications for patient outcomes.

Table 1. ***Patterns of Antibiotic Prescription Changes for Therapy of VAP from Initial to Final***

	Increased	No Change	Decreased
Number of antibiotics	7.0%	70.1%*	22.7%
Spectrum of antibiotics	12.1%	72.6%*	14.3%

*57.0% of patients started and finished therapy on the same regimen.

DISCLOSURE: Marin Kollef, Grant monies (from industry related sources), The ALARM Study has been funded by a grant from Elan Pharmaceuticals.

PREDICTORS OF DEATH AMONG PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA: AN ANALYSIS OF THE ASSESSMENT OF LOCAL ANTIMICROBIAL RESISTANCE MEASURES (ALARM) STUDY DATA

Lee E. Morrow MD* Marin H. Kollef MD Kenneth V. Leeper MD Antonio Anzueto MD Lisa Benz-Scott PhD Frank J. Rodino MS Michael S. Niederman MD Creighton University Medical Center, Omaha, NE

PURPOSE: To identify predictors of death among patients with clinically diagnosed ventilator-associated pneumonia.

METHODS: ALARM was a prospective, observational cohort study from 5/1/03 to 12/31/04. Investigators from 20 U.S. medical centers identified 398 adults meeting the ACCP criteria for ventilator-associated pneumonia. Clinical, diagnostic, treatment, and outcomes data were recorded for the duration of ICU stay. Escalation and de-escalation of antibiotic therapy were defined using a novel classification system that incorporated spectrum and number of drugs prescribed (Figure 1).

Ventilator Associated Infections, continued

Patients were classified based on the presence of risk factors for multidrug-resistant pathogens using ATS criteria. Multivariate logistic regression was used to identify variables associated with death.

RESULTS: The study population was 60.8% male and had a mean age of 58.3 years. The final model (Chi^2=172, p<0.001) included five predictors of death: increased APACHE II score at ICU admission (1 unit increments, RR 1.05, 95% CI 1.40-1.06); inability to de-escalate antibiotic therapy (no change in therapy vs. de-escalation, RR 2.85, 95% CI 2.08-3.89; escalation vs. de-escalation RR 10.75, 95% CI 6.65-17.15); lack of a response to therapy as demonstrated by persistence of or increase in the CPIS score from baseline to 72 hours (RR 1.40, 95% CI 1.33-1.48); failure to use a BAL to diagnose VAP (RR 2.32, 95% CI 1.75-3.03); presence of risk factors for multidrug-resistant pathogens (RR 2.19, 95% CI 1.49-3.23).

CONCLUSION: This multicenter study confirms several single-center reports that increased severity of illness, failure to use an invasive diagnostic strategy employed, and poor response to therapy are significant predictors of death. Our analysis also validates the recent ATS recommendation that risk factors for multidrug-resistant pathogens should be considered when selecting empiric VAP therapy.

CLINICAL IMPLICATIONS: Several predictors of death are modifiable and provide opportunities for improving patient care. Diagnosis of VAP should be aggressively pursued using invasive methods if feasible. Empiric therapy should consider risk factors for multidrug-resistant pathogens and should be de-escalated when possible. Serial CPIS monitoring identifies patients who are failing therapy and have a poor prognosis.

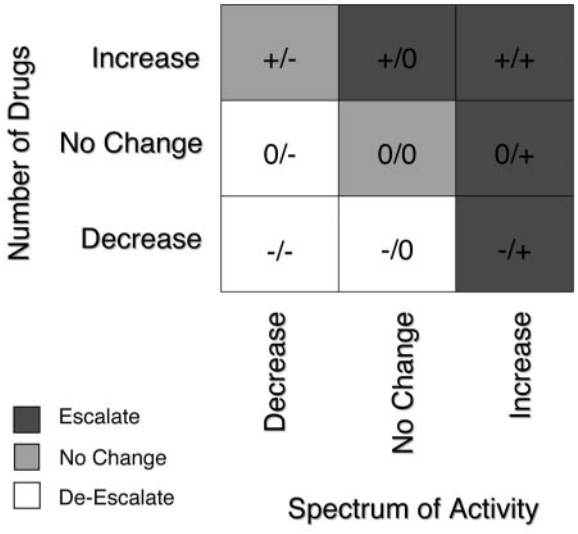


FIGURE 1. Classification of Antibiotic Therapy Escalation/De-Escalation. Chart notation indicates number of drugs/spectrum of activity. Spectrum of activity was defined using the following hierarchy of drug categories: carbapenems > cefepime > ureidopenicillin/monobactam > fluoroquinolone > other/none.

DISCLOSURE: Lee Morrow, Grant monies (from industry related sources) Elan Pharmaceuticals.

PSEUDOMONAS AERUGINOSA VENTILATOR-ASSOCIATED PNEUMONIA: A COMPARISON OF CLINICAL OUTCOMES AMONG RESISTANT VERSUS SUSCEPTIBLE ORGANISMS AT EMORY-CRAWFORD LONG HOSPITAL

Cheryl M. Weyers MD* Seth Clemens MD Kenneth V. Leeper MD
Emory University School of Medicine, Atlanta, GA

PURPOSE: Pseudomonas aeruginosa is the leading cause of nosocomial pneumonia in the USA. Treating infections caused by this organism is challenging given the organism's inherent resistance potential. It is unclear, however, if clinical outcomes are affected by the organism's resistance profile. As such, the purpose of this study was to describe the clinical impact of antibiotic resistance in a group of patients with ventilator-associated pneumonia due to Pseudomonas aeruginosa.

METHODS: All VAP cases between September 2001 and February 2005 that had Pseudomonas aeruginosa recovered from a respiratory culture were included in the analysis. Only the first episode of pneumonia was studied and VAP was defined according to criteria established by the American College of Chest Physicians."Multi-drug resistant" was defined by resistance to at least 3 classes of anti-pseudomonal antibiotics.

RESULTS: Of the 54 cases identified, 21 (39%) were multi-drug resistant isolates.Mortality did not differ significantly between the 2 groups (50% resistant vs 44% sensitive; p=0.72). Patients with VAP caused by resistant strains, however, had longer ICU stays (53 days vs 31days; p=0.004) and were less likely to receive adequate, initial antibiotic therapy (29% vs 100%; p < 0.001). Additionally, they were more likely to be discharged to an LTAC facility (48% vs 15%; p=0.01). No antibiotic combination was associated with improved outcomes, but use of a fluoroquinolone was associated with a trend toward increased mortality and increased risk for inadequate, initial therapy.

CONCLUSION: VAP caused by resistant strains of pseudomonas aeruginosa is not associated with increased mortality as compared to VAP caused by sensitive strains. Resistant cases, however, are more often associated with longer lengths of stay and inadequate, initial antimicrobial therapy.

CLINICAL IMPLICATIONS: Fluoroquinolones should not be used as initial therapy for VAP when Pseudomonas aeruginosa is suspected.

DISCLOSURE: Cheryl Weyers, None.

TRACHEAL COLONIZATION IN NEWLY INTUBATED PATIENTS

Lakshmi Durairaj MBBS* Janice Launspach Joseph Zabner MD University of Iowa Hospitals and Clinics, Iowa City, IA

PURPOSE: Tracheal colonization has been associated with subsequent development of ventilator-associated pneumonia. Little is know about the density of and change in colonization over time.We did a prospective study to examine the pattern and density of tracheal colonization during the initial days of mechanical ventilation in the intensive care unit (ICU).

METHODS: Subjects were enrolled if they were intubated for less than 24 hours and were predicted to stay intubated for 4 days and had a legally authorized representative that signed consent. Tracheal aspirates were collected everyday for the first 4 days of intubation via sterile in-line suction catheter on to a sputum trap using 2ml of saline. Specimen was transported immediately to microbiology laboratory and quantitative cultures obtained. Density of colonization is reported as microbial index which is the sum of log colony forming units of all growth.

RESULTS: 29 subjects (16 men) have been recuited thus far. Mean age is 56 years. Mean ICU and hospital stay is 9 and 20 days respectively. 19/29 were receiving antibiotics on the first day of intubation. Proportion colonized was 63%, 72%, 76% and 93% on Days 1, 2, 3 and 4 respectively. Mean microbial index increased progressively (2.9 on day 1 and 4.2 on day 4). When subjects were colonized from day 1 (n=19), the colonization was persistent for all 4 days. Among those who were sterile on day 1 (n=11), 3 subjects remained sterile and 2 subjects had transient colonization. Among the early colonizers, there was very little acquisition of new bacteria.

CONCLUSION: About two thirds of subjects are already colonized within 24 hours of intubation. Density of colonization increases with the duration of intubation. Initial colonizers are relatively resistant to acquisition of new bacteria.

CLINICAL IMPLICATIONS: Future studies should explore for differences in susceptibility to nosocomial pneumonia between early and late colonizers.

DISCLOSURE: Lakshmi Durairaj, None.

COLONIZATION SURVEILLANCE PREDICTS MICROBIAL ETIOLOGY OF INFECTION IN THE CRITICALLY ILL

Flora V. Kontopidou MD Evangelos D. Papadomichelakis MD Effrosyni D. Manali MD* Anastasia Antoniadou MD Sofia Athanassia MD Evangelos Koratzanis MD Irini Mavrou MD Apostolos Armaganidis MD Helen Giamarellou MD Attikon University Hospital, Athens, Greece

PURPOSE: To study if respiratory and gastrointestinal tract (RT and GIT) colonization surveillance predicts microbial etiology of infections

Ventilator Associated Infections, continued

and permits timely and adequate empiric treatment in the intensive care unit (ICU).

METHODS: The study was performed in a new 5-bed medical-surgical ICU over a year. Infection control policy included weekly surveillance cultures of bronchial secretion and stool samples. All infectious episodes were recorded, analyzing the relationship between infectious etiology and adequacy of empiric treatment, based on most recent colonization results.

RESULTS: We recorded 55 documented infectious episodes, 10 ventilator-associated pneumonias (VAP), 38 bacteremias (18 catheter-related), 3 intra-abdominal and 4 soft-tissue infections. VAP pathogens correlated with bronchial or stool colonizers in 88% (RT being most important). Acinetobacter spp colonization of the RT predicted VAP etiology with a sensitivity of 75% and a specificity of 100%. Primary bacteremia pathogens were colonizers in 73% of the cases, mostly of the GiT. Klebsiella spp colonisation predicted bacteremia etiology with a sensitivity of 57% and a specificity of 92%. In catheter-related isolates 87% of Gram (-) previously colonized bronchial secretions or stool. Fecal or bronchial colonisation predicted etiology in all intra-abdominal or soft tissue infections, respectively. Empiric antibiotic treatment based on colonization results permitted 90% adequacy in VAP and 80% in primary bacteremia treatment.

CONCLUSION: RT and GIT colonization is strongly related to microbial etiology of subsequent infection.

CLINICAL IMPLICATIONS: Systematic weekly colonization surveillance of RT and GIT specimens could be helpful in predicting microbial etiology of infection and guiding appropriate empiric treatment in the critically ill.

DISCLOSURE: Effrosyni Manali, None.

PROBIOTIC MANIPULATION OF THE NATIVE FLORA IN CRITICALLY ILL PATIENTS: AN OPPORTUNITY FOR VENTILATOR-ASSOCIATED PNEUMONIA PROPHYLAXIS?

Lee E. Morrow MD* Marin H. Kollef MD James B. Bowers DO Thomas B. Casale MD Creighton University Medical Center, Omaha, NE

PURPOSE: The pathogenesis of ventilator-associated pneumonia (VAP) involves a shift from the host's native, non-pathogenic flora, to an opportunistic, ICU-acquired flora rich in pathogens. We evaluated whether probiotic therapy maintained a non-pathogenic flora in critically ill patients.

METHODS: 40 mechanically ventilated adults were stratified by APACHE II score and randomized to double-blinded administration of 10(9) CFU of Lactobacillus GG or placebo (inactive plant starch inulin) suspended in vehicle and applied to the oropharynx and stomach every 12 hours. Prior to the first dose of study medication (baseline) and 12 hours after the sixth dose of study medicine (72-hour surveillance), semi-quantitative cultures were obtained via oral swab and gastric aspiration while quantitative cultures were obtained by non-bronchoscopic bronchoalveolar lavage (mini-BAL). Patients received study drug and had cultures collected in addition to standard care. Delta scores were calculated from baseline and 72-hour surveillance culture densities. Two-sample t-tests were used to assess between group differences in the mean delta scores.

RESULTS: Baseline characteristics were not different between the groups. Compared to placebo (n=21), Lactobacillus (n=19) was statistically superior at preserving the normal oral flora (Delta semi-quantitative cultures 0.37 vs. −0.45, p=0.03). Although the Lactobacillus group demonstrated trends toward less pathogenic colonization of the mouth (Delta semi-quantitative cultures -0.21 vs. 0.32) and stomach (Delta semi-quantitative cultures -0.11 vs. 0.32), these results were not statistically significant (p=0.45 and 0.35 respectively). Although twice as many placebo patients as Lactobacillus patients had a ≥10(3) increase in quantitative cultures from surveillance mini-BAL (16% vs. 32%) this difference was not statistically significant (p=0.34). Trends toward less clinically diagnosed VAP (26% vs. 45%, p=0.21) and microbiologically confirmed VAP (11% vs. 33%, p=0.08) were seen in the Lactobacillus group. No adverse events attributable to Lactobacillus administration were encountered.

CONCLUSION: Administration of the probiotic agent Lactobacillus GG to critically ill patients is safe and appears to favorably alter the microbiotic flora in this population.

CLINICAL IMPLICATIONS: Probiotic therapy may provide a novel, inexpensive, non-antibiotic opportunity for VAP prevention.

DISCLOSURE: Lee Morrow, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Lactobacillus GG administration; Other Lactobacillus GG and placebo capsules were generously provided by ConAgra Foods Inc.

Advances in Non-Pulmonary Thoracic Surgery
2:30 PM - 4:00 PM

ROBOTIC THORACIC SURGERY: WHERE WE STAND IN 2005

Robert C. Ashton MD* Cliff P. Connery MD Scott Belsley MD Charles Ro MD Sanju Balaram MD Joseph J. DeRose MD St Luke's Roosevelt Hospital, New York, NY

PURPOSE: Robotic thoracic surgery has slowly gained acceptance over the past 4 years. While a wide variety of case are able to be performed robotically, the advantages for each procedure has been questioned. The purpose of our review is to identify the lessons learned from our experience as we move forward to the future.

METHODS: A retrospective review of our prospective database was performed from Jan 2002 until May 2005. All thoracic robotic procedures were included. The robotic system used for all cases was the da Vinci Surgical System.

RESULTS: A total of 35 cases have been performed encompassing all areas of general thoracic surgery. No complications related to the robot occurred. One conversion occurred secondary to bleeding, which did not require a transfusion. Length of stay for each procedure was short as compared to open procedures for most procedures including: thymectomy, mediastinal mass resection and Heller myotomy.

CONCLUSION: Robotic thoracic procedures can be safely performed using the current robotic system. For various procedures including thymectomy /anterior mediastinal mass resections, Heller myotomy and brachytherapy, robotic assistance appears to offer advantages over open procedures at our institution. Necessary components that are needed to build a successful robotic program including dedicated OR personnel and a dedicated surgical team. Learning curves are yet to be defined; however they appear to be shorter as compared to standard laparoscopic and thoracoscopic procedures.

CLINICAL IMPLICATIONS: The future of robotic cardiothoracic surgery is dependent upon measuring objective outcomes in comparison to other minimally invasive procedures rather than open procedures. Learning curves and teaching protocols need to be defined and developed to ensure the continued growth and safety of robotic surgery.

Procedure	Cases	Conversion
Esophageal resection	11	0
Thymectomy	9	0
Heller myotomy	6	0
Mediastinal mass resection/biopsy	5	1
Brachytherapy	3	0
Lobectomy	1	0

DISCLOSURE: Robert Ashton, Consultant fee, speaker bureau, advisory committee, etc. Procotor for cases by members of the department.

APPLICATION OF ROBOTICS IN THE CHEST: INITIAL EXPERIENCE

Ramzi K. Deeik MD* Robert R. Klingman MD Queen of the Valley Hospital, Napa Medical Center, Napa, CA

PURPOSE: Robotic technology is the most advanced development of minimally invasive surgery that holds significant promise, but there are still some unresolved issues concerning its use in a clinical setting. Robotic surgical systems allow the surgeon to perform more complex maneuvers

Advances in Non-Pulmonary Thoracic Surgery, continued

with increased precision and accuracy. These systems are also costly to purchase and maintain and they provide the surgeon with essentially no tactile feedback. The purpose of this study was to demonstrate the efficacy and safety of using the da Vinci Robotic Surgical System to perform minimally invasive cardiothoracic procedures.

METHODS: Between October 2002 and May 2005, prospective data were maintained on 71 Robotic-assisted surgical procedures. Of the 71 procedures, 30 cardiothoracic minimally invasive robotic procedures were performed (18 men and 12 women). The average age was 64.5 years (range, 22-86 years). The cardiothoracic robotic surgical operations included Robotic-assisted minimal invasive direct coronary artery bypass (MIDCAB, n=12), epicardial lead placement (n=5), nissen fundoplication (n=5), esophagectomy (n=4), heller myotomy (n=1), thymectomy (n=1), posterior mediastinal/paravertebral mass resection (n=1) and pericardial window (n=1).

RESULTS: All procedures were completed successfully without conversion to open surgery. All Robotic-assisted MIDCAB patients had post-operative coronary angiogram and/or Computed Tomography angiogram to confirm LIMA-LAD patency. The postoperative mortality rate was zero. The morbidity rate was 13%. Complications included pulmonary embolus (n=1), pneumonia (n=1) and gastrostomy leak (n=1)which required a re-operation. The length of hospital stay ranged from 1 day to 29 days. 21 patients were discharged home within 36 hours.

CONCLUSION: Our preliminary experience suggests that Robotic-assisted cardiothoracic Surgery, although still in its infancy, is safe and feasible. However, the best indications still have to be defined. The cost-benefit ratio is being evaluated at our institution.

CLINICAL IMPLICATIONS: The da Vinci Robotic Surgical System is an important tool in the surgical armamentarium. It expands the application of minimally invasive cardiothoracic surgery by providing the tools necessary to perform delicate complex maneuvers through port incisions.

DISCLOSURE: Ramzi Deeik, None.

ADVANCES IN SURGICAL APPROACHES TO MEDIASTINAL MASSES: A THREE-YEAR EXPERIENCE

John N. Afthinos MD* Charles Y. Ro MD Cliff P. Connery MD Karen M. McGinnis MD Christopher W. Adams MD Maureen Reyes Other R. J. A. Nabong Other Joseph J. DeRose Jr. MD Robert C. Ashton Jr. MD St. Luke's-Roosevelt Hospital Center, New York, NY

PURPOSE: Mediastinal masses can be approached through a variety of surgical techniques, including sternotomy, thoracotomy, and thoracoscopy, depending on indication, location, and extent of disease. Our experience reflects the current advances in surgical techniques for diagnosis and treatment of mediastinal masses.

METHODS: A retrospective comparative study of the surgical approaches to anterior and posterior mediastinal mass resection was performed using our thoracic surgery database for patients treated between January 2002 and December 2004. Forty patients presented with anterior pathology (25 sternotomy, 3 thoracotomy, 9 robotic thoracoscopy, and 3 video-assisted thoracoscopy (VATS)). Eleven patients had posterior pathology (3 thoracotomy, 1 sternotomy, 1 transcervical approach, and 6 VATS). Data was analyzed with Mann-Whitney U-test, Student's T-test, and Chi-square.

RESULTS: Tissue of thymic origin (including thymoma, hyperplasia, and cysts) represented 80% (32/40) of anterior pathology. Schwannomas and neurofibromas represented 45% (5/11) and 27% (3/11), respectively, of posterior pathology. Patients who underwent minimally invasive approaches (VATS and robotic-assisted) for anterior mediastinal masses had shorter length of chest tube days and length of hospital stay (p=0.016 & p=0.002, respectively). Similarly, patients who underwent VATS for posterior mediastinal masses had shorter operative times, length of chest tube days, and length of hospital stay but no statistical significance was achieved. No significant difference in other patient demographics or immediate post-op and 30-day mortality was noted in either anterior or posterior groups.

CONCLUSION: Minimally invasive approaches offer advantages compared to traditional open resection in selected cases. A decision analysis for patients presenting with mediastinal masses needs to be made on an individual basis and is dependent upon, size of the mediastinal mass, body habitus, co-morbidities, and surgeon comfort with the approach.

CLINICAL IMPLICATIONS: Thoracic surgeons should be familiar with all surgical techniques especially thoracoscopic and robotic approaches for the management of mediastinal disease.

	Anterior Mediastinal Masses			Posterior Mediastinal Masses		
	OPEN N=28	VATS/ROBOT N=12	p	OPEN N=5	VATS N=6	p
# Pack-years	10.5	0.92	0.101	3.0	6.7	NS
OR time (min)	186	165	NS	245	205	NS
Chest tube (days)	2.5	1.7	0.016	3.0	2.5	NS
LOS (days)	6.1	3.4	0.002	7.0	3.8	0.157

DISCLOSURE: John Afthinos, None.

VIDEO-ASSISTED THYMECTOMY FOR MYASTHENIA GRAVIS

Erich Hecker MD* Klinikum Bremen-Ost, Bremen, Germany

PURPOSE: Thymectomy is an effective, but radical therapy for myasthenia. Traditionally, thymectomy for myasthenia gravis has been performed using either a transcervical approach or a median sternotomy. The excision of the thymic tissue by video-assisted thoracoscopic (VATS) surgery is less aggressive and recovery is faster. The aim of this study was to evaluate the usefulness and outcomes of VATS thymectomy for myasthenia gravis in a unit specializing in advanced VATS techniques.

METHODS: Over the past 2 years, we have performed 41 video-assisted thoracoscopic thymectomies on patients with myasthenia gravis at our unit. This study included 29 women and 12 men, with a mean age of 36.6 years (range, 18-55 years). Only left-side thoracoscopic surgery was performed, with a mean intervention time of 99 minutes (range, 72-122 minutes).

RESULTS: There was no perioperative mortality and all procedures were concluded successfully, with one patient requiring sternotomy in case of intraoperative bleeding. No patient required assisted ventilation postoperative and the maximum stay in intensive care was less than 24 hours. Postoperative there was no necessity for any surgical intervention. Mean time of hospital stay was 6.2 days (range, 5 -9). The clinical outcome was excellent in 25 cases (medical treatment no longer required), good in 10 (reduced medical treatment), and poor in 6 (no changes).

CONCLUSION: Video-assisted thoracoscopic thymectomy is effective in the treatment of myasthenia gravis and improves patient recovery. In addition, the excellent surgical view allows the thymectomy to be performed with absolute safety.

CLINICAL IMPLICATIONS: We recommend VATS-thymectomy in every case of myasthenia gravis without thymoma or paraneoplastic myasthenia .

DISCLOSURE: Erich Hecker, None.

MULTIDISCIPLINARY TREATMENT FOR ADVANCED INVASIVE THYMOMA WITH CISPLATIN, DOXORUBICIN, AND METHYLPREDNISOLONE

Kohei Yokoi MD* Haruhisa Matsuguma MD Rie Nakahara MD Tetsuro Kondo MD Yukari Kamiyama MD Kiyoshi Mori MD Nagoya Graduate School of Medicine, Nagoya, Japan

PURPOSE: Advanced thymomas (stage III with great vessel involvement and Stage IV) are not usually manageable by surgical resection and radiotherapy, and effectiveness of multimodality therapy including chemotherapy has been recently reported. However, the optimal treatment strategy has not been determined. We reviewed our experience with a multidisciplinary approach and evaluated the chemotherapy in the treatment of invasive thymoma.

METHODS: Seventeen patients were treated with multimodality therapy consisted of chemotherapy, surgery, and/or radiotherapy. Four patients had stage III disease with superior vena cava invasion, 9 had stage IVa disease, and 4 had stage IVb disease. The chemotherapy regimen

Advances in Non-Pulmonary Thoracic Surgery, continued

consisted of cisplatin (20 mg/m2/day on days 1 - 4), doxorubicin (40 mg/m2 on day 1), and methylprednisolone (1,000 mg/day on days 1- 4 and 500 mg/day on days 5, 6) (CAMP). Chemotherapy was administered in a neoadjuvant setting to the 14 patients and in an adjuvant setting to the remaining 3 patients with stage IVa disease. Surgical resection was intended in all patients. After those treatments, chemotherapy and/or radiation therapy were performed.

RESULTS: All but one of the 14 patients with induction chemotherapy had responded to the CAMP therapy, and the response rate (CR: 1, PR: 13) was 92.8%. One patient with MG, PRCA, and hypogammaglobulinemia died during the chemotherapy. Eight patients of them had a CR after surgical resection and chemoradiotherapy. All three patients treated with surgical resection followed by chemotherapy with or without radiotherapy achieved also a CR. Recurrences occurred in 6 patients, but 4 of them are now alive after re-treatment. The 10-year survival of all the patients was 80.7%, and 11 patients with a complete remission after the multidisciplinary treatment are all alive 9 to 193 months after initiation of the therapy.

CONCLUSION: The CAMP therapy was highly effective to invasive thymomas. The multidisciplinary treatment containing this chemotherapy is considered a justifiable treatment strategy for patients with advanced thymoma.

CLINICAL IMPLICATIONS: The high efficacy of chemotherapy will contribute to improve the outcomes of patients with unresectable invasive thymoma.

DISCLOSURE: Kohei Yokoi, None.

STERNAL NEOPLASMS: PROGNOSIS AFTER RESECTION AND REPAIR

Cosimo Lequaglie MD* Gabriella Giudice MD Centro di Riferimento Oncologico Basilicata, Rionero, Italy

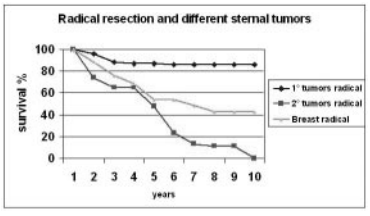
PURPOSE: To target the standard to sternal resections for cancer even in apparently extreme situations and to report the better treatment for the better prognosis.

METHODS: Our experience is 102 sternal tumor resections during last decade: 37 primary tumors, 31 local relapses or metastases from breast cancers, 19 other tumors and 15 radionecroses. There were 11 total sternectomies, 39 subtotal (>50%), and 52 partial (<50%). The procedure was associated to 70 rib resections, 16 of the clavicles, 26 of the lung, 20 of the pericardium. The breaches in the soft tissue and bone were repaired using: prosthetic materials covered by myocutaneous or muscle tissue in 64 patients, prosthetic material in 18, myocutaneous or muscle flaps in 5, and other in 15. A radical resection was in 92 cases and palliative in 10.

RESULTS: There were 2 peri-operative deaths, and 3 necroses of the flap. Sixty-two patients with radical surgery were alive and disease free at the end of the follow-up, 86% of survival in primary tumors, 11.6vs0% in secondary tumors and 42.7% in breast cancer relapses.

CONCLUSION: The treatment of sternal tumors by means of a broad sternal resection followed by a reconstruction based on the use of prosthetic materials is an efficacious and safe solution that improves the quality of life and makes it possible to perform curative broad radical resections in the case of primary tumors. Major en bloc resections can be performed with zero mortality, minimal morbidity and acceptable hospitalisation times provided that all of the steps are standardised. Resection offers a significant and permanent palliative solution in breast cancer relapse and radionecroses.

CLINICAL IMPLICATIONS: All patients with sternal neoplasms must be valued by oncologic surgeon not only by medical oncologic point of view.



DISCLOSURE: Cosimo Lequaglie, None.

Asthma Evaluation
2:30 PM - 4:00 PM

ROLE OF EXHALED NITRIC OXIDE AND SPIROMETRY IN PREDICTING ASTHMA EXACERBATIONS

Arthur F. Gelb MD* Colleen Flynn Taylor MA Chris M. Shinar PharmD Carlos Gutierrez MD Noe Zamel MD Lakewood Regional Medical Center, Lakewood, CA

PURPOSE: This study explores the complementary roles of spirometry and FENO to identify asthmatics at risk for exacerbations.

METHODS: We prospectively studied 44 nonsmoking asthmatics (24 F) age 51 ± 21 yr (mean ± SD), clinically stable for 6 weeks and on fluticasone 250/salmeterol 50 ug or equivalent for 3 years. Over the next 18 months we documented asthma exacerbations requiring ≥ 1 tapering course of corticosteroids. Total exhaled nitric oxide (FENO), small airway/alveolar nitric oxide (CANO), large airway nitric oxide flux (J'awNO) and spirometry were measured.

RESULTS: Baseline FEV1 was 2.1 ± 0.7L, 70 ± 20% predicted post 180 ug albuterol. When baseline FEV1 ≤ 76% predicted, exacerbations occurred in 20 of 30 (67%); whereas if > 76% predicted, only in 2 of 14 (14%), p = 0.003 chi-square. Using ROC curve for first exacerbation, with cutoff point of FEV1 76%, predicted the AUC = 67%, sensitivity = 0.91, specificity = 0.50, PPV = 0.65, NPV = 0.85, likelihood ratio = 1.8. When baseline FENO was abnormal (≥ 28 ppb), exacerbation occurred in 13 of 17 (76%); whereas when FENO < 28 ppb, in 9 of 27 (33%), p = 0.003 chi-square. Using ROC curve for first exacerbation, with cutoff point FENO = 28 ppb, the AUC = 71%, sensitivity = 0.59, specificity = 0.82, PPV = 0.77, NPV = 0.87, likelihood ratio = 3.3. Controlling baseline FEV1, an abnormal FENO increased the relative risk (RR) for exacerbation by 2.4 (95% CI, 1.1 - 4.5) Mantel-Haenszel, p = 0.011. Abnormal increase in CANO increased RR 3.0 (0.9 - 9.9) p = 0.036 and abnormal J'awNO increased RR 2.4 (1.0 - 5.6) p = 0.04. Controlling baseline FENO, FEV1 ≤ 76% predicted increased RR 1.7 (1.1-2.7) p = 0.02.

CONCLUSION: Baseline FENO ≥ 28 ppb and FEV1 ≤ 76% predicted identifies stable asthmatics at risk for exacerbations requiring ≥ 1 tapering course of corticosteroids over 18 months.

CLINICAL IMPLICATIONS: Asthma exacerbations can be more effectively predicted.

DISCLOSURE: Arthur Gelb, None.

GENE EXPRESSION AFTER ENDOBRONCHIAL INSTILLATION OF ENDOTOXIN (LPS) AND HOUSE DUST MITE ANTIGEN (HDM) IN ASTHMATIC AND NON-ASTHMATIC SUBJECTS

Jaspal Singh MD* John Tomfohr PhD John S. Sundy MD Catherine M. Foss RRT Erin McElvania-Tekippe BS David A. Schwartz MD Duke University Medical Center, Durham, NC

PURPOSE: Endotoxin (LPS) and house dust mite antigen (HDM) contribute to asthma development and are well-studied models of asthma pathogenesis. Though both LPS and HDM can induce asthmatic phenotypes in susceptible individuals, it is not clear as to what mechanisms are shared and which are different with these two agents. We believe that with simultaneous localized instillation of both agents we will gain insight into mechanisms of asthma development and pathogenesis.

METHODS: 11 atopic, mild asthmatic and 11 nonatopic, nonasthmatic adult subjects were identified by routine screening studies. Subjects underwent an initial bronchoscopy with instillation of saline, LPS, and house dust mite antigen (D farinae) in separate subsegmental bronchi. Four hours later, a repeat bronchoscopy with bronchoalveolar lavage (BAL) and endobronchial brush biopsy was performed in each subsegmental bronchus. Inflammatory and epithelial cells from these specimens were separated, RNA was extracted, and microarray analysis was performed using the Agilent whole human genome array.

RESULTS: After instillation of LPS, there was increased inflammatory cell gene expression in both asthmatics and control subjects. Specifically, genes involved with innate immunity and other mechanisms of cell injury were upregulated. In contrast, after instillation of HDM we found much less dramatic changes in gene expression. However, we noted that genes involved in the adaptive immune response were upregulated both in atopic and nonatopic individuals after instillation of HDM.

CONCLUSION: We demonstrate that asthmatics and control subjects have similar gene expression changes in inflammatory cells following LPS installation. The changes after instillation of HDM do not appear as robust, but those genes that are upregulated may lead to fundamental understanding of mechanisms of asthma development based on different environmental exposures.

Asthma Evaluation, continued

CLINICAL IMPLICATIONS: Asthma is a heterogeneous group of disorders with various inciting agents and a variety of responses to treatment. It is possible that gene expression technologies can serve as important clinical aides to phenotype patients with asthma and their response to treatment as well as lead to better understanding of the genetics of asthma susceptibility.

DISCLOSURE: Jaspal Singh, None.

EOSINOPHILIC INFLAMMATION AND BASEMENT MEMBRANE THICKNESS (BMT) IN ATOPIC AND IN GER-RELATED ASTHMA

Claudio Micheletto MB, BCh* Silvia Tognella MD Fiorenza Trevisan MD Marilia Visconti MD Roberto W. Dal Negro MD Lung Dept - Orlandi Hospital, Bussolengo, Italy

PURPOSE: The inflammatory and remodelling processes that underlie asthma result from a highly complex interaction between various cell types. Through the release of mediators, cytokines, chemokines and growth factors, epithelial and mesenchymal cells cause persistence of the inflammatory infiltrate and induce structural changes in the airway wall, such as increased thickness of the basement membrane, leading to a reduced baseline airway calibre and exaggerated airway narrowing. Aim of the study was to compare the BMT and the BAL eosinophil count in mild and moderate atopic asthma; in mild and moderate non-atopic GER-related asthma, never previously investigated to our knowledge.

METHODS: After their informed consent, 8 mild atopic asthmatics (MIAA, 32–63y, 4 m., FEV1 = 94.8% pred. ± 9.9sd), 8 moderate atopic asthmatics (MOAA, 30–64 y, 4 m., FEV1 = 68.6% pred. ± 8.8 sd), 8 non-atopic GER-related mild asthmatics (MIAGER, 24-64 y, 2 m, FEV1 = 96.2 % pred. ± 7.7sd), 7 non-atopic GER – related moderate asthmatics (MOAGER, 36–64y, 3 m., FEV1 = 66.6 % pred. ± 4.7 sd), non-smoker, underwent endobronchial biopsy and BAL for eosinophil count (EOS). BMT was expressed in mm, and EOS in % total cell count. Statistics: Wilcoxon test, $p < 0.05$ accepte.

RESULTS: Results (mean ± sd) in tab. 1.

CONCLUSION: 1) when GER-related, mild asthma seems characterized by a much smaller BMT than atopic asthma; 2) also eosinophilic inflammation proves lower in these circumstances; 3) in moderate-asthma, when eosonophilic inflammation is predominant, atopic and ger-related asthma the basement membrane thickness is similar.

CLINICAL IMPLICATIONS: Present data lead to suggests GER-related asthma as a peculiar nosologic entity in the earlier phase of the disease.

DISCLOSURE: Claudio Micheletto, None.

THE RELATIONSHIP BETWEEN ASTHMA AND RHINITIS/ RHINOSINUSITIS

Anne E. Dixon MD* David A. Kaminsky MD Janet T. Holbrook PhD Robert A. Wise MD David M. Shade Charles G. Irvin PhD University of Vermont, Burlington, VT

PURPOSE: Rhinitis and rhinosinusitis (R/RS) are frequently associated with asthma. Small cohort studies suggest that R/RS are associated with severe asthma, and can worsen asthma control. The purpose of the current study was to determine the impact of rhinitis and rhinosinusitis on disease in the lower airway in a large cohort of subjects with well-characterized asthma.

METHODS: We studied data from subjects enrolled in two trials of the American Lung Association-Asthma Clinical Research Centers ("SIIVA" and "LoDo"). At baseline subjects reported the presence of rhinitis or sinusitis, and had measures of lung function and asthma control.

RESULTS: Data were available on a total of 2031 subjects in SIIVA and 488 subjects in the LoDo. Over 70% of subjects reported rhinitis or sinusitis. Disease was more common in females (Adjusted OR 1.3, CI 1.05-1.61, SIIVA), those with gastro-esophageal reflux disease (Adjusted OR 1.81, CI 1.39-2.35, SIIVA) and less common in those of non-white race (Adjusted OR 0.82, CI 0.74-0.91, SIIVA). In LoDo asthma symptoms as measured by the Asthma Symptom Utility Index were slightly worse in subjects with R/RS (0.67 versus 0.73, $p=0.0008$). However, there was no difference in asthma severity as measured by lung function tests in LoDo subjects whereas SIIVA subjects with R/RS actually had higher baseline lung function than those without R/RS (FEV1 87.5% versus 84.0 % and FVC 91.8% versus 88.8% predicted, $p<0.05$).

CONCLUSION: Rhinitis and rhinosinusitis are common in asthma. They affect symptoms, but do not adversely affect lung function. Future studies evaluating the impact of treating upper airway disease in asthma should carefully evaluate symptoms using validated questionnaires.

CLINICAL IMPLICATIONS: Disease of the nose and sinuses is a frequent co-morbidity in subjects with asthma and may contribute to more severe symptoms, but does not adversely affect asthma severity as measured by lung function.

DISCLOSURE: Anne Dixon, None.

CHLAMYDIA PNEUMONIAE INFECTION AND POSSIBLE RELATIONSHIP TO ADULT ONSET ASTHMA

Amira F. Amer MD Malaka M. El Mofty MD Iman A. Hatata MD* Alexandria University Faculty of Medicine, Alexandria, Egypt

PURPOSE: The work entailed 40 patients with adult onset asthma divided into two matched groups, 20 patients with acute asthma exacerbation, and 20 patients with chronic stable asthma.

METHODS: Serum samples from from all studied patients were tested for the presence of C.pneumoniae specific antibodies (IgG,IgM)using enzyme linked immuonosorbent assay.Seropositive samples for IgG-were further examined with microimmunofluorescence(MIF)test for titration of IgG antibodies against c.pneumoniae.An IgG titer of ≥512 was inerperted as evidence of acute primary infection or re- infection,and IgG titer of 64-256 for chronic infection .Nasopharyngeal swab specimens for detection of c.pneumoniae by polymerase chain reaction assay,sputum culture and pulmonary function tests were also performed.

RESULTS: Seropositivity to c.pneumoniae specific IgG was found in 85% and in 80% of patients with acute exacerbation and chronic asthma respectively.In seropositive cases ,MIF test illustrated IgG titers consistent with acute infection in 8/17(47.1%)of cases with acute exacerbation versus 3/16(18.8%)with chronic asthma.IgG titers indicating chronic infection were detected in 9/17(52.9%)cases with acute exacerbation compared to 13/16(81.3%)with chronic stable asthma.The mean log titer of IgG was significanly higher in acute asthma than in chronic asthma.IgM could not be detected in any of the studied patients suggesting that acute infection was due to re-infection.PCR detected c.pneumoniae infection in 5 cases with acute exacerbation and had serological evidence of acute infection.All patients with acute infection showed severe airway obstruction.Significant inverse relationship was found between IgGtiterand indices of airway obstuction in both studied groups. Stepwise regression analysis revealed that IgG titer was mainly related to FEF 25-75%.

CONCLUSION: Re-infection and chronic infection with c.pneumoniae are common in adult onset asthma .C.pneumoniae could be a triggering factor for asthma exacerbation.The high IgG titeres of IgG antibody to C.pneumoniae and its strong relationship with the pulmonary physiological impairment in patients with acute and chronic asthma provide evidence that c.pneumoniae can play role in the immunopathogenesis and severity of asthma presentation.

CLINICAL IMPLICATIONS: Effort aiming at evaluating and eradicating infection with c.pneumoniae are recommended for proper asthma control.

DISCLOSURE: Iman Hatata, None.

PREVALENCE OF *MYCOPLASMA PNEUMONIAE* INFECTION IN ASTHMATIC ADULTS IN INDIA

Nazima Nisar PhD * Randeep Guleria MD Arvind K. Singh MD Tirlok C. Chawla PhD Niranjan Nayak MD Nihar R. Biswas MD Department of Ocular Pharmacology, Dr. R.P.Centre for Ophthalmic Sciences, All I, New Delhi, India

PURPOSE: Mycoplasma pneumoniae (M . pneumoniae), primarily recognized as a causative agent of community acquired pneumonia has recently been linked to asthma pathogenesis. The lack of awareness and appropriate diagnostic facilities handicap the current understanding of their true prevalence in asthma . Polymerase chain reaction (PCR) is emerging as one of the most accurate methods for the rapid identification of M. pneumoniae in asthmatics. The purpose of present study is to see the prevalence of M. pneumoniae in asthmatics using PCR , culture and serology.

METHODS: Seventy nine adults (Aged 15-58 years) with stable asthma and 20 age matched healthy controls without any respiratory illness were evaluated for the presence of M. pneumoniae infection. Throat swabs collected from both the groups were subjected to culture as well as PCR for P1/P-30 gene. Serum samples were analyzed for IgM and

Asthma Evaluation, continued

IgG antibodies to M. pneumoniae using gelatin particle agglutination test and enzyme linked immunosorbent assay respectively.

RESULTS: Seventeen (21.5%) asthmatics were found to be positive by PCR amplifying 153 bp and 825 bp fragments of P1 and P-30 genes respectively. Only 9 (11.4%) patients were positive for culture. High levels of IgG antibodies to M. pneumoniae were detected in the paired sera of 14 (17.7%)patients and 6 (7.6%) patients were positive for IgM antibodies. In normal controls, one sample was positive for only IgM antibodies at a titre of 1:80. This titre was taken as a cut off value while analyzing sera of patients with asthma.

CONCLUSION: This is the first report from India showing the presence of M. pneumoniae in a significant group of asthmatics. Carefully controlled prospective studies are warranted to confirm this association in asthma using highly sensitive techniques.

CLINICAL IMPLICATIONS: Given the possibility that M. pneumoniae is involved in the etiopathogenesis of asthma, treatment with antimicrobials active against M.pneumoniae in addition to standard therapy may help in better control of asthma.

DISCLOSURE: Nazima Nisar, None.

Community Acquired Pneumonia
2:30 PM - 4:00 PM

EFFICACY AND SAFETY OF 23-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE IN PREVENTION OF LOWER RESPIRATORY TRACT INFECTIONS IN THE CHINESE ELDERLY: A PROSPECTIVE CONCURRENT CONTROLLED TRIAL

Bi R. Dong PhD* Yin Xu MD Yan L. Zhang MD Ji R. Yue MD West China Hospital, Chengdu, Peoples Rep of China

PURPOSE: The aime of the study is to assess the efficacy, safety and cost-effectiveness of this vaccine in prevention of lower respiratory tract infections (LRTIs) in Chinese elderly.

METHODS: 600 subjects of 60 years old were divided into experimental and control groups(300 each group). Data on name, sex, age, smoking and exercise habits, monthly per capita income, living conditions, influenza vaccine status, immunoenhancers use and diseases – particularly LRTIs – 3 months prior to the study were collected for baseline comparison. During a 1-year follow-up period, both groups were observed for incidence and severity of LRTIs, hospitalization rates, length of hospital stay, antibiotic use and direct medical costs.

RESULTS: Overall, the vaccine reduced LRTIs, antibiotic use and hospitalization by 69.7%, 72.6% and 65.9%, respectively. Stratified analysis showed vaccine reduced the incidence and severity of LRTIs as well as rates of antibiotic use and hospitalization in subjects with COPD or CHD. In subjects who had diabetes mellitus, hypertension or were inoculated with the influenza vaccine, the vaccine was a protective factor in LRTIs and rate of antibiotic use, but reductions in hospitalization rates were not significant. The vaccine did not reduce the incidence and severity of LRTIs or the rates of antibiotic use and hospitalization in subjects classified as healthy. Side effects were noted in 91 subjects, including 80 with local reactions at the injection site, 9 with systemic reactions, and two with both local and systemic reactions. All adverse reactions were mild and resolved within 1 to 3 days by local stupe or rest.The benefit-cost ratio was 2.06, with a net benefit of ¥66,471.65.

CONCLUSION: 23-valent pneumococcal polysaccharide vaccination among the elderly community is effective in reducing the incidence and severity of LRTIs. It also decreases antibiotic use the frequency and duration of hospitalization.

CLINICAL IMPLICATIONS: The protective efficacy of this vaccine is particularly significant in patients with COPD and CHD and it is cost-effective and safe.

DISCLOSURE: Bi Dong, None.

IMPACT OF GUIDELINE-CONCORDANT ANTIBIOTIC THERAPY ON MORTALITY WITHIN 48 HOURS OF ADMISSION FOR PATIENTS HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

Eric Mortensen MD* Marcos Restrepo MD Antonio Anzueto MD Jacqueline Pugh MD South Texas Veterans Health Care System, San Antonio, TX

PURPOSE: National clinical practice guidelines have recommended specific empiric antimicrobial regimes for patients with community-acquired pneumonia (CAP). However, there is controversy over whether there are modifiable factors that may impact mortality during the first 48 hours after admission, and little evidence whether the use of guideline-concordant antimicrobials during this time may be beneficial. Our aim was to determine whether the use of guideline-concordant antibiotic therapy is associated with decreased mortality within the first 48 hours after admission for patients with CAP.

METHODS: Eligible patients were admitted with a diagnosis of CAP between 1/1/1999 and 12/1/2001 from two tertiary teaching hospitals, had a chest x-ray consistent with CAP, and had a primary or secondary ICD-9 diagnosis of pneumonia. Patients were excluded if they were "comfort measures only" or transferred from another acute care hospital. A propensity score was used to balance the covariates associated with the use of guideline-concordant antimicrobial therapy. A multivariable logistic regression model was used to assess the association between mortality within 48 hours, and the use of guideline-concordant antibiotic therapy, after adjusting for potential confounders including the propensity score and severity of illness.

RESULTS: Information was obtained on 787 patients with CAP. The median age was 60 years, 79% were male, and 20% were initially admitted to the ICU. At presentation 52% of subjects were low risk, 34% were moderate risk, and 14% were high risk. 20 patients died within the first 48 hours. After adjusting for potential confounders, the use of guideline-concordant antimicrobial therapy (odds ratio 0.37, 95% confidence interval 0.14-0.95) was significantly associated with decreased mortality at 48 hours.

CONCLUSION: Using initial empiric guideline-concordant antimicrobial therapy is associated with decreased mortality at 48 hours after admission.

CLINICAL IMPLICATIONS: Further research is needed to determine what are appropriate empiric antimicrobial therapies for patients with CAP.

DISCLOSURE: Eric Mortensen, None.

THE LONG-TERM IMPACT OF SEVERE ACUTE RESPIRATORY SYNDROME (SARS) ON PULMONARY FUNCTION, EXERCISE CAPACITY, AND QUALITY OF LIFE IN A COHORT OF SURVIVORS

David S. Hui MD* Fanny W. Ko MB, ChB Doris P. Chan BSc Joan P. Fok MB, ChB Michael C. Chan MB, BCh Kin W. To MB, BCh Joseph J. Sung MD Chinese Univ of HK, Shatin, Hong Kong PRC

PURPOSE: To examine pulmonary function, exercise capacity, and health-related quality of life (HRQoL) among SARS survivors.

METHODS: We evaluated survivors with confirmed SARS at the Prince of Wales Hospital, HK, at 3, 6, 12, and 18 months after symptom onset. Our assessment included: lung volume (TLC, VC, RV, FRC), spirometry (FVC, FEV1), diffusing capacity (DLCO), 6-minute walk distance (6MWD), and HRQoL by SF-36 questionnaire.

RESULTS: 86 patients completed the serial assessments. There were 27 males, 59 females, and half were healthcare workers with age 39.9(SD11.5) years and BMI 23.7(3.9) kg/m2. At 18 months, 8(9.3%), 3(3.5%), and 24 (27.9%) patients had FVC, TLC, and DLCO below 80% of predicted values respectively. The 6MWD at 18 months was 492.8(85.7)m, which was higher than at 3 months [452.9(80.7)m but not different from 12 months [494.8(85.4)m]. The 6MWD was lower than normal controls of the same age groups and there was impairment of HRQoL at 18 months. Patients who required ICU admission (n=20) showed lower % predicted DLCO than those who did not [78.1(21.1) vs 88.6(15.1), p=0.048] but there were no differences in 6MWD and health status.

CONCLUSION: Significant impairment in diffusing capacity was noted in 27.9% of survivors 18 months after illness onset. The exercise capacity and health status of SARS survivors was still remarkably lower than that of a normal population.

CLINICAL IMPLICATIONS: SARS causes significant long-term adverse impact on pulmonary function, exercise capacity, and quality of life among the survivors.

DISCLOSURE: David Hui, Grant monies (from sources other than industry) Research Fund for the Control of Infectious Diseases (Health, Welfare and Food Bureau, HKSAR).

Community Acquired Pneumonia, continued

FULMINANT COMMUNITY ACQUIRED *ACINETOBACTER BAUMANNII PNEUMONIA* AS A DISTINCT CLINICAL SYNDROME

Wah S. Leung MB, ChB* Chung M. Chu MBBS Veronica L. Chan MB, ChB Judy Y. Lam MBBS Pak L. Ho MD Department of Medicine, United Christian Hospital, Kowloon, Hong Kong PRC

PURPOSE: In previous uncontrolled studies, acinetobacter baumannii appears to be a rare but important cause of community acquired pneumonia (CAP-AB), that may run a fulminant course. We performed a retrospective study of CAP-AB to characterize its clinical course and outcome, by comparing it with a control group of patients with hospital acquired pneumonia caused by acinetobacter baumannii (HAP-AB).

METHODS: This is a retrospective case-control study comparing CAP-AB with HAP-AB between July 2000 and December 2003. Clinical, laboratory, radiological and microbiological data were analyzed.

RESULTS: There were 19 cases of CAP-AB (16 male and 3 female, mean age 72.6 ± 9.6 years) and 74 cases of HAP-AB during the 42-month study period. When compared to HAP-AB group, CAP-AB group has more ever smokers (84.3% vs. 55.4%, $p = 0.031$), more patients with COPD (63.2% vs. 29.7%, $p = 0.014$), and lower number of past hospitalization in the previous year (range: 0-0 vs. 0-6, $p = 0.049$). CAP-AB group had a higher prevalence of bacteremia (31.6% vs. 0%, $p < 0.001$). Strains causing HAP-AB were generally more resistant. There were higher frequencies of adult respiratory distress syndrome (ARDS) (84.2% vs. 17.6%, $p < 0.001$) and disseminated intravascular coagulation (DIC) (57.9% vs. 8.1%, $p < 0.001$) in the CAP-AB group. Moreover, the median survival was only 8 days in the CAP-AB group, versus 103 days in the HAP-AB ($p=0.0026$). Unexpectedly, early appropriate antibiotics in CAP-AB was not assoicated with better survival. Factors associated with higher mortality in the CAP-AB group included the presence of AB bacteremia ($p = 0.040$), platelet count < 120 x 10^9/L ($p = 0.026$), pH< 7.35 on presentation ($p = 0.047$) and presence of DIC ($p = 0.004$).

CONCLUSION: CAP-AB appears to be a distinct clinical entity with a high incidence of bacteremia, ARDS, DIC and death, when compared to HAP-AB. Early appropriate antibiotics in CAP-AB was not assoicated with better survival.

CLINICAL IMPLICATIONS: Further studies are needed to investigate the mechanism of the fulminant nature of CAP-AB.

DISCLOSURE: Wah Leung, None.

COMPARISON OF NATIONAL, REGIONAL, AND STATE SUSCEPTIBILITIES OF *STREPTOCOCCUS PNEUMONIAE* ISOLATES TO CLINDAMYCIN AND ERYTHROMYCIN: RESULTS OF THE ANTIMICROBIAL RESISTANCE MANAGEMENT (ARM) PROGRAM, 1997-2004

John G. Gums PharmD* University of Florida, Gainesville, FL

PURPOSE: The ARM Program, an ongoing project of the University of Florida, documents trends in antimicrobial susceptibility patterns in inpatient/outpatient isolates to track antibiotic resistance. To date, 358 institutions from 6 US geographic regions have been enrolled at no cost. Each provides a minimum of 3 years of antibiogram/sensitivity report data in a HIPAA-compliant non-identifying format. These data comprise a national aggregate database containing 28.3 million isolates, 250,423 of which are S pneumoniae.

METHODS: The database was interrogated to determine resistance patterns for S pneumoniae isolates against clindamycin and erythromycin as surrogate markers for macrolide resistance at the national, regional, and state level for data collected from 1997-2004. States were stratified in terms of resistance rates; only states with 5 or more institutions in the database were included.

RESULTS: Nationally, pneumococcal isolate susceptibility to clindamycin was 89% (range, 86.9% in Southwest to 91.4% in North Central). The 5 states with isolates most susceptible to clindamycin were Illinois (97.6%), Maryland (94.9%), Tennessee (93%), Arkansas (92.4%) and West Virginia (92%); the 5 states with isolates least susceptible to clindamycin were Virginia (87.9%), Georgia (86.5%), Alabama (83.9%), Florida (83.8%), and Nevada (76.9%). For erythromycin, national susceptibility was 67.8% (range, 62.1% in Southeast to 76.2% in Southwest). The 5 states with isolates most susceptible to erythromycin were Arizona (79.8%), Indiana (78.8%), Massachusetts (78.8%), Kansas (76.4%), and Pennsylvania (76.1%); the 5 states with isolates least susceptible to erythromycin were Virginia (62.7%), South Carolina (62.5%), Georgia (62.2%), Florida (60.5%), and West Virginia (57.9%). Virginia, Georgia, South Carolina, and Florida had low susceptibility to both erythromycin and clindamycin; West Virginia, Tennessee, Arkansas, South Carolina, and Virginia had the largest difference between clindamycin and erythromycin.

CONCLUSION: Susceptibility patterns for S pneumoniae isolates against clindamycin and erythromycin suggest the highest level of methylation-induced resistance (MLS-b) is in Nevada, while the highest level of efflux-mediated resistance (M-type) is in West Virginia.

CLINICAL IMPLICATIONS: Surveillance programs such as ARM provide the ability to track both frequency and severity of macrolide resistance.

DISCLOSURE: John Gums, None.

EVALUATION OF ICU ADMISSION CRITERIA FOR PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA: CURRENT PRACTICE SURVEY

Marcos I. Restrepo MD* Antonio Anzueto MD Eric M. Mortensen MD Jacqueline A. Pugh MD Mark L. Metersky MD Patricio Escalante MD Richard G. Wunderink MD Bonita T. Mangura MD on behalf Chest Infections Network VERDICT/STVHCS/UTHSCSA, San Antonio, TX

PURPOSE: Community acquired pneumonia (CAP) is a common problem in clinical practice. Different recommendations regarding who should be admitted to the intensive care unit (ICU) are found in CAP guidelines from various professional societies. Our specific aim was to describe how clinicians decide which CAP patients to admit to the ICU.

METHODS: Self-administered survey to assess physician preferences regarding admission to the ICU in patients with CAP. We generated items for this instrument by reviewing recent literature on criteria to admit CAP patients to the ICU. All items were reviewed by the Chest Infections Network Steering Committee. We asked whether the following criteria to make the admission decision: American Thoracic Society (ATS) 1993 and 2001, British Thoracic Society (BTS, CURB, CURB-65), Pneumonia severity index (PSI class IV and V), APACHE II or III and SAPS I or II. The survey was e-mailed to ACCP members (in Chest Infections and Critical Care networks) in 2004.

RESULTS: 393 questionnaires were returned. The most common criteria used to admit patients to the ICU were ATS 2001 (50%), APACHE II or III (28%) and PSI class V (27%). Responders were aware of ICU criteria (SAPS (74%), ATS 1993 (68%), and APACHE (67%)) but did not use it in clinical practice. However, responders were not aware and did not use the CURB (77%) or the CURB-65 (72%). Academic practitioners (n=182) used more often BTS criteria (63% vs. 51%; $p=0.04$), PSI Class IV (69% vs. 56%; $p=0.02$), and SAPS to admit patients to the ICU (87% vs. 71%; $p<0.01$) than non-academic practitioners (n=203). No other statistical significant differences were observed between groups.

CONCLUSION: Important differences were found in academic practitioners vs. non-academic practitioners regarding the criteria used to admit patients to the ICU with CAP.

CLINICAL IMPLICATIONS: There is a need for more unified and appropriate criteria to define which patients with CAP require admission to the ICU.

DISCLOSURE: Marcos Restrepo, None.

Critical Care Outcomes
2:30 PM - 4:00 PM

HEPCIDIN IS THE PRINCIPLE MEDIATOR OF ANEMIA OF INFLAMMATION

Seth Rivera MD* Tomas Ganz MD University of California Los Angeles, Studio City, CA

PURPOSE: Anemia of inflammation (AI, anemia of chronic disease) is a common occurrence in the ICU and in pulmonary inflammatory diseases. The principal finding of AI is decreased serum iron with preserved tissue stores. The iron regulatory hormone hepcidin is most likely the mediator of AI. Hepcidin blocks iron absorption, release of recycled iron from macrophages and mobilization of stored iron from liver. We sought to determine whether hepcidin recapitulates the acute

hypoferremia seen in anemia of inflammation and to determine the inflammatory mediators that regulate its expression.

METHODS: We have shown that IL-6 is necessary for the upregulation of hepcidin in acute sterile inflammation (Nemeth et al, JCI 2004). In this study, we created a model of infectious peritonitis in IL-6 deficient mice and WT controls. We treated primary human hepatocytes with various cytokines to further study the regulation of hepcidin. Finally, we injected hepcidin and inactive peptide into mice to test whether they cause hypoferremia.

RESULTS: Both WT and IL-6 knockouts increased hepcidin significantly and developed anemia but there was no difference between the two groups. In primary hepatocytes, TGFβ-1 induced hepcidin mRNA to a similar degree as IL-6 and the effect could not be blocked by the addition of anti-IL-6 antibody. IL-1 also induced hepcidin but this was IL-6-dependent since the anti-IL-6 antibody blocked the effect. IFN-gamma, BMP, and IL-10 did not affect hepcidin expression. A single IP dose of hepcidin and showed a dose-dependent fall in serum iron from 32 ± 8 μM in control mice to 6.4 ± 1.2 μM in mice injected with 50 μg hepcidin (Spearman R=-0.929, $p<0.001$). The effect was rapid, with maximal suppression achieved within 1 hour of hepcidin administration and lasting at least 48 hours.

CONCLUSION: This is the first evidence that hepcidin can directly cause the acute hypoferremia seen in AI. Hepcidin increase in inflammation is mediated by IL-6, but other cytokines, such as TGFβ, may be important during infection.

CLINICAL IMPLICATIONS: Targeting hepcidin may help prevent AI without interfering with important inflammatory regulators.

DISCLOSURE: Seth Rivera, None.

COMBATING "GRADE INFLATION" IN MEASURING RISK-ADJUSTED MORTALITY: UPDATED APACHE MORTALITY PREDICTIONS

Andrew A. Kramer PhD* Jack E. Zimmerman MD Douglas S. McNair MD Fern M. Malila MS Cerner Corporation, Vienna, VA

PURPOSE: Over time changes in medical practice and therapy can result in improvements in hospital mortality. This can lead to systematic overestimation of mortality by prognostic systems based on 10-20 year old outcome data. Upon subsequent evaluation most ICUs' performance will look good as the standardized mortality ratio (SMR) will be below 1.00, i.e. "grade inflation". The purpose of this study is to compare results from two earlier versions of the APACHE III hospital mortality equation with a newly remodeled APACHE IV hospital mortality equation in order to examine how the performance of predictive models can change over time.

METHODS: The APACHE III-h equation was based on outcomes from 16,662 patients admitted to ICUs during 1988-1989, and the APACHE III-i equation for 40,264 patients from 1993-1996. Each of these equations had good accuracy at the time of development. A new APACHE hospital mortality equation was built using patients admitted to an ICU during 2002 and 2003. The updated equation includes a new variable for patients who were sedated, adjusts for ventilation on ICU day 1, measures prior length of stay more accurately, and increases the number of disease groups from 94 to 116. The model was built on 66,270 patients and then validated on 44,288 patients.

RESULTS: The observed mortality was 13.51% and the predicted mortality was 13.55% yielding a standardized mortality ratio = 0.997 ($p=0.79$). The previous APACHE models when applied to the 2002-2003 data did not calibrate well. The predicted hospital mortality for version III-i was 14.64% for an SMR = 0.923 ($p<0.001$). Version III-h predicted hospital mortality to be 16.90% for an SMR = 0.799 ($p<0.001$). Thus, the older the model the worse its performance.

CONCLUSION: Prognostic models require repeated assessment and updating to adjust for changes in disease specific outcomes, to incorporate advances in statistical methods, and new knowledge about outcome prediction.

CLINICAL IMPLICATIONS: ICU performance comparisons using risk-adjusted hospital mortality should be based on models developed on contemporary data.

DISCLOSURE: Andrew Kramer, Shareholder Cerner Corporation stock.; Employee Cerner Corporation.

UTILIZATION OF A NURSE DIRECTED INSULIN DRIP PROTOCOL FOR TIGHT GLUCOSE CONTROL IN THE ICU

Thaddeus Golden MD Daniel Albrandt PharmD Melissa Means-Markwell MD Caitriona Buckley MD Tet Wei-Chan MD James Morton MD Tara Roque MD Thomas G. Rainey MD Leo C. Rotello MD* Suburban Hospital, Rockville, MD

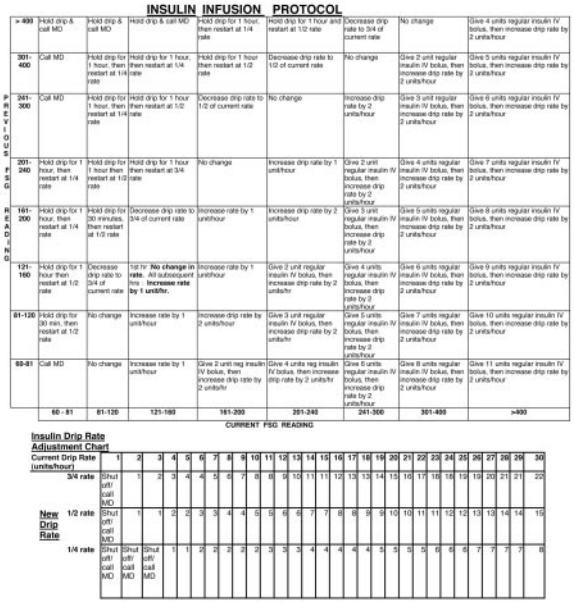
PURPOSE: Although tight glucose control in the ICU has been shown to significantly impact outcomes, it remains a labor intensive intervention to apply broadly. We developed a protocol which allows the nurse to control an insulin infusion to maintain tight glucose control with only minimal input from the physician.

METHODS: Our insulin drip protocol is included in Figure 1. The protocol is initiated when blood glucose measurements on a sliding scale insulin regimen were > 140 for 24 hours. The physician writes the order to initiate the insulin drip protocol and the starting infusion rate. The numbers on the left side of the chart refer to the previous glucose measurement; those on the bottom refer to the current reading. The nurse matches up previous reading with the current reading and follows the instructions in the table. Blood glucose is monitored Q1 hour for 4 hours, then Q2 hours thereafter if blood sugar stabilizes to less than 140. For any rate change, the blood glucose readings are rechecked Q1 hour x 2 hours and then resumed at Q2 hour checks.

RESULTS: From May 2004 to May 2005 94 patients were started on the protocol. The average time to achieve a blood glucose of < 140 was approximately 10 hours (r 5-21), with an average length of stay on the protocol of 3.4 days (r 5-21). 3(3.2%) patients developed hypoglycemia (blood glucose < 40). Blood glucose levels of < 140 were acheived in 95% of patients.

CONCLUSION: Our nurse directed insulin infusion protocol for the tight control of blood glucose in the ICU is a safe and effective means of achieving goal glucose levels in critically ill patients. Once stabilized the patient can have glucose monitoring as inferequently as every 2 hours which significantly decreases the workload on the bedside nurse.

CLINICAL IMPLICATIONS: Utilization of a nurse directed protocolized insulin infusion can afford safe and effective blood glucose control in the ICU without causing a significant increase in nursing workload.



DISCLOSURE: Leo Rotello, None.

Critical Care Outcomes, continued

POSTOPERATIVE INTENSIVE-CARE INTERVENTIONS IN PATIENTS UNDERGOING CAROTID ENDARTERECTOMY: A FIVE-YEAR RETROSPECTIVE ANALYSIS

Rim I. Atoui MD* Sanjeev Bansal MD Sergio Zanotti MD Cooper University Hospital, University of Medicine & Dentistry of New Jersey, Camden, NJ

PURPOSE: Routine intensive-care unit admission post-carotid endarterectomy (CEA) has been the standard of care in various institutions. In recent years the cost-effectiveness of this practice has come under question. the aim of this analysis was to study the need for intensive-care admission in the post-operative period of patients undergoing CEA, and to identify risk factors predictive of need for prolonged intensive-care intervention (> 12 hours).

METHODS: Retrospective analysis of clinical data from patients undergoing CEA at Cooper University Hospital during the time period of 1999-2004.Intensive-care interventions included: administration of vasoactive drugs, intravenous fluids for low blood pressure, myocardial ischemia, arrhythmia that required intravenous medication, congestive heart failure, need for re-operation for stroke or hematoma, administration of aggressive bronchodilator therapy, high-flow oxygen, and endotracheal intubation.

RESULTS: A total of 219 patients who underwent isolated CEA were studied. Mean age was 69.5 (±9.4) years, 61% of patients were male, and co morbidities included: hypertension 87%, cardiac disease 61%, and diabetes 31%. Of the total group 57.1% required some form of intensive-care intervention; and only 22.8% required an intensive-care intervention more than 12 hours after surgery. The most common intervention was the administration of vasoactive drugs for elevated blood pressure (81.6%). Preoperatively the presence of hypertension and diabetes were associated with the need for intensive-care intervention > 12 hours. Intraoperative characteristics such as type of anesthesia and length of surgery were not associated with increased need for intensive-care intervention > 12 hours. However, intraopretative administration of continuous vasoactive drugs was strongly associated with the need for intensive-care intervention > 12 hours ($p = 0.0001$).

CONCLUSION: Patients undergoing CEA frequently receive intensive-care interventions in the early post-operative period (<12 hours). Intraoperative use of vasoactive drugs is a strong predictor of need for prolonged intensive-care intervention (> 12 hours).

CLINICAL IMPLICATIONS: Patients undergoing CEA require short term monitoring in an intensive-care setting.the intraoperative use of vasoactive drugs predict the need for a prolonged intensive-care intervention.

DISCLOSURE: Rim Atoui, None.

COAGULATION STATUS AND RESPONSE TO TIFACOGIN IN COMMUNITY-ACQUIRED PNEUMONIA

Richard G. Wunderink MD* Lona Poole MD Fang Xie PhD Pierre-Francois Laterre MD Steven Opal MD Northwestern University Feinberg School of Medicine, Chicago, IL

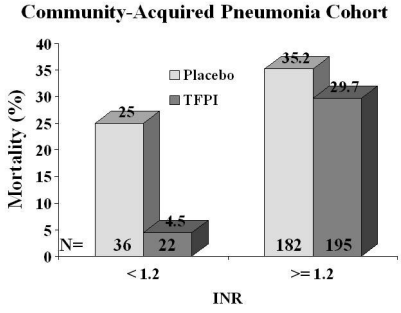
PURPOSE: Phase II trials of tifacogin (rTFPI) had suggested greater efficacy in severe sepsis patients with evidence of coagulopathy, as suggested by an abnormal International Normalized Ratio (INR) test. This subset of patients was therefore the primary study group of the subsequent multicenter Phase III trial of rTFPI in severe sepsis. A concurrent, separately randomized substudy of patients with INR < 1.2 was also completed. While the overall study did not demonstrate efficacy for rTFPI in the primary study group, subgroup analysis identified patients with community-acquired pneumonia (CAP) as having a favorable response to rTFPI. We therefore examined the CAP subgroups in both the primary (elevated INR) and secondary (normal INR) study cohorts to determine if the response to rTFPI was affected by coagulation status.

METHODS: Cases of CAP were extracted from the closed and locked clinical database from the Phase III trial. CAP patients were defined as those with pneumonia as the source of infection and start of study drug infusion was < 48 hours after hospital admission.

RESULTS: 58 of 201 patients in the secondary cohort had CAP (36 placebo, 22 rTFPI) while 377 or 1754 in the primary cohort had CAP (182 placebo, 195 rTFPI). While baseline INR did correlate with mortality (placebo low INR 22.9% vs. high INR 33.9%), no favorable response to rTFPI was seen in the primary cohort(placebo 33.9% vs. rTFPI 34.2%) while a positive response to rTFPI was seen in the secondary cohort (placebo 22.9% vs. rTFPI 12%, $p = 0.051$). In the CAP subgroups from both (Figure), the baseline INR did not distinguish between patients regarding respond to rTFPI.

CONCLUSION: Coagulation status, as determined by an elevated admission INR, does not determine responsiveness to rTFPI in patients with severe CAP.

CLINICAL IMPLICATIONS: Exclusion of patients based on normal INR is not needed for the Phase III trial of rTFPI in severe CAP. INR is an inadequate marker to select patients for immunomodulatory therapy directed at the coagulation system.



DISCLOSURE: Richard Wunderink, University grant monies Clinical Research grant for Phase III trial for Drs. Wunderink, Opal, Laterre; Employee Drs. Poole and Xie; Consultant fee, speaker bureau, advisory committee, etc. Drs. Wunderink, Opal, Laterre.

COMPARISON OF DEPTH OF SEDATION MEASURED BY PSA 4000 AND RICHMOND AGITATION-SEDATION SCALE (RASS)

Curtis N. Sessler MD* Marin Kollef MD Anne Hamilton RN Mary Jo Grap PhD Deborah Jefferson RN Virginia Commonwealth University, Richmond, VA

PURPOSE: To investigate the relationship between electroencephalogram (EEG)-based Patient State Index (PSI) (a computed EEG variable using the PSA 4000 device (Physiometrix)) with the sedation or agitation level subjectively measured by Richmond Agitation-Sedation Scale (RASS) score in intubated and mechanically ventilated medical ICU patients.

METHODS: After obtaining informed consent, PSI was measured continuously for up to 8hrs. RASS testing was performed at 2 hr intervals. PSI readings, obtained 5 minutes before, and immediately prior to RASS testing were documented for correlation with RASS (Pearson Correlation Coefficient). The distribution of PSI values for three clinically relevant RASS categories: A. 0 to +2 (alert, restless, or agitated); B. -1 to -3 (drowsy, light sedation, moderate sedation); C. -4 and -5 (deep sedation, unarousable) was also determined (ANOVA).

RESULTS: Patients (n=20; 40% male; age 52 +17 years; APACHE II 27.5 + 6.5) underwent RASS testing on 78 occasions. Mean (+SD) RASS was -2.86 + 2.08, range = -5 to +2. PSI 5 minutes before RASS (66.1+19.8, range 13 to 99) and PSI immediately prior to RASS (66.7+20.1, range 12 to 99) were similar, and both correlated highly with RASS ($r = 0.539$, $p < .0001$, and $r = 0.562$, $p < .0001$, respectively). ANOVA revealed significant differences in PSI scores among clinical RASS categories at both time periods (both: n=78; $p<0.0001$). PSI values (mean, 95% confidence interval) are displayed for RASS categories in the Table.

CONCLUSION: The significant associations between PSI and RASS support the validity of the PSA 4000 as a tool to monitor the level of sedation in the ICU.

CLINICAL IMPLICATIONS: Additional research in larger populations and relevant subgroups, including further investigation of PSA 4000 as a clinical tool for sedation management, will further define its role in intensive care.

PSI immediately prior to RASS

RASS Category	n	Mean PSI	95% Confidence Intervals
A (alert/agitated)	13	82.3	73.1/91.6
B (mild-moderate sedation)	26	73.9	68.9/78.8
C (deep sedation)	39	56.8	50.1/63.5

DISCLOSURE: Curtis Sessler, Grant monies (from industry related sources) Physiometrix, Baxter.

Cystic Fibrosis and Bronchiectasis
2:30 PM - 4:00 PM

INCIDENCE AND RISK FACTORS FOR MULTIPLE ANTIBIOTIC RESISTANT PSEUDOMONAS AERUGINOSA (MARPA) IN CYSTIC FIBROSIS

Christian A. Merlo MD* Michael P. Boyle MD Marie Diener-West PhD Noah Lechtzin MD The Johns Hopkins University School of Medicine, Baltimore, MD

PURPOSE: Pseudomonas aeruginosa is the most common infection in patients with cystic fibrosis (CF). Over time these bacteria become resistant to multiple classes of antibiotics. There is concern that multiple antibiotic resistant Pseudomonas aeruginosa (MARPA) may be associated with worse clinical outcomes in CF. However, very little is known about the incidence and risk factors for MARPA. The purpose of this study is to estimate the incidence of MARPA and understand the risk factors that may be associated with developing resistance.

METHODS: Cohort study of patients followed in the US CF Foundation Patient Registry from 1998 through 2002. Individuals were included if they were 6 years of age or older and if they were culture negative for Pseudomonas during the first 90 days of enrollment. MARPA was defined as any strain of Pseudomonas resistant to at least two of the following antibiotics: tobramycin, ciprofloxacin, and/or meropenem.

RESULTS: 4,458 patients developed infection with Pseudomonas and were included in the study. Mean age for the cohort was 15.7 years (range: 6-61.8) with a mean follow-up time of 1545.2 days (range: 7-1821). A total of 638 patients developed MARPA during the study period. The overall incidence of MARPA among CF individuals infected with Pseudomonas was 393.8 cases/1000 patients per year. In multivariable analyses using Cox proportional hazards models after adjusting for important physiologic and clinical confounders, higher baseline FEV1 was associated with a decreased risk of developing MARPA (HR: 0.68; 95%CI: 0.58-0.80). Diabetes (HR: 1.54; 95%CI: 1.21-1.97), inhaled tobramycin usage (HR: 1.41; 95%CI: 1.17-1.71), greater than 5 acute exacerbations/year (HR: 4.69; 95%CI: 3.20-6.87), and being cared for by a CF center in the top quartile for MARPA prevalence (HR: 3.79; 95%CI: 2.76-5.21) independently increased the risk of developing MARPA.

CONCLUSION: Resistant Pseudomonas is common among patients with CF. Diabetes, inhaled tobramycin usage, and frequent acute exacerbations increase risk of developing resistance.

CLINICAL IMPLICATIONS: Identification of potentially modifiable risk factors for MARPA may help to decrease the incidence of resistant Pseudomonas among patients with CF.

DISCLOSURE: Christian Merlo, None.

AN AIRWAY SPECIFIC ANTIBACTERIAL PROTEIN THAT IS OVER-EXPRESSED IN CYSTIC FIBROSIS

Lina Lukinskiene MS Joseph Pilewski MD Y.P. Peter Di PhD* University of Pittsburgh, Pittsburgh, PA

PURPOSE: To characterize the antimicrobial function of an airway specific gene, spurt, which is induced by retinoic acid and to examine the levels of expression and secretion of spurt in Cystic Fibrosis patients.

METHODS: Antibacterial activity was evaluated by colony formation units (CFU) against gram negative P. aeruginosa (PAO1). Cell culture supernatant from CMV-spurt stably transfected airway cells, BAL from CCSP-spurttg transgenic mice, and specific peptides from SPURT were used to compare with their respective controls for CFU counts. Western blotting analysis, immunohistological staining, real time PCR, and ELISA were used to examine levels of secretion, gene and protein expression.

RESULTS: Higher antibacterial activity against P. aeruginosa using cell culture supernatant from CMV-spurt stably transfected spurt-overexpressing cells than those from wildtype and CMV vector control cells. BAL fluid from unchallenged CCSP-spurttg mice that overexpress SPURT (spurt protein) exhibited enhanced antibacterial activity than control group using BAL from wildtype mice. Lower numbers of CFUs in CCSP-spurttg transgenic mice than wildtype littermates were also observed in both 4h and 24h after both groups of mice were challenged with aerosolized P. aeruginosa infection. We also identified a region within SPURT peptide sequence that effectively killed P. aeruginosa at ng concentration range. Furthermore, we observed significant higher gene and protein expression levels of spurt in tissues and epithelial cell cultures originated from Cystic Fibrosis (CF) patients. The secretion of spurt was also consistently higher in BAL samples from CF patients and in apical cell culture supernatants.

CONCLUSION: SPURT is a novel BPI-like antibacterial protein that may play a critical role in airway specific innate immunity and the significant higher expression and secretion in CF epithelium may represent a response of airway epithelial cells to colonized and increased bacteria exist in CF patients.

CLINICAL IMPLICATIONS: Functional role of spurt may associate with pathogenesis of lung diseases such as cystic fibrosis. Aerosolized SPURT may be used to enhance airway specific antibacterial activity.

DISCLOSURE: Y.P. Peter Di, None.

BURKHOLDERIA GLADIOLI: FIVE YEAR EXPERIENCE IN A CYSTIC FIBROSIS REFERRAL AND LUNG TRANSPLANTATION CENTER

Marcus P. Kennedy MD* Raymond D. Coakley MD Scott H. Donaldson MD Robert M. Aris MD Kathy Hohneker RN Eric L. Olson MD Isabelle P. Neuringer MD Peter H. Gilligan PhD Michael R. Knowles MD James R. Yankaskas MD University of North Carolina, Chapel Hill, NC

PURPOSE: There is a paucity of information available about the prevalence and clinical relevance of disease related to Burkholderia gladioli, a gram-negative organism identified in at risk patient populations including patients with cystic fibrosis (CF) and other chronic airway diseases and immunosuppressed patients.

METHODS: A retrospective review was performed using patient medical records for all patients who had one or more positive B. gladioli cultures from any organ, at UNC hospital between September 1999 and September 2004. Medical records of all cases were reviewed and data recorded about age, sex, ethnicity, comorbidities, pulmonary function tests, frequency of positive cultures, length of follow-up, sensitivity testing, other organisms cultured, and evidence of complications including mortality and inpatient therapy. FEV1 in CF patients age 10-30 was compared to the national median FEV1 for age.

RESULTS: A total of 26 patients had cultures (all respiratory) that grew B. gladioli including 24 CF patients (sputum positive prevalence of 3.6%), one patient with primary ciliary dyskinesia and one trauma patient on mechanical ventilation. Lung disease in CF patients was variable as reflected by FEV1 in comparison to the national median FEV1 for age. Repeat sputum cultures were available in 19/21 CF patients who were not transplanted of which 6 were continuously culture positive (32%) and 13 (68%) cultured positive on one (n=9) or more occasion with subsequent negative cultures. 22/24 CF patients had mycobacterial cultures (n=15≥2 cultures) and all were negative (expected prevalence=15-20% [Oliver et al AJRCCM 167, 2003]). Three CF patients cultured positive for B. gladioli pre and post bilateral lung transplantation, two with no complication and one complicated by a mediastinal abscess secondary to B. gladioli treated successfully with combined medical and surgical intervention. 48% of isolates were generally susceptible to TMP/SMX, ciprofloxacin, aminoglycosides, carbapenem, anti-pseudomonal penicillens and cephalosporins.

CONCLUSION: The majority of patients' culture positive for B. gladioli at our center have CF with variable severity of pulmonary disease.

CLINICAL IMPLICATIONS: B. gladioli infection does not appear to contraindicate lung transplantation.

DISCLOSURE: Marcus Kennedy, None.

Cystic Fibrosis and Bronchiectasis, continued

CORRELATION OF CHEST XRAY FINDINGS, SEX, AND GENOTYPE IN ADULT CYSTIC FIBROSIS PATIENTS: PRELIMINARY SINGLE CENTER REVIEW

Vaidehi Kaza MD* Marcia Katz MD Baylor College of Medicine, Houston, TX

PURPOSE: Striking differences in the radiological patterns in patients with cystic fibrosis (CF)are seen. CT scans have been correlated with spirometry and mortality. Chest Xrays(CXR) are usually the first and commonest method of following these patients. CXR patterns have not been correlated with genotype, sex, age or outcome. CXRs on 110 adult CF patients at a single center were reviewed and the pattern of CF changes were correlated with these demographics. We present the preliminary data on the first 36 patients.

METHODS: Three independent reviewers graded CXRs as having one of the following patterns: diffuse bilateral(DB), unilateral, upper lobe(UL-)vs.lower lobe predominant disease or normal. When the reviewers disagreed the CXR was assigned to the DB category. Genotyping was done at a central CF reference laboratory. These data was then compared to genotype, sex, age. Age and genotype, and sex (male[M], female [F]) vs. genotype were compared.

RESULTS: The most common radiological appearances were of DB(58%)and UL(31%)of cases. The commonest genotype was homozygous for δF508 (64%)[2F508]; 8 patients (22%)were heterozygous for F508 with an unidentified second allele(F508/No ID). The other radiological patterns and genotypes were infrequently seen. No association was seen between genotype and CXR pattern. 74% M vs. 53% F expressed the 2F508 gene. Pts. less than 30 yrs old more commonly expressed the 2F508 gene than those 30 and over [75% vs. 50%]. DB pattern was more commonly seen in F(70%) vs. M (47%). UL was seen predominantly in M(42%) vs. only 18% of F.

CONCLUSION: In this small preliminary evaluation of CF patients, genotype does not appear to predict radiological disease pattern. However UL and DB disease are associated with M and F sex respectively. Interestingly the 2F508 genotype is less predominant in the older pts. suggesting a possible negative survival impact.

CLINICAL IMPLICATIONS: Chest Xrays pattern though inexpensive and simple to obtain and assess may prove a useful adjunct in risk assessment particularly when combined with age and sex in evaluation and management of CF patients.

DISCLOSURE: Vaidehi Kaza, None.

LITHOPTYSIS AND PULMONARY CALCIFICATION IN PRIMARY CILIARY DYSKINESIA

Marcus P. Kennedy MD* Peadar G. Noone MD Paul L. Molina MD Andy J. Ghio MD John L. Carson PhD Maimoona Zariwala PhD Susan L. Minnix RN Michael R. Knowles MD Unviersity of North Carolina, Chapel Hill, NC

PURPOSE: Primary ciliary dyskinesia (PCD) is characterized by sino-pulmonary disease associated with abnormal ciliary structure and function leading to defective airway host defense. It is an autosomal recessive trait with a prevalence of ~1/12000-1/17000 [Noone et al. AJRCCM 169, 2004]. Broncholiths (stones in the bronchial lumen) and intraluminal calcification have been previously reported in idiopathic bronchiectasis [Hirashima et al. Nihon Kyobu 31, 1993]. After identifying two adult PCD patients (ages 60 and 65) with lithoptysis (expectoration of a stone) and pulmonary calcification, we tested the hypothesis that lithoptysis related to pulmonary calcification is associated with PCD.

METHODS: From our total population of 128 PCD patients, we reviewed the histories and questioned 20 contactable patients of 27 age>40. If a history of lithoptysis was reported, radiographic, microbiologic and laboratory data were reviewed. In one patient, broncholiths were examined by routine and electron microscopy. Electron dispersive X-ray analysis (EDXA) was performed and stones were decalcified and stained for fungi. Chest CT scans were reviewed for calcification in 31 PCD patients, including 12 patients age>40.

RESULTS: 5/20 (25%) PCD patients age>40 reported lithoptysis. Chest CT scans in 3/4 of these patients displayed intraluminal and peribronchial calcification without mediastinal nodal or abdominal calcification. Chest CT is pending in the 5th patient. Two other PCD patients were identified with intraluminal and peribronchial calcification without a history of lithoptysis. Broncholiths were composed of calcium carbonate (calcite) without evidence of positive staining for fungi in one patient. Sputum culture and history was negative for mycobacterial and fungal infection and positive for P. aeruginosa in all 7 patients (n=5 mucoid).

CONCLUSION: There is an association between lithoptysis and pulmonary calcification without nodal calcification in PCD that has not been previously reported.

CLINICAL IMPLICATIONS: We hypothesize that the formation of calcium stones in PCD is a biomineralization response to chronic airway inflammation and retention of infected airway secretions.

DISCLOSURE: Marcus Kennedy, None.

ASSOCIATION BETWEEN RISK OF ACUTE EXACERBATIONS AND AGE IN PATIENTS WITH BRONCHIECTASIS

Derek Weycker PhD* John Edelsberg MD Gerry Oster PhD Gregory Tino MD Policy Analysis Inc. (PAI), Brookline, MA

PURPOSE: Advanced age is widely believed to be a risk factor for acute exacerbations in patients with bronchiectasis. However, few data exist supporting this association.

METHODS: Data were obtained from a medical claims database containing information from >30 US health plans with a combined membership of >10 million lives annually. Study subjects consisted of all patients aged ≥18 years with diagnoses of bronchiectasis between July 1998 and June 2002 and continuous medical coverage between July 2002 and June 2003 ("follow-up"); patients with cystic fibrosis were excluded. Study subjects were stratified based on age (<65 vs ≥65 years). Acute exacerbations were defined to consist of respiratory hospitalizations and respiratory-related outpatient encounters with subsequent receipt of antibiotic therapy, and were identified during the one-year period of follow-up. Bivariate analyses were undertaken to examine the relationship between risk of acute exacerbations and age; statistical comparisons were performed using a chi-square test.

RESULTS: A total of 667 persons were identified who met study entrance criteria (age <65 years, n= 490; age ≥65 years, n=177). Mean (±SD) age among those <65 years was 52 (±10); among those ≥65 years, it was 76 (±8). During the one-year follow-up period, the percentage of patients experiencing one or more acute exacerbations did not differ by age (32.9% for age <65 years vs. 32.8% for age ≥65 years, p=0.98). The risks of respiratory hospitalization (9.2% vs. 10.7% respectively, p=0.55) and respiratory-related outpatient encounters with subsequent receipt of antibiotic therapy (29.2% vs. 27.1%, p=0.60) also did not differ across age groups.

CONCLUSION: Risk of acute exacerbations among patients with bronchiectasis does not differ by age.

CLINICAL IMPLICATIONS: Our study suggests that age is not important in predicting the risk of acute exacerbations in patients with bronchiectasis.

DISCLOSURE: Derek Weycker, Grant monies (from industry related sources) Funding for this research was provided by Chiron BioPharmaceuticals to Policy Analysis Inc. (PAI), an independent contract research organization.

Lung Cancer: From the Bench to the Bedside
2:30 PM - 4:00 PM

SUCCESS OF BRONCHOSCOPICALLY EXTRACTED SMALL CELL LUNG CANCER (SCLC) SAMPLE IN ESTABLISHING PRIMARY SCLC XENOGRAFTS: A PRECLINICAL AERODIGESTIVE CANCER MODEL TO ESTABLISH BIOMARKER PROFILE AND RESPONSE TO NOVEL THERAPIES

Rex C. Yung MD* David N. Watkins MD Vincent C. Daniel MD Eric Syphard BA Gregory S. Gessel Stephen Ames BA Ed Gabrielson MD Paul Flint MD David Berman MD Malcolm V. Brock MD Craig D. Peacock Johns Hopkins University, Baltimore, MD

PURPOSE: For the study of translational tumor biology, human lung cancer cell lines are convenient but limited models as they don't reproduce the three-dimensional cellular interactions of tumors in-vivo. Recent studies suggest the utility of primary human cancer xenografts as better models for cancer biology and therapeutics. Examples include

Lung Cancer: From the Bench to the Bedside, continued

demonstration of genetic changes such as EGFR amplification in primary brain tumors that are maintained in xenograft tumors but not in tissue cultures (Pandita, 2004); at our institution, primary pancreatic cancer xenograft lines can model preclinical responses to Hedgehog pathway inhibitors (Berman, 2004). Such xenografts usually require surgically resected samples, unlikely situation for Small Cell Lung Cancers (SCLC). We are reporting on what we believe are the first series of human SCLC xenografts grown from bronchoscopically retrieved samples, their biologic properties and preliminary translational studies.

METHODS: Suspected cases of primary SCLC are confirmed by specific stains. Samples are collected either by Trans Bronchial Needle Aspiration (TBNA) of mediastinal lymph nodes or tumor masses or endobronchial tumors. In two cases, visible exophytic tumor cells are collected by physical debulking with forceps or mechanical microdebrider. Tumor cells are collected by collagenase disaggretion and subsequently injected with MatrigelTM subcutaneously into NOD/SCID mice. Subcutaneous tumors are passed into subsequent mice, or cryo-preserved and reinjected multiple times.

RESULTS: All five xenograft tumor cell lines show classic SCLC histology and immunohistochemical staining. Three of five subcutaneously injected tumors demonstrate organ trophism by growing as large mediastinal masses without detectable extrathoracic disease. Preliminary studies demonstrate biomarker expression of the Sonic Hedgehog pathway.

CONCLUSION: Bronchoscopically obtained samples from SCLC are successfully cultured as tumor xenografts that demonstrate typical SCLC characteristics and surprising organ trophism. These xenograft lines represent a novel and more accurate preclinical model of SCLC.

CLINICAL IMPLICATIONS: Viable SCLC xenograft models will provide mechanisms for validating SCLC biomakers, and direct pathways towards logical design and testing of targeted therapies. It may be useful as test systems of novel combination therapies, and has potential for SCLC tumor-specific vaccine development.

DISCLOSURE: Rex Yung, None.

ROLE OF STAT1 IN THE PERMISSIVE EFFECT OF INTERFERON-GAMMA ON FAS-INDUCED APOPTOSIS OF NON-SMALL CELL LUNG CANCER CELLS

J. R. Brewer BA Christopher Spradley MD* Jeremy L. Nickolai BS Richard E. Winn MD George W. Booz PhD Scott & White Hospital and Clinic, Temple, TX

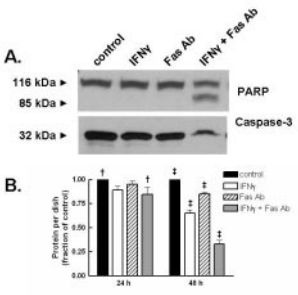
PURPOSE: One of the most lethal cancers is non-small cell lung carcinoma (NSCLC), which is resistant to chemotherapy- and irradiation-induced programmed cell death or apoptosis. Our objective is to define processes in NSCLC opposing apoptosis. Previously, we showed IFNγ potently inhibits proliferation of human NSCLC A549 cells under optimal growth conditions by a process involving transcription factor STAT1. Here we investigated whether IFNγ made A549 cells susceptible to activation of the death receptor FAS.

METHODS: A549 cells grown with 10% serum were treated as follows: vehicle, 10 ng/ml IFNγ, 70 ng/ml activating FAS antibody, or 10 ng/ml IFNγ and 70 ng/ml FAS antibody. After 48 h, apoptosis was measured by DNA laddering, annexin V binding, and Western immunoblotting for PARP and caspase 3 cleavage. FAS was measured by Westerns, protein by BioRad DC assay. Cells were transfected with siRNA STAT1 using lipofectamine. Statistical significance ($P < 0.05$) was determined by ANOVA.

RESULTS: IFNγ did not induce apoptosis of A549 cells as indexed by PARP or caspase 3 cleavage, DNA laddering, or annexin V binding. Neither did the agonistic anti-FAS antibody. However, together, they induced marked apoptosis as indexed by all 4 assays and loss of protein from culture dishes. The permissive effect of IFNγ on FAS-induced apoptosis was not due to upregulation of FAS, as A549 cells expressed FAS and its expression was not affected by IFNγ. To assess the role of STAT1, cells were transfected with STAT1 siRNA or lipofectamine alone (control) prior to treatment. Although STAT1 expression was downregulated with siRNA, PARP and caspase 3 cleavage were still observed with the combination of IFNγ and FAS antibody.

CONCLUSION: IFNγ plays a permissive role in FAS-mediated apoptosis of NSCLC A549 cells by a process downstream of FAS and independent of STAT1. Further studies are underway to determine which STAT1-independent mechanism sensitizes A549 cells to apoptosis.

CLINICAL IMPLICATIONS: The combination of IFNγ and activating FAS antibody could be a novel therapeutic strategy in the treatment of non-small cell lung cancer.



DISCLOSURE: Christopher Spradley, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. The combination of IFNγ and activating FAS antibody in the treatment of non-small cell lung cancer.

CAN EARLY LUNG CANCER BE DETECTED FROM BUCCAL MUCOSA SCRAPINGS?

Roger A. Kemp PhD* Bojana Turic MD Perceptronix Medical Inc., Vancouver, BC, Canada

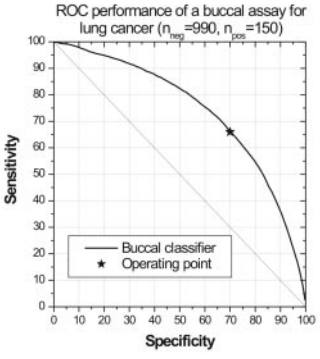
PURPOSE: We have studied whether it is possible to detect lung cancer in high risk patients using information that is present in the buccal mucosa. The goal is to create a simple, inexpensive test—an assay that could be used by GPs and dentists to screen for lung cancer. Recent studies have shown that normal appearing buccal mucosa can be analyzed to predict the presence of not only adjacent oral malignancies but also of distant tumors as well. We believe this effect extends to the lung.

METHODS: We have developed an automated system for cytometry of quantitatively (Feulgen-thionin) stained specimens of buccal mucosa scrapings. Dubbed Automated Quantitative Cytometry (AQC), the system analyzes nuclear conformation and chromatin texture that reflect subtle DNA distributional changes in buccal cell nuclei. Several thousand cells are analyzed per specimen and the data reduced to a single score that predicts the likelihood of the presence of cancer. No manual pathological review is done as part of the AQC analysis. The system was developed through a field study of buccal specimens collected from 150 confirmed lung cancer patients and 990 high-risk negatives. The two groups were matched for smoking status (mean pack years, 52 versus 54; median pack years, 45 versus 42). An automated analysis system and decision rule was created to separate the two groups.

RESULTS: The cross validated performance on the 1140 field study specimens was 66% sensitivity at 70% specificity. Sensitivity for Stage I lung cancer (which comprised 47 of the 150 cases) was 61%.

CONCLUSION: Buccal mucosa contains information that separates patients with lung cancer from high risk negatives. Further study is warranted to turn this analysis approach into an early detection test.

CLINICAL IMPLICATIONS: Analysis of buccal mucosa may become a regular part of screening for lung cancer.



DISCLOSURE: Roger Kemp, Employee Perceptronix Medical Inc.

Lung Cancer: From the Bench to the Bedside, continued

ABERRANT METHYLATION OF RASSF1A IN SMALL-SIZED LUNG ADENOCARCINOMA AND ITS RELATIONSHIP TO CLINICOPATHOLOGICAL FEATURES

Kuniharu Miyajima MD* Yasuhiro Suga MD Tatsuo Ohira MD Masahiro Tsuboi MD Norihiko Ikeda MD Takashi Hirano MD Harubumi Kato MD Shinichi Toyooka MD Riichiro Maruyama MD Makoto Suzuki MD Hisayuki Shigematsu MD Adi Gazdar MD Tokyo Medical University, Tokyo, Japan

PURPOSE: Aberrant methylation of CpG islands in promoter regions of tumor cells is one of the major mechanisms for silencing of tumor suppressor genes. Chromosome 3p is deleted frequently in lung cancer. The RAS association domain family 1A (RASSF1A) gene was isolated from the 3p21.3 region homozygously deleted in lung cancer cell lines, and it was shown to be inactivated by hypermethylation of the promoter region in lung cancers. In this study, we investigated the clinicopathological significances of RASSF1A methylation in the development and/or progression of small-sized (less than 2.0cm) lung adenocarcinoma. It is important to identify a marker for high-risk early stage patients who should benefit from new investigational adjuvant therapies.

METHODS: Surgically resected specimens from 260 primary lung adenocarcinoma 77 cases of small-sized adenocarcinoma. We determined the frequency of aberrant promoter methylation of the RASSF1A genes in 77 small-sized lung adenocarcinoma. Aberrant promoter methylation was examined using methylation-specific PCR (MSP).

RESULTS: Twenty-five of 77 (32.5%) tumors showed RASSF1A methylation. RASSF1A methylation was dominantly detected in smoker ($P < 0.03$). There was no significant correlation of RASSF1A methylation with gender, age, T stage, N stage and pathological stage. RASSF1A methylation correlated with adverse survival by univariate analysis ($P < 0.005$; log-rank test) as well as multivariate analysis ($P = 0.0062$; risk ratio 4.251; 95% confidence interval, 1.507-11.993). Furthermore, RASSF1A promoter hypermethylation in resected stage I small-sized lung adenocarcinoma was associated with impaired patient survival ($P < 0.01$).

CONCLUSION: Aberrant promoter methylation of the RASSF1A was present in 25 of 77 (32.5%) of small-sized lung adenocarcinoma by MSP assay. These results indicated that epigenetic inactivation of RASSF1A plays an important role in the progression of small-sized lung adenocarcinoma, and that RASSF1A hypermethylation appears to be a useful molecular marker for the prognosis of patients with small-sized and stage I lung adenocarcinoma.

CLINICAL IMPLICATIONS: RASSF1A is a potential tumor suppressor gene that undergoes epigenetic inactivation in lung adenocarcinoma through hypermethylation of its promoter region. RASSF1A methylation was significantly related to unfavorable prognosis in small-sized lung adenocarcinoma.

DISCLOSURE: Kuniharu Miyajima, None.

ION MOBILITY SPECTROMETRY: A NEW METHOD FOR THE DETECTION OF LUNG CANCER AND AIRWAY INFECTION IN EXHALED AIR? FIRST RESULTS OF A PILOT STUDY

Michael Westhoff MD* Patrick Litterst Lutz Freitag MD Vera Ruzsanyi PhD Sabine Bader Wolfgang Urfer PhD Jörg I. Baumbach PhD Lungenklinik Hemer, Hemer, Germany

PURPOSE: Lung cancer and airway infections gain increasing importance. Early diagnosis is desirable. We examined if volatile metabolites occurring in human exhaled air can be correlated directly to different kinds of diseases.

METHODS: An ion mobility spectrometer (IMS) coupled to a multicapillary-column (MCC) was used to identify and quantify volatile metabolites occurring in human breath down to the ng/L- and pg/L-range of analytes within less than 500 s and without any pre-concentration. The IMS investigations are based on different drift times of swarms of ions of metabolites formed directly in air at ambient pressure.

RESULTS: During a pilot study data were obtained from 36 patients suffering with lung cancer and 54 healthy persons in a control group. A reduction from more than one million data points per IMS-chromatogram to 25 variables enabled a classification and differententiation of these two groups with an error of 1.3 %.In a further study IMS-chromatograms were obtained from 30 patients with different airway infections (COPD-exacerbations, bronchiectasis, pneumonia). In comparison to healthy persons typical clusters of bacterial metabolites could be found.

CONCLUSION: These first clinical data show, that ion mobility spectrometry allows precise detection of airway infections as well as a distinction of patients with lung cancer from healthy people with high accuracy.The preliminary data need further confirmation by studies with greater populations.

CLINICAL IMPLICATIONS: Ion mobility spectrometry seems to be a promising tool in the diagnostic approach to lung cancer and airway infections.

DISCLOSURE: Michael Westhoff, None.

DISCOVERY OF SERUM PROTEOMIC PATTERNS FOR LUNG CANCER

Jonathan Heller PhD* John Stults PhD Shawn Becker MD Glenn Rosen MD Heather Wakelee MD Pierre P. Massion MD William L. Bigbee MD Predicant Biosciences, South San Francisco, CA

PURPOSE: Lung cancer is most often detected at late stages where treatment options are limited and outcomes are poor. Furthermore, common chest imaging tests detect significant numbers of lesions, of which most are found to be benign. As a result, there is a significant demand for a blood test for lung cancer diagnosis.

METHODS: We analyzed a cohort of serum samples from patients with biopsy-confirmed non-small cell lung cancer, along with control samples from cancer-free patients, matched for gender, age, smoking status (active, ex-smoker, never-smoker) and smoking history. Serum samples were processed to remove high abundance proteins, and analyzed by capillary electrophoresis-electrospray ionization mass spectrometry using a proprietary microfluidic chip-based platform and an ultra-high sensitivity mass spectrometer. Samples were blinded and randomized during sample preparation and analysis in order to remove bias in the measurement. After signal pre-processing of the data, the resulting intensities of ~1000 molecular species in the MS profiles were analyzed using pattern recognition methods.

RESULTS: Preliminary results for 93 samples show that a pattern of 24 molecular components yields an error rate of 18% (76% sensitivity, 87% specificity) for distinguishing cancer from non-cancer.

CONCLUSION: This system for proteomic analysis provides increased sensitivity and reliability for protein peak identification, substantially increasing the number of proteins observed and reducing inter- and intra-sample variability.

CLINICAL IMPLICATIONS: This approach holds promise as a new method for diagnosing lung cancer. This advanced system facilitates discovery of molecular signatures, and will lead to the roll-out of clinically practical, high-throughput cancer detection methodologies.

DISCLOSURE: Jonathan Heller, Employee Vice President, Information and Project Planning

Management Strategies in Pleural Effusions
2:30 PM - 4:00 PM

THE RELATIONSHIP BETWEEN PLEURAL PRESSURE CHANGES AND PATIENT SYMPTOMS DURING THORACENTESIS

Allan J. Walkey MD* David Berkowitz MD Rabih Bechara MD William Lunn MD Momen Wahidi MD Armin Ernst MD David J. Feller-Kopman MD Beth Israel Deaness Medical Center, Boston, MA

PURPOSE: To determine whether patients' symptoms during thoracentesis correspond to changes in pleural pressure.

METHODS: Data was collected prospectively during thoracenteses performed from 9/2002-12/2004. Of 468 patients, 169 had pleural manometry and were included in this study. Pleural pressures were measured with either a simple water manometer or an electronic transducer system. End expiratory pleural pressures were recorded after the withdrawal of 5cc of fluid (opening pressure), and until either there was no more fluid present or the patient developed chest discomfort (closing pressure).

RESULTS: Twenty eight of the 169 patients (16%) developed symptoms during thoracentesis: 10/169(5%) with cough, 18/169(11%) with chest discomfort. Total volume of pleural fluid removed was not different between the three groups (asymptomatic 1219±76ml, cough 1338±286ml, pain 1136±213ml), nor were opening pressures. Closing

Management Strategies in Pleural Effusions, continued

pleural pressures were significantly lower in patients with chest pain (-13±2.4cmH20) than in those without symptoms (-6.8±0.8cmH20) p=0.04, but not in those with cough (-6.8±3.2cmH20) p=0.1. The total change in pleural pressure (opening-closing pressure) was significantly greater in patients with chest pain (-20±1.7) than those without symptoms (-12.4±0.6) and those with cough (-9.5±2.2), p<0.001. There were no differences in pleural pressures between patients with cough and without symptoms.

CONCLUSION: This study is the first to demonstrate a relationship between patient symptoms and pleural pressure changes during thoracentesis. Chest discomfort was associated with large negative pleural pressure changes, which may increase risk for re-expansion pulmonary edema, and should be a signal to terminate thoracentesis. Cough was not associated with increased changes in pleural pressure and may be a sign of resolving atelectasis during volume removal. Manometry is recommended to prevent pressure-related complications and maximize volume of fluid removal during thoracentesis. However, if unavailable, patient symptoms may be a surrogate for pleural manometry.

CLINICAL IMPLICATIONS: Symptoms during thoracentesis correspond to pleural pressure changes. Cough is not related to high-risk negative pleural pressure. Chest discomfort is associated with large negative-pleural pressure changes and should lead to termination of thoracentesis.

DISCLOSURE: Allan Walkey, None.

IS IT A TRANSUDATE OR AN EXUDATE? DYSYNCHRONY BETWEEN PLEURAL FLUID PROTEIN AND LDH IN 211 INITIAL THORACENTESES

Jay T. Heidecker MD* John T. Huggins MD Peter Doelken MD Steven A. Sahn MD Medical University of South Carolina, Charleston, SC

PURPOSE: Though traditional cutoffs for protein levels and LDH values were reported in the 1970s to reliably distinguish between exudates and transudates, more recent ROC analyses have questioned this assumption. The purpose of this study was to determine the incidence of pleural effusions that were exudative by either protein or LDH and transudative by traditional cutoff values. Further, we wanted to identify specific diagnoses which occurred within the dysynchronous groups.

METHODS: A database has been collected of all pleural procedures performed at the Medical University of South Carolina for safety purposes. We retrospectively examined this data from July 2001 to October 2004. We included all initial thoracenteses provided that the pleural protein, LDH, and serum protein values were obtained. We defined an exudate by protein as a pleural fluid/protein ratio of ≥.51 and by LDH as an LDH value of ≥161 (2/3 of our upper limits of normal). We classified effusions as synchronous exudates, synchronous transudates, dysynchronous effusions with elevated protein ratios only, and dysynchronous effusions with elevated LDH levels only. We then reviewed all available clinical data and assigned diagnoses to the effusions.

RESULTS: Table 1 shows the characteristics of these 211 effusions that met criteria for study.

CONCLUSION: Pleural fluid dysynchrony was found in 39% of effusions. The most common causes were parapneumonic, paramalignant, and malignant, effusions. Trapped lung, entrapped lung, chylothorax and post-liver transplant effusions were dysynchronous effusions with high protein ratios and low LDH levels; these processes are characterized by minimal inflammation with abnormal pleural lymphatics. The high incidence of dysynchronous pleural effusions confirms that isolated values in the pleural fluid analysis are not consistently reliable diagnostically.

CLINICAL IMPLICATIONS: Pleural fluid analysis must be used in conjunction with the clinical presentation in determining the cause of a pleural effusion. Pleural fluid dysynchrony can indicate whether an exudative effusion is primarily due to a lymphatic abnormality with elevated protein or to inflammation (increased LDH). Traditional transudates, like CHF, rarely cause pleural fluid dysynchrony except following intense diuresis.

Diagnosis	Dysynchronous-high protein	Dysynchronous-high LDH
Total n=211		
Synchronous transudates n=73		
Synchronous exudates n=79		
Dysynchronous n=59		
Parapneumonic (13)	5	8
Paramalignant (12)	8	4
Malignant (9)	7	2
Ideopathic (7)	5	2
CHF (4)	3	1
Post liver transplant (3)	3	0
Chylothorax (2)	2	0
Trapped lung (2)	2	0
Entrapped lung (2)	2	0
Post cardiac surgery (2)	0	2
Tuberculosis (2)	0	2
Acute pancreatitis (2)	0	1
Total	37	22

DISCLOSURE: Jay Heidecker, None.

LARGE VOLUME THORACENTESIS AND THE RISK OF RE-EXPANSION PULMONARY EDEMA

David M. Berkowitz MD* Rabih I. Bechara MD William Lunn MD Momen M. Wahidi MD Armin Ernst MD David J. Feller-Kopman MD Beth Israel Deaconess Hospital, Boston, MA

PURPOSE: Re-expansion Pulmonary Edema (RPE) is a well described, but rare complication after large volume thoracentesis. The creation of excessive negative pleural pressures (Ppl) has been postulated as a mechanism for the development of RPE. Previous studies in animal models have suggested that RPE is not seen when Ppl is kept greater than -20 cmH20. Similarly, an arbitrary cut-off of 1L has been suggested as a volume limit to minimize the risk of RPE. To date, no large series has examined the safety of large volume thoracentesis and risk of RPE in humans.

METHODS: Data was collected prospectively during thoracentesis performed by the division of Interventional Pulmonology at Beth Israel Deaconess Medical Center from October 2001 to April 2005. Thoracentesis was performed using Pleura-Seal thoracentesis kit (Arrow-Clark) and pleural pressures were recorded either by simple water manometer or electronic transducer system (Biobench, National Instruments). Complications of thoracentesis were evaluated by medical record review and analysis of post-thoracentesis radiographic examinations.

RESULTS: Of the 602 patients in the database, 245 had greater than or equal to 1L of pleural fluid removed (range 1000-6550mL) and were included in analysis. Of those, 55 had greater than or equal to 2L removed and 12 had greater than 3L removed. Closing Ppl ranged from +15.6 to -29 cmH20. Nine cases (3.7%) had closing pleural pressures equal to -20 cmH20, and 10 cases (4.0%) had a closing Ppl less than -20 cmH20. One case (0.4%) of RPE was described radiographically, however, the patient suffered no adverse clinical outcomes, and specific treatment for RPE was not required. No case of hemodynamic instability was noted post-thoracentesis. Pneumothorax occurred in only 5 of 245 cases (2.0%).

CONCLUSION: Pleural fluid in excess of 6L has been safely removed without hemodynamic compromise or clinically significant RPE. The previously suggested pleural pressure cut-off of -20 cmH20 appears to confer a very low risk for RPE.

CLINICAL IMPLICATIONS: Large volume thoracentesis may be safely performed as long as attention is paid to pleural pressures.

DISCLOSURE: David Berkowitz, None.

Management Strategies in Pleural Effusions, continued

THORACOSCOPY AND PLACEMENT OF AN INDWELLING CATHETER FOR THE MANAGEMENT OF MALIGNANT PLEURAL EFFUSION: A DAY CASE

Ahmed S. Al-Halfawy MD* Faculty of Medicine, Cairo University, Cairo, Egypt

PURPOSE: The purpose of this study was to evaluate the possibility of performing diagnostic thoracoscopy for patients with pleural effusions and inserting an indwelling catheter at the end of the procedure when intrapleural pathology was identifiable as possible malignancy, and discharging those patients on the same day of the procedure on domiciliary self drainage.

METHODS: Diagnostic thoracoscopy was performed under local anesthesia and conscious sedation. when a lesion was observed and judged to be the possible cause of the effusion and when it was thought that it was most probably malignant, a second skin incision was made 5 cm dorsal to the first incision. An indwelling catheter was tunnelled under the skin with the outer part of the catheter with the valve at its end coming out from the first incision. The fenestrated end was inserted into the pleural cavity through the second incision. Through the first incision, an intercostal tube was also placed. When patients recovered, they were asked to cough repeatedly until air stopped bubbling in the underwater seal. The intercostal tube was then removed and the indwelling catheter connected to surgivac pump to produce continuous negative pressure.

RESULTS: This technique was performed in eight patients with malignant pleural effusions who were diagnosed during thoracoscopy. all patients were discharged on the same day of the procedure. the intercostal tube was removed after a short period that ranged from 1 to 12 hours.

CONCLUSION: It is possible to minimize hospital stay after thoracoscopy for malignant pleural effusions by inserting an indwelling catheter to complete the draining of the effusion on an outpatient basis.

CLINICAL IMPLICATIONS: Patients with malignant pleural effusions can undergo thoracoscopy and be discharged home on the same day. This technique also abolished the need for chemical pleurodesis as the indwelling catheter have a comparable success rate in producing spontaneous pleurodesis.

DISCLOSURE: Ahmed Al-Halfawy, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. placement of an indwelling pleural catheter at the same sitting of thoracoscopy for malignant pleural effusiosns and discharging the patient on the same day of the procedure.

EVALUATION OF INTRAPLEURAL STREPTOKINASE FAILURE CRITERIA USED IN MIST1 FOR THE TREATMENT OF COMPLICATED PLEURAL EFFUSIONS

Kelvin K. Shiu DO* Paul H. Mayo MD Mark J. Rosen MD Beth Israel Medical Center, New York, NY

PURPOSE: Recently reported results in the New England Journal of Medicine from the Multicenter Intrapleural Sepsis Trial (MIST1) showed that intrapleural administration of streptokinase does not improve mortality, rate of surgery, or length of stay among patients with pleural infection. Referral to surgical drainage was one of the primary studied outcomes. The decision to refer was made by managing physicians locally at the 52 centers. Our study investigated the potential effects and contributions from procedure and practice variance on the surgical drainage referral decision.

METHODS: Criteria for surgery referral from MIST1 were based on persistent fever and/or raised blood inflammatory markers, and residual pleural fluid. Probabilistic risk assessment (PRA) was used to model and quantify the surgical drainage decision making process. Event tree analysis was employed to simulate different decision branch points based on the referral criteria. Each of these branch points were evaluated by fault tree analysis. The MIST1 result was adopted as the baseline reference case in our study.

RESULTS: Results from PRA analysis show that the decision to refer to surgical drainage is complex and depends on the managing physician's perceived importance of several parameters, including the severity and duration of fever, the extent of elevated blood inflammatory markers, and the degree of residual effusion. The non ambiguous decisions of referral or no referral constitute between 60 to 80 percent of the total. The balance is more arbitrary. This introduced a substantial variability and uncertainty into the final results. Our study further shows that by refining the definitions of fever, residual effusion, and inflammatory markers, the relative contributions to the streptokinase and placebo groups could vary up to 40 percent.

CONCLUSION: This study suggests that the primary outcome selected in MIST1 to compare streptokinase with placebo may be sensitive to how the surgical drainage referral criteria are defined.

CLINICAL IMPLICATIONS: Modified definitions of residual effusion, fever, and elevated inflammatory markers could potentially alter the conclusion on the efficacy of streptokinase as a fibrinolytic agent for complicated pleural effusions.

DISCLOSURE: Kelvin Shiu, None.

CHARACTERISTICS OF TRAPPED LUNG: MANOMETRY, PLEURAL FLUID ANALYSIS, AND AIR-CONTRASTED COMPUTED TOMOGRAPHY

John T. Huggins MD* Jay Heidecker MD Peter Doelken MD Steven A. Sahn MD MUSC, Charleston, SC

PURPOSE: Trapped lung results from a remote inflammatory process leading to development of a fibrous pleural membrane on the visceral pleura which prevents normal lung expansion. Pleural fluid persistence is due to hydrostatic equilibrium in the presence of an irreducible pleural space. Diagnosis of trapped lung implies chronicity and the absence of active inflammation or bronchial obstruction. Pleural fluid analysis, manometry, and radiographic data of 10 patients with trapped lung are presented.

METHODS: Manometry was performed on 202 consecutive patients referred for therapeutic thoracentesis at the Medical University of South Carolina between 10/2001 and 3/2005. Mean pleural liquid pressure (Ppl) was obtained initially and at aliquots of 50-250cc. In the absence of malignancy or active pleural inflammation, air is introduced to allow for safe removal of all pleural fluid and to evaluate visceral pleura thickness by CT.

RESULTS: Abbreviations: C= cirrhosis, L=lymphocyte, Mac= macrophages, NC= nucleated cells, CS=Cardiac Surgery,Plp= pleural liquid pressure, U=Uremia, R=Radiation, *=lab error, ** PLel= pleural space elastance (pressure change)/(volume removed); cmH2O/L.

CONCLUSION: Prevalence of trapped lung was 10/202 (5%). Cardiac surgery was the most common cause partially due to its frequency. All cases had evidence of visceral pleural restriction with PLel≥16 cmH2O and visceral pleural thickening by air-contrast CT. Pleural fluid protein values greater than 4 mg/dl were seen in two cases suggesting abnormal protein transport. Cell counts were low with lymphocyte predominance in most. Together with a low LDH, these findings indicate minimal or absent pleural inflammation. The present series documents a benign and chronic clinical and pathophysiological syndrome distinct from the more common active malignant or infectious pleural processes complicated by lung entrapment.

CLINICAL IMPLICATIONS: The diagnosis of trapped lung requires documentation of visceral pleural restriction by pleural manometry or CT combined with the history of a remote inflammatory insult. Pleural fluid analysis typically reveals a transudate with a paucity of nucleated cells, although the protein level at times may be slightly above the cut-points due to abnormal protein transport.

Pleural Fluid Characteristics of Trapped Lung

Case	1	2	3	4	5	6	7	8	9	10
Diagnosis	CS	U	CS	CS	U	CS	C	U	CS	R
pH	7.44	7.42	7.26	7.33	7.38	*	7.39	7.46	7.40	7.33
Total protein (g/dl)	4.2	2.2	3.6	3.6	4.1	2.0	2.0	2.0	3.2	2.8
LDH	99	114	100	153	170	132	107	155	57	118
NC	214	192	1837	148	315	235	538	21	352	213
Differential	64% Mac	94% L	96% L	39% L	67% L	63% L	70% L	74% Mac	76% L	69% L
Initial Plp (cmH_2O)	-2.7	-8.0	-34.0	+6.6	-1.0	+3.0	+4	+2.2	+4.5	-1.2
PL_{el} ** (cmH_2O/L)	24	149	86	19	30	42	22	17	16	89

DISCLOSURE: John Huggins, None.

Prognostic Markers in COPD
2:30 PM - 4:00 PM

LUNG FUNCTION DECLINE AND OUTCOMES IN AN ELDERLY POPULATION: FINDINGS FROM THE CARDIOVASCULAR HEALTH STUDY

David M. Mannino MD* Kourtney J. Davis PhD University of Kentucky, Lexington, KY

PURPOSE: We sought to determine the risk factors for and outcomes associated with rapid lung function decline in a cohort of subjects followed for up to 11 years.

METHODS: We analyzed data from 4,923 adult participants, aged 65 and older at baseline, in the Cardiovascular Health Study (CHS). We classified subjects using a modification of the GOLD criteria for COPD, and added a "restricted" category (FEV1/FVC > 70% and FVC < 80% predicted). We used Cox proportional hazard models to determine the risk of lung function decline over four years on subsequent mortality and COPD hospitalizations, after adjusting for age, race, sex, smoking status, and other factors.

RESULTS: Of the participants in our initial cohort, 3388 (68.8%) had spirometry at the Year 4 visit. Participants with GOLD Stages 3 or 4 COPD at baseline were less likely than normal subjects to have follow-up spirometry (52.7% vs. 77.9%, $p < 0.01$) and were more likely to be in the most rapidly declining quartile of FEV1 (28.2% vs, 21.3%, $p < 0.01$), with an FEV1 loss of at least 3.4% annually. Overall, membership in the most rapidly declining quartile of FEV1 from baseline to Year 4 was modestly associated with risk of COPD hospitalization (adjusted Hazard Ratio [HR] 1.6, 95% confidence interval [CI] 1.3, 2.0) and all-cause death (adjusted HR 1.5, 95% CI: 1.2, 1.7) over an additional seven years of follow-up.

CONCLUSION: More rapid decline of lung function was independently associated with a modest increased risk of COPD hospitalizations and deaths in an elderly cohort of US participants.

CLINICAL IMPLICATIONS: Monitoring changes in spirometry may be useful in determining the risk if exacerbations and death in elderly patients with COPD.

DISCLOSURE: David Mannino, Grant monies (from industry related sources) GlaxoSmithKline, Pfizer; Consultant fee, speaker bureau, advisory committee, etc. GlaxoSmithKline, Pfizer, Ortho Biotech, Boehringer Ingelheim.

AMBULATORY MONITORING OF OXIMETRY AND ACTIVITY IN PATIENTS WITH ADVANCED LUNG DISEASE: A NEW APPROACH TO OPTIMIZE LONG-TERM OXYGEN THERAPY

Miriam D. Cohen MSN* Sakshi Pawa MD Ravindra Mehta MD Michael Cutaia MD VA, New York Harbor Health Care Service, Brooklyn, NY

PURPOSE: Long-term oxygen therapy (LTOT) improves survival in hypoxemic patients with advanced lung disease. The LTOT prescription is based on an evaluation of oxygen saturation at rest and during exercise, although this evaluation may not reflect the usual daily activity of these patients. The impact of routine daily activity on oxygen desaturation is unknown. We conducted this study to assess the daily activity profile of LTOT patients and its relationship to oxygen saturation.

METHODS: 25 daytime ambulatory oximetry monitoring (AOM) studies were performed on 11 patients with resting hypoxemia on continuous oxygen (COT) and 14 patients who desaturated only with ambulation (AOT). Accelerometers defined 3 categories of activity: walking, active-not-walking, and inactive. Oximetry confirmed desaturation events defined as oxygen saturation <90% for >30 seconds. Using a scoring method similar to polysomnography, a temporal profile of oxygen saturation linked to activity was defined for each patient.

RESULTS: See charts 1 and 2.

CONCLUSION: Both the COT and AOT patients spent the majority of their time "active-not-walking". Both groups spent a very small percentage engaged in "walking". The COT patients spent a significantly more time "inactive" than the AOT patients; the AOT patients spent a significantly more time "active-not-walking". In both groups, the greatest duration of oxygen desaturation occurred during "active-not-walking". The COT group desaturated for more minutes when "inactive" compared to AOT. Although both groups desaturated while "walking", desaturation time linked to walking contributed little to the total time. The severity of hypoxemia for each linked desaturation event was similar.

CLINICAL IMPLICATIONS: This is the first detailed study to define the activity profile of patients with advanced lung disease on LTOT. Standard rest and walk testing is a limited evaluation on which to base the LTOT prescription. This approach does not assess oxygen saturation when patients are "active-not-walking" – the most common activity of these patients. AOM with activity monitoring provides patient-specific data on the temporal profile of oxygen saturation linked to usual activity, which may be used to optimize LTOT prescriptions.

Desaturation Minutes Linked to Activity (mean minutes ± standard error and mean O2 saturation)

	Total Minutes of Daytime DS (± SE)	Walking (min) (± SE)	Active-not-walking (min) (± SE)	Inactive (min) (± SE)
AOT	103 (± 31.4)	35 (± 9.5) Mean O2 = 87	61 (± 23.5) Mean O2 = 87	7 (± 5.8) Mean O2 = 75
COT	242 (± 49.2)	39 (± 6.6) Mean O2 = 86	133 (± 31.6) Mean O2 = 87	70 (± 27.1) Mean O2 =78
p Value for DS (min)	<.02	NS	NS	<.02

Accelerometer Profile of Daytime Activity (% time in activity ± standard error)

	Walking	Active-not-walking	Inactive
AOT	3.7 % (± 0.79)	89.5 % (± 1.4)	6.6 % (± 1.4)
COT	2.2 % (± 0.39)	78.7 % (± 3.1)	18.9 % (± 3.2)
p Value	NS	<.004	<.002

DISCLOSURE: Miriam Cohen, Grant monies (from sources other than industry) VA, Veterans Network #3; Grant monies (from industry related sources) Nonin Medical, Inc.

BRONCHODILATOR-RESPONSIVENESS AS A PROGNOSTIC FACTOR IN COPD

M.M. Ismail MD* M. Moammar MD H. Aziz MD M. Shubair MD V. DeBari PhD M.A. Khan MD St. Joseph's Regional Medical Center, Paterson, NJ

PURPOSE: Bronchodilator-responsiveness in COPD patients (defined as a 12% and ≥200 ml improvement in FEV1) has rarely been studied as a prognostic factor in patient outcomes. In order to correlate bronchodilator-responsiveness and frequency of hospitalizations in COPD patients, we retrospectively reviewed our experience with two groups of patients with COPD.

METHODS: We retrospectively reviewed the pulmonary function studies of 166 patients with the diagnosis of COPD between 2000 and 2003 and divided them into two groups, based on the above-outlined criteria: Group I: Non-Responders (NR): 123 patients, and Group 2: Responders (R): 43 patients. We then contacted all patients by phone and reviewed their hospital records about the frequency of COPD-related admissions during 2004.

RESULTS: There were 33 hospitalizations among 123 patients in NR Group and only 3 hospitalizations among 43 patients in R Group. Using Fischer Exact Test to compare the two groups, we found a statistically significant difference (P value: 0.0052, odds ratio: 0.218, and 95% confidence interval: 0.06-0.71).

CONCLUSION: COPD patients who are non-responders (NR) to bronchodilators have a more complicated course than responders (R) as evidenced by a significantly greater frequency of hospitalizations due to acute exacerbations.

CLINICAL IMPLICATIONS: Bronchodilator-responsiveness in COPD patients predicts better prognosis.

Classification	Responders	Non-Responders
No. of patients	43	123
No. of hospitalizations	3	33

DISCLOSURE: M.M. Ismail, None.

OSTEOPOROSIS IN PATIENTS WITH OBSTRUCTIVE LUNG DISEASE ON INTERMITTENT ORAL STEROIDS

Bernard J. Roth MD* Suzette Gagnon-Bailey MSN Madigan Army Medical Center, Tacoma, WA

PURPOSE: Very little is known about the possible osteopenic effect of intermittent courses of oral prednisone. This prospective study sought to compare the bone density in patients taking chronic oral steroids (OS), intermittent oral steroids (IOS) or inhaled steroids alone (IS).

METHODS: Computerized pharmacy records were used to identify patients in a military medical center pulmonary clinic who were prescribed oral or inhaled steroids. 100 patients with obstructive lung disease participated in the study with a telephone survey, review of their computerized patient record and dual energy X-ray absorptiometry of the vertebral spine and proximal femur. Patients were divided up into 14 OS, 48 IOS and 38 IS. The T and Z scores were compared between groups and the effect of various confounding factors such as age, sex, menopause, exercise, calcium supplementation and steroid dose were evaluated.

RESULTS: No significant difference was noted in any of the descriptive factors. The average femur T score was -2.043 for OS, -1.402 for IOS and -1.168 for IS (difference significant only for OS vs IS, $p< 0.0244$). The average lumbar T score was -1.421 for OS, -1.217 for IOS and -0.410 for IS (difference significant for IOS vs IS and OS vs IS, $p< 0.0108$ and $p<0.0259$ respectively). The average femur Z score was -1.193 for OS, -0.444 for IOS and -0.646 for IS (difference significant only for OS vs IOS, $p< 0.0117$). The average lumbar Z score was -1.229 for OS, -0.404 for IOS and -0.053 for IS (difference significant only for OS vs IS, $p< 0.0098$). 33% of OS, 23% of IOS and 15% of IOS patients met WHO criteria for Osteoporosis based on a T score of -2.5 or less.

CONCLUSION: Osteopenia and osteoporosis trended to be greater in IOS patients compared with IS patients but not as severe as in OS patients, suggesting a clinically significant osteopenic effect from intermittent oral steroids.

CLINICAL IMPLICATIONS: Patients taking intermittent oral steroids should be screened for osteoporosis.

DISCLOSURE: Bernard Roth, Grant monies (from industry related sources) This study was partially funded by a grant from the Geneva Foundation.

COMPARISON OF RESPIRATORY DISEASE BURDEN FOR CHRONIC OBSTRUCTIVE LUNG DISEASE VERSUS AN "AT-RISK" GROUP: EARLY FINDINGS FROM THE RESPIRATORY HEALTH PROMOTION STUDY (RHPS)

Jeno P. Marton MD* Joseph Menzin PhD Jeffrey S. Brown PhD Barrett Kitch MD Mark Friedman MD Lisa Guadagno MS Jianwei Xuan PhD Pfizer, Inc., New York, NY

PURPOSE: To assess the comparative respiratory disease burden among subjects with COPD versus an at-risk population in worksite and community settings.

METHODS: A prospective, longitudinal, study was initiated as part of employer and community wellness activities offered by a local health plan. Subjects aged 25+ years are eligible if they provide valid spirometry readings and complete a Respiratory Health Questionnaire. This questionnaire includes items related to respiratory symptoms, activity limitations, healthcare resource use, and perceived health status (as measured by a Visual Analog Scale [VAS]). Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria are used to group enrollees as COPD subjects (FEV1/FVC <0.70; stages 1-4) or at-risk subjects (chronic respiratory symptoms and FEV1/FVC >0.70; stage 0).

RESULTS: 589 subjects were enrolled through December 2004: 70% at worksites, 17% at senior centers, and 13% at community sites. 102 subjects (17%) met the criteria for GOLD stages 0 to 4: 30 in the at-risk group, 26 with mild COPD (stage 1), 32 with moderate COPD (stage 2) and 14 with severe or very severe COPD (stages 3 and 4). Subjects in the at-risk group were, on average, younger than those with COPD (52 versus 63 years old). At-risk subjects were as likely as those with COPD to report wheezing (37% versus 33%) or shortness of breath (47% and 44%) as somewhat, moderately, or very bothersome. Respiratory-related activity limitations were reported by 37% of at-risk subjects versus 31% of COPD subjects. At-risk subjects were less likely as those with COPD to report use of respiratory medications (17% versus 32%), and equally likely to report use of respiratory-related emergency room or hospital services (10%). Mean VAS scores were similar (75), although the median score was lower for the at-risk group (75 versus 80).

CONCLUSION: Subjects with chronic respiratory symptoms and normal lung function reported similar symptom burden and quality of life to those with COPD.

CLINICAL IMPLICATIONS: At-risk subjects, classified based on GOLD criteria, experience a substantial respiratory disease burden.

DISCLOSURE: Jeno Marton, None.

COMPUTED TOMOGRAPHIC MEASUREMENT OF CARTILAGINOUS AIRWAY WALL THICKENING AS A PREDICTOR OF INSPIRATORY FLOW RESISTANCE

George R. Washko MD* Raul S. Estepar PhD Carl-Fredrik Westin PhD Ron Kikinis MD Stephen H. Loring MD John J. Reilly MD Brigham and Women's Hospital, Boston, MA

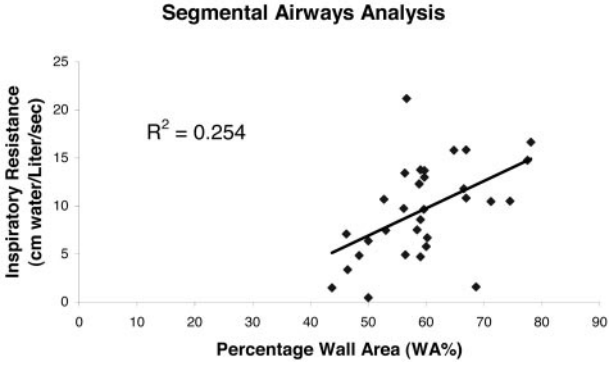
PURPOSE: Emphysematous subjects whose airflow obstruction is due to loss of parenchymal tethering of the airways experience greater benefit from lung volume reduction surgery (LVRS) than individuals with fixed small airway obstruction. Inspiratory resistance is a useful measure of intrinsic airway disease and has been used in subject selection for LVRS. In-vivo radiologic assessment of airway remodeling in chronic obstructive pulmonary disease (COPD) is challenging because the size of the peripheral airways (<2mm) exceeds the capabilities of current CT techniques for accurate assessment. We hypothesized that cartilaginous airway wall thickening as assessed by CT scan correlates with inspiratory resistance.

METHODS: Chest CT scans, pulmonary function tests, and inspiratory resistance measurements were examined in 152 subjects assessed at Brigham and Women's Hospital between 1998 and 2005. Thirty two scans demonstrated the origin of the apical segment of the right upper lobe without wall interruption or motion artifact in one slice, conditions necessary for accurate measurement. Automated lung mask detection and manual wall delineation of 5, 8, or 10mm thickness images were performed using Slicer. (http://www.slicer.org). Airway wall area is expressed as the percentage wall area (WA%) where WA%=Wall area/Lumen area*100.

RESULTS: The Pearson Correlation coefficient for the linear regression of percentage wall area and inspiratory resistance is 0.51 ($p = 0.0039$).

CONCLUSION: The percentage airway wall area of cartilaginous airways correlates with a subject's inspiratory resistance.

CLINICAL IMPLICATIONS: This relationship may assist in the determination of the degree of a subject's airway disease and potential benefit from LVRS. Further investigation with high resolution CT scans is necessary to confirm these results.



DISCLOSURE: George Washko, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Slicer is open

source software which provides a visualization and processing environment allowing segmentation and quantification of medical data for research.

Therapeutic Update in Pulmonary Hypertension
2:30 PM - 4:00 PM

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ILOPROST INHALATION AS ADD-ON THERAPY TO BOSENTAN IN PULMONARY ARTERIAL HYPERTENSION (PAH)

Vallerie V. McLaughlin MD* Ronald Oudiz MD Adaani Frost MD Victor Tapson MD Srinivas Murali MD Richard Channick MD David Badesch MD Robyn Barst MD Henry Hsu MD Lewis Rubin MD University of Michigan, Ann Arbor, MI

PURPOSE: Inhaled iloprost, a prostacyclin analogue, is safe and effective monotherapy for PAH. Combination therapy may enhance treatment options for PAH. We assessed the safety and efficacy of adding inhaled iloprost to bosentan in PAH.

METHODS: In this prospective multicenter study, PAH patients on a stable dose of bosentan were randomized to inhaled iloprost 5 mcg or placebo 6 times daily up to 9/day for 12 weeks. Patients were evaluated for safety and the following efficacy measures: change in 6-minute walk distance (6-MWD), Borg Dyspnea Score, NYHA Class, time-to-clinical-worsening, and hemodynamics.

RESULTS: Fifteen U.S. centers enrolled 67 PAH patients (55% idiopathic PAH, 45% associated PAH). The mean age was 50 years and 79% were female. Most patients were in NYHA class III (94%) with a mean baseline 6-MWD of 338 m. Inhalation dosing compliance was 94% in both groups, with most taking 6 inhalations/day and 125 mg BID bosentan. At Week 12, patients receiving iloprost had a mean increase of 30 m in their 6-MWD compared to baseline ($p = 0.0013$), while those on placebo had a mean increase of 4 m ($p = 0.69$), with a placebo-adjusted difference of +26 m ($p = 0.0513$). This was accompanied by a reduction in Borg Dyspnea Score in the iloprost group (P=0.03 vs baseline). NYHA class improved by one Class in 34% iloprost patients compared with 6% placebo ($p = 0.0023$). Iloprost delayed time-to-clinical-worsening ($p = 0.0219$) with 0/32 iloprost patients and 5/33 (15%) placebo patients experiencing clinical deterioration. Improvements were noted in placebo adjusted change in mPAP, 8 mmHg ($p < 0.0001$), and PVR, 244 dynes•sec•cm-5 ($p = 0.0007$). Adverse events with combination therapy were consistent with the known safety profile of inhaled iloprost and included cough, headache, jaw pain, and flushing. Syncope was infrequent overall (1 iloprost, 2 placebo).

CONCLUSION: Combination therapy with inhaled iloprost and bosentan was safe and provided additional efficacy compared with bosentan alone.

CLINICAL IMPLICATIONS: Inhaled iloprost may be a useful adjunct therapy to bosentan in PAH patients.

DISCLOSURE: Vallerie McLaughlin, Grant monies (from industry related sources); Consultant fee, speaker bureau, advisory committee, etc.

ONE YEAR EXPERIENCE WITH INTRAVENOUS TREPROSTINIL IN PULMONARY ARTERIAL HYPERTENSION (PAH) PATIENTS

Vallerie V. McLaughlin MD* Robyn Barst MD Mardi Gomberg-Maitland MD Victor Tapson MD Abby Krichman RRT Allison Widlitz Stuart Rich MD Raymond Benza MD Univeristy of Michigan, Ann Arbor, MI

PURPOSE: Intravenous (IV) epoprostenol improves exercise tolerance, symptoms, hemodynamics, and survival in PAH. IV treprostinil, a prostacyclin analogue, may have similar clinical benefits and a better safety profile with a longer (4 ½ hour) elimination half-life. Previous reports from this investigator initiated study have demonstrated favorable 12 week results. The purpose of this study was to assess the clinical efficacy of IV treprostinil after one year of therapy.

METHODS: In this open label, multicenter study, PAH patients were treated with IV treprostinil either as initial therapy for PAH (de novo) or transitioned to treprostinil from epoprostenol (transition). The goal of therapy was improvement in de novo patients and maintenance of functional capacity and symptoms in the transition patients. Patients were assessed with six minute walk distance (6MWD) and right heart catheterization at baseline and 1 year using a paired t-test.

RESULTS: Forty-seven patients (16 de novo, 31 transition), mean age 43.4 years, (81% female) were enrolled. PAH was idiopathic in 62%, related to connective tissue disease 25%, and related to congenital heart disease in 13%. At baseline 49% were FC II , 47% were FC III and 4% were FC IV. Transition patients were on epoprostenol for 55 ± 44 months at a mean dose of 40 ± 23 ng/kg/min. At one year, the mean treprostinil dose was 111 ± 29 ng/kg/min in de novo patients and 124 ± 57 ng/kg/min in transition patients. One year data was available in 16 patients. Data was not available in the remaining 31 for the following reasons: death (4), discontinuation of IV treprostinil (7), and duration of IV treprostinil therapy <1 year (20). 6MWD and hemodynamic results are displayed in the table. Side effects associated with treprostinil were typical of prostacyclins, eg. headache, jaw pain, leg pain, and diarrhea.

CONCLUSION: The clinical efficacy of IV treprostinil appears to be maintained at one year.

CLINICAL IMPLICATIONS: IV Treprostinil may be an effective alternative to IV epoprostenol in selected PAH patients.

	De Novo (n=5)			Transition (n=11)		
Parameter	Baseline	1 year	P value	Baseline	1 year	P value
6MWD (meters)	323±35	454±43	0.06	482±18	482±12	0.96
PAPm (mmHg)	66±9	48±7	0.006	45±4	50±3	0.08
CI (L/min/m^2)	1.5±0.1	2.5±0.2	0.04	2.9±0.2	3.0±0.2	0.71
PVRI (Wood units•m^2)	37±5	16±4	0.01	13±2	14±2	0.5

M ± SE

DISCLOSURE: Vallerie McLaughlin, Grant monies (from industry related sources) United Therapeutics; Consultant fee, speaker bureau, advisory committee, etc. United Therapeutics.

SITAXSENTAN IMPROVES TIME TO CLINICAL WORSENING IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

David Badesch MD* Nazzareno Galie MD David Langleben MD Robert Naeije MD Gerald Simonneau MD Robyn Barst MD University of Colorado, Denver, CO

PURPOSE: Sitaxsentan (SITAX), an oral, once-daily, highly selective (>6500:1) ETA endothelin receptor antagonist has been studied in 2 previously reported, pivotal, randomized, PBO-controlled PAH studies (STRIDE-1, 12 week duration, Barst AJRCCM, 2004; and STRIDE-2, 18 week duration, Barst, ATS, 2005). Here, we report a prospectively defined combined analysis of clinical worsening events from both studies. This combined analysis has been submitted to the November, 2005 American College of Rheumatology meeting.

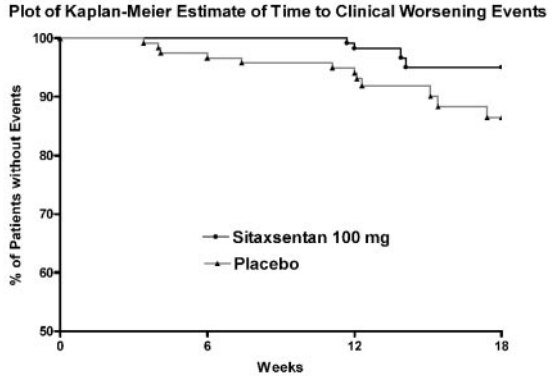
METHODS: STRIDE-1 (n=178) and STRIDE-2 (n=246) included PAH pts with WHO Class II, III, and IV: idiopathic PAH (56%) or associated with connective tissue disease (28%) or congenital heart defects (16%). While the 2 pivotal studies evaluated 100mg and 300mg in STRIDE 1 and 50mg and 100mg in STRIDE 2, the 100 mg dose was evaluated in both trials and has been shown to be the optimal dose based on overall risk-benefit considerations. Clinical events were defined as hospitalization for worsening PAH, death, transplantation, addition of new chronic PAH treatment, or a combined deterioration in WHO functional class and ≥ 15% decrease from baseline in 6MW. Time to clinical worsening events was assessed from the date of the first dose of study drug through the first clinical event. Subjects were censored at study completion.

RESULTS: 115 pts were treated with SITAX 100mg and 119 with PBO. Time to clinical worsening was better in the SITAX 100mg vs PBO group (p=0.0464) with no events in 96% of the SITAX 100mg pts vs no events in 89% of the PBO pts.

Therapeutic Update in Pulmonary Hypertension, continued

CONCLUSION: Sitaxsentan 100 mg once daily improves time to clinical worsening in patients with PAH.

CLINICAL IMPLICATIONS: Sitaxsentan 100mg once daily has been shown to be effective and safe in the treatment of PAH.



DISCLOSURE: David Badesch, Grant monies (from sources other than industry) American Lung Association, American Heart Association, National Institutes of Health, and the Scleroderma Foundation; Grant monies (from industry related sources) Glaxo Wellcome/GlaxoSmithKline, UnitedTherapeutics, Boehringer Ingelheim, Actelion, ICOS/Texas Biotechnologies, Encysive, Pfizer, Myogen, CoTherix.; Consultant fee, speaker bureau, advisory committee, etc. Glaxo Wellcome/GlaxoSmithKline, Actelion, Berlex, Astra-Merck, Astra-Zeneca, Myogen, Intermune, Forest Labs, Encysive, Exhale Ther; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Sitaxsentan.

LONG-TERM FOLLOW UP AFTER SUCCESSFUL DISCONTINUATION OF PROSTACYCLIN ANALOGUES IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH)

Enrique Diaz Guzman Zavala MD* Omar Minai MD Nancy Bair RN Svetlana Banjac RN Alejandro Arroliga MD Cleveland Clinic Foundation, Cleveland, OH

PURPOSE: Previous reports have indicated that the addition of bosentan to the treatment regimen of patients with PAH may allow the successful discontinuation of parenteral prostacyclin analogues. There are no reports of long-term outcomes in such patients.

METHODS: We reviewed the medical records of patients in whom prostacyclin analogues were successfully discontinued after the addition of bosentan. Data collected included demographics, cause of PAH, NYHA class, BNP, echocardiography, and 6 minute walk (6MW).

RESULTS: With the addition of bosentan, prostacyclin analogues were successfully discontinued in eight patients with PAH, mean age 44 yrs. (range 33-61), 7 females/1 male. Etiology of PAH included iPAH (N=4), SLE-PH (N=3), and HIV-PH (N=1). Six patients were taken off intravenous epoprostenol and 2 were taken off subcutaneous remodulin. Mean duration of follow-up after discontinuation of therapy was 27.5 months (range: 12-33). During the course of follow-up 2 patients required the addition of sildenafil. All patients have continued to do very well clinically at last follow-up in NYHA II (N= 7) or NYHA I (N=1), mean 6MW distance 1329 ft, mean BNP 95 pg/ml (range 5-164), and mean RVSP 63 mmHg (range 34-93).

CONCLUSION: With the addition of bosentan, intravenous or subcutaneous prostacyclin analogues may be successfully discontinued in selected patients with PAH.

CLINICAL IMPLICATIONS: In appropriately selected patients, the addition of bosentan helps to the successful discontinuation of prostacyclin analogues without deterioration of the functional capacity over long-term follow up.

DISCLOSURE: Enrique Diaz Guzman Zavala, None.

LONG-TERM BENEFITS OF SILDENAFIL TREATMENT ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

Joanna Pepke-Zaba MD Martin C. Brown Other* Tamiza Parpia PhD Claire Gilbert Gary Burgess MD Pfizer Ltd, Sandwich, United Kingdom

PURPOSE: Sildenafil inhibits PDE5, enhancing cGMP-mediated relaxation of pulmonary vasculature. We report the effects of 6 months oral sildenafil therapy on health-related quality of life (HR-QoL) in pulmonary arterial hypertension (PAH) patients.

METHODS: We assessed the HR-QoL effects of sildenafil (20, 40, or 80 mg tid) in a 12-week, double-blind, placebo-controlled study (SUPER-1) and an open-label extension (SUPER-2). Patients recorded their assessment of HR-QoL using SF-36 and EQ-5D questionnaires. Open-label data are presented for patients who received sildenafil for 24 weeks.

RESULTS: Improvement from baseline to Week 12 was observed in all HR-QoL domains for sildenafil-treated patients, and these benefits were maintained for 24 weeks.

CONCLUSION: Sildenafil improves HR-QoL of PAH patients, and these improvements appear to be maintained for at least 6 months. Effects are strongest in domains addressing the physical impact of health on daily activities and the patient's overall perception of health.

CLINICAL IMPLICATIONS: These patient-reported outcome data demonstrate the benefits of continued sildenafil treatment for PAH.

Mean (95% CI) change in HR-QoL domains from SUPER-1 baseline, for patients who received placebo or sildenafil for 12 weeks (SUPER-1), and patients who received sildenafil for 24 weeks (SUPER-2)

	SUPER-1		SUPER-2
	Placebo (n=70)†	Sildenafil (n=200)†	Sildenafil (n=184)†
SF-36			
Physical functioning	4.5 (0.7, 8.3)	13.7*** (11.0, 16.4)	16.4 (13.5, 19.2)
Role-physical	15.4 (5.6, 25.3)	19.8 (14.2, 25.3)	20.2 (14.0, 26.3)
Bodily pain	4.9 (0.1, 9.7)	7.1 (3.2, 11.1)	6.6 (2.6, 10.6)
General health	0.3 (-3.4, 4.0)	8.0*** (5.7, 10.3)	7.9 (5.5, 10.3)
Vitality	5.5 (1.4, 9.6)	11.7* (8.5, 14.9)	11.4 (7.8, 14.9)
Social functioning	7.3 (1.4, 13.2)	12.9 (9.2, 16.6)	13.9 (9.8, 18.0)
Role-emotional	12.3 (0.9, 23.7)	14.7 (8.1, 21.4)	17.0 (10.3, 23.6)
Mental health	5.3 (1.5, 9.2)	9.2 (6.3, 12.0)	8.9 (5.8, 12.0)
EQ-5D			
Current health state	0.6 (-3.1, 4.3)	7.9** (5.6, 10.2)	10.4 (7.9, 13.0)
Utility index	0.005 (-0.048, 0.059)	0.101** (0.065, 0.136)	0.079 (0.044, 0.115)

†n-numbers varied slightly for each domain due to missing responses

DISCLOSURE: Martin Brown, Grant monies (from industry related sources) Actelion, Encysive, Myogen, Pfizer Ltd, United Therapeutics and Schering AG; Employee Papworth Hospital; Consultant fee, speaker bureau, advisory committee, etc. Actelion, Encysive.

THE ADDITION OF SILDENAFIL TO BOSENTAN THERAPY IN THE TREATMENT OF PULMONARY ARTERIAL HYPERTENSION

Stephen C. Mathai MD* Micah R. Fisher MD Traci Housten-Harris RN Reda E. Girgis MB, BCh Paul M. Hassoun MD Johns Hopkins University, Baltimore, MD

PURPOSE: Pulmonary arterial hypertension (PAH) is a progressive disease that often results in right heart failure and death. Combination therapy targeting several pathways involved in the pathogenesis of pulmonary hypertension has been recommended. In this study, we review

Therapeutic Update in Pulmonary Hypertension, continued

our experience with the addition of sildenafil to bosentan therapy in patients with PAH.

METHODS: Eighteen patients with pulmonary hypertension (12 with PAH related to connective tissue disease, 4 with IPAH, 2 with PAH related to anorexigen use) who received combination therapy with bosentan and sildenafil between January 2002 and April 2005 were included. Bosentan was used as first-line therapy. Sildenafil was added for clinical deterioration based upon symptoms, New York Heart Association (NYHA) assessment, and/or deterioration in six minute walk distance (6MWD). Demographics, clinical data, and hemodynamic data were collected at baseline; clinical data were again collected just prior to adding sildenafil and 1-3 months after starting sildenafil.

RESULTS: Of 18 patients in whom sildenafil was added to bosentan therapy, 4 (22.2%) discontinued therapy due to side effects. One patient died from complications related to progressive right heart failure. Five patients required additional therapy due to disease progression. Prior to starting bosentan therapy, the mean 6MWD was 281.5±115.2m. The mean 6MWD after initiation of sildenafil improved significantly compared to 6MWD prior to initiation (223.6±106.5m vs. 307.6±122.5m, p=0.04). The proportion of patients who were considered NYHA class I or II after the addition of sildenafil therapy versus prior to initiation also increased significantly (0% vs. 27.7%, p = 0.02).

CONCLUSION: Overall, the addition of sildenafil to bosentan therapy improved NYHA class and functional capacity assessed by 6MWD in this group of patients with pulmonary arterial hypertension. However, a significant proportion of patients had to discontinue sildenafil due to adverse effects or required escalation in therapy due to clinical deterioration.

CLINICAL IMPLICATIONS: Addition of sildenafil to bosentan therapy may be of benefit in patients with pulmonary arterial hypertension. Long-term follow-up is needed to ascertain the clinical efficacy and tolerability of this combination of therapies.

DISCLOSURE: Stephen Mathai, None.

Advances in Interventional Bronchoscopy 10:30 AM - 12:00 PM

A MULTI-CENTER TRIAL OF THE INTRABRONCHIAL VALVE FOR TREATMENT OF SEVERE EMPHYSEMA: ONE YEAR RESULTS

Daniel H. Sterman MD* Douglas E. Wood MD Robert J. Mckenna MD Atul C. Mehta MD David E. Ost MD Xavier Gonzalez MD Steven C. Springmeyer MD University of Pennsylvania Medical Center, Philadelphia, PA

PURPOSE: Lung Volume Reduction Surgery for patients with severe emphysema improves pulmonary function, exercise capacity and quality of life, but with significant morbidity and mortality. Minimally invasive therapy could provide palliation with less risk to patients not considered for surgical therapy. The Intrabronchial Valve (IBV, Spiration, Inc., Redmond, WA) blocks distal airflow when placed into bronchi leading to areas of severe emphysema, and is designed to allow passage of secretions and allow removal. We report 12 month results of the initial 30 patients in this pilot trial.

METHODS: Thirty patients with severe upper-lobe predominant emphysema underwent endoscopic placement of multiple IBV into upper lobes via flexible bronchoscopy. Follow-up bronchoscopy was done in all patients after 1 month. Patients were followed at data collected at 1, 3, 6, and 12 month intervals.

RESULTS: Five centers treated 30 patients over a 6 month period between January and July 2004. Patient follow-up ranged from 6 to 12 months. A mean of 6.5 valves per patient were placed bilaterally in the desired segments without difficulty. The procedure ranged from 15 to 120 minutes (mean 61). Discharge occurred within 2 days of the procedure in 28 of 30 patients. Follow-up bronchoscopy at 1-2 months resulted in additional valves, or valve revision, in 17 patients. All valves designated for removal were easily removed up to 3 months after original placement. There have been no deaths, no device migration, no device erosion, and no significant bleeding. Of the 30 patients, 24 or 80%, had no adverse events judged possibly or probably related to the device. Efficacy results are currently being collected and tabulated for the 12 month results.

CONCLUSION: The IBV device is safe, easy to use, and has acceptable procedural complications. Further clinical studies are planned to evaluate its clinical effectiveness for palliation of severe emphysema.

CLINICAL IMPLICATIONS: The IBV may be a minimally invasive alternative to surgical LVRS with substantially less morbidity and mortality.

DISCLOSURE: Daniel Sterman, Consultant fee, speaker bureau, advisory committee, etc. Member (unpaid) of Scientific Advisory Board for Spiration, Inc.; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Spiration Intrabronchial Valve.

ENDOSCOPIC AND SURGICAL TREATMENT OF TRACHEOBRONCHIOMALACIA: A PROSPECTIVE OUTCOME ANALYSIS

Adnan Majid MD* Rabih Bechara MD Yoshihiro Nakamura MD David Feller-Kopman MD Simon Ashiku MD Malcom Decamp MD Armin Ernst MD Tufts-New England Medical Center, Boston, MA

PURPOSE: To demonstrate subjective and objective improvement in patients undergoing central airway stabilization with moderate to severe tracheobronchomalacia (TBM).

METHODS: Single center prospective observational study from July / 2004 to June /2006 of patients referred for evaluation of TBM. Patients were evaluated at baseline (1st visit)and the following information was obtained: demographic data (age, race, gender); co-morbid conditions; spirometry (FEV1); dynamic airway CT and bronchoscopy. If patients were considered for a stent trial based on their symptoms as well as on the bronchoscopic and CT findings then a 6 Minute Walk Test (6MWT) and standardized questionnaires were done: St George's Respiratory Questionnaire (SGRQ), Baseline Dyspnea Index (BDI), ATS dyspnea score and Karnosfsky Performance Status (KPS). Silicone stents were placed in the trachea, main bronchus or both. Patients were scheduled for post-stent follow up after 4-6weeks. On that visit a 6MWT and standardized questionnaires were performed. If symptoms improved (less cough,less dyspnea, better clearing of secretions,less O2 or Off MV) and the patient had a low/intermediate surgical risk, stents were removed and they were scheduled for tracheobronchoplasty in 2 weeks.Patients were scheduled for post-surgical follow up (3rd Visit) at 3 months. At that time patient underwent spirometry (FEV1),dynamic airway CT, bronchoscopy, 6 MWT and standardized questionnaires.

RESULTS: Number of patients:18; patients stented:13; patients with tracheoplasty:10; SGRQ: Mean Score (Baseline N=7): 79, (Post-stent N=7):68, (Post-surgery N=1):54 ;BDI: Mean score (Baseline N=5): 1.8, (TDI post-stent N=5): +3.6, (TDI post-surgical N=2): +8.5; ATS dyspnea score: Mean Score (Baseline N=6):3.3, (Post-stent N=6): 1.5, (Post-surgical N=2): 0.5; KPS: Mean score (Baseline N=6): 63, (Post-stent N=6):81, (Post-surgical N=2): 80; 6MWT: (Baseline N=1): 1200ft, (post-surgical N=1):1500 ft.

CONCLUSION: These results suggest that in carefully selected patients central airway stabilization improves: respiratory symptoms, health related quality of life, functional status and 6 minute walk distance.

CLINICAL IMPLICATIONS: A carefully selected group of patients with symptomatic, moderate to severe TBM should be considered for central airway stabilization.

DISCLOSURE: Adnan Majid, None.

COMPARISON OF FIDUCIAL PLACEMENT FOR CYBERKNIFE® STEREOTACTIC RADIOSURGERY USING CT-GUIDANCE OR FLEXIBLE BRONCHOSCOPY

Cristina A. Reichner MD* Brian T. Collins MD Gregory J. Gagnon MD Shakun Malik MD Carlos Jamis-Dow MD Eric D. Anderson MD Georgetown University Hospital, Washington, DC

PURPOSE: CyberKnife Frameless Image-Guided Radiosurgery with the Synchrony™ Motion Tracking Module is now available for the treatment of thoracic malignancies. CyberKnife offers an alternative for patients with lung cancer or thoracic metastatic disease who are inoperable, poor candidates for conventional radiotherapy because of compromised lung function or have received previous radiotherapy. Gold fiducial markers are required for the treatment planning and aiming of CyberKnife therapy. Fiducials have traditionally been placed under CT-guidance. We describe a novel use of the transbronchial needle aspiration needle (TBNA) for placing these fiducials and report our center's experience compared to CT-guidance.

Advances in Interventional Bronchoscopy, continued

METHODS: We conducted a retrospective review of patients referred for CyberKnife stereotactic radiosurgery at Georgetown University Hospital for treatment of thoracic malignancies. All patients underwent fiducial placement via CT-guidance or flexible bronchoscopy. Fiducials placed by bronchoscopy were loaded in the 19-gauge needle of a 19/21-gauge transbronchial needle. At the desired location, the 19-gauge needle was advanced into the tumor. The 21-gauge needle was extended and the fiducial deployed under fluoroscopic guidance. Data collected included patient demographics, number and location of fiducials placed, and complications associated with their placement.

RESULTS: Twenty-six patients underwent fiducial placement, 11 under CT-guidance and 15 via flexible bronchoscopy. The main diagnosis was non-small cell lung cancer (69%) and the main reason for choosing CyberKnife therapy was previous radiotherapy to the chest. In the CT group, there were 4 pneumothoraces (36%), 50% of them required chest tube drainage. One patient developed a small hemothorax. In the bronchoscopy group, there was no incidence of pneumothorax or significant bleeding. One fiducial embolized via the pulmonary artery without adverse clinical consequence and 1 patient developed bronchospasm requiring mechanical ventilation for 48 hours.

CONCLUSION: Flexible bronchoscopy using a TBNA needle for fiducial placement appears to be safe, especially for central tumors. More experience is needed to determine its applicability for peripheral tumors where CT-guidance is still favored.

CLINICAL IMPLICATIONS: Fiducial placement for CyberKnife stereotactic radiosurgery can be performed under CT-guidance or via flexible bronchoscopy.

DISCLOSURE: Cristina Reichner, None.

BRONCHOSCOPIC IMPLANTATION OF GOLD FIDUCIALS FOR ESTIMATING LUNG TUMOR MOTION DURING GATED RADIATION THERAPY

Rodolfo C. Morice MD* Leendert Keus Carlos A. Jimenez MD Georgie A. Eapen MD Christopher Nelson MS Craig W. Stevens MD George Starkschall PhD The University of Texas MD Anderson Cancer Center, Houston, TX

PURPOSE: Advances in radiation therapy permit high-dose, 3D-focused irradiation to lung tumors. This may improve tumor eradication and reduce normal tissue damage. Tumor motion due to respiration remains a significant problem. The accuracy of breathing gating techniques that depend on abdominal or chest wall motion as surrogates for lung tumor motion have not been well defined. We studied the feasibility of implantating gold markers bronchoscopically in and around lung tumors and evaluated its usefulness for estimating tumor motion during gated radiotherapy.

METHODS: Patients with lung tumor motion greater than 1cm were recruited. Sterile, gold fiducials (ACCULOC®, NMPE) with a diameter of 1.0 –2.0 mm were implanted in a tetrahedral spread around primary lung tumors in 3 patients. Each fiducial was loaded at the tip of a plastic catheter with an inner wire to serve as a releasing plunger. Up to 5 fiducials per patient were placed under fluoroscopic guidance. Respiratory gating dependent on abdominal displacement was used during radiation (RPM, Varian Medical Systems).Images were also captured continuously during the gated treatment to determine fiducials' motion and location relative to the treatment field.

RESULTS: No complications occurred during bronchoscopic implantation of fiducials. Each procedure lasted approximately 15 minutes. In patient #1, three of the five fiducials migrated to the stomach leaving only two for daily imaging. Fiducial #1 was located directly in the tumor and fiducial #2 was located between the posterior chest wall and the tumor. Table 1 displays mean(SD) and maximum fiducial excursions for left-right(LR),superior-inferior (SI),and anterior-posterior(AP)directions as measured on portal images.

CONCLUSION: Bronchoscopic placement of fiducials in and around lung tumors is safe and useful for detecting lung tumor motion. Detection of tumor motion by externally acquired respiratory trace may not be sufficiently accurate for reducing the field margin and may result in inadequate tumor coverage during treatment.

CLINICAL IMPLICATIONS: The use of bronchoscopically-implanted lung fiducials is a promising aid to improving accuracy, better target coverage, and spare more healthy tissue during 3D-conformal radiotherapy for moving tumors.

Fiducial Excursions (cm) - - Patient 1x35 Fractions						
	LR		SI		AP	
Fiducial	1	2	1	2	1	2
Mean	0.23	0.14	0.33	0.57	0.37	0.52
St. Dev.	0.10	0.07	0.15	0.38	0.21	0.36
Max	0.38	0.31	0.59	1.42	0.70	1.29

DISCLOSURE: Rodolfo Morice, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Technique used for implantation of fiducials in the lung is experimental. This protocol was approved by our institutional IRB.

ANESTHESIA FOR FLEXIBLE BRONCHOSCOPY

Andre G. Leite PhD* Rogerio Xavier PhD José Silva PhD Pompéia, Caxias Do Sul, Brazil

PURPOSE: To define which anesthetic method used during flexible bronchoscopy determines better results to facility the procedure, besides to verify which they present minors rates of complications.

METHODS: Eighty patients were analyzed. They were divided in four groups of twenty patients according to drugs used: 1. 200mg of topical lidocaine (LID group); 2. . 200mg of topical lidocaine plus 2mg/kg of propofol (PPF group); 3. 200mg of topical lidocaine plus 20mcg/kg of alfentanil (ALF group); and 4. . 200mg of topical lidocaine plus 0,5mg/kg of midazolam (MID group). The patients were analyzed following some variables showed during and after the bronchoscopy (cardiac dysrhythmia, hypoxemia, cough, additional necessity, lidocaine intoxication, restlessness, respiratory failure, laryngospasm, hypotension, dizziness, vomiting, conscience level and change of anesthetic method). Each variable was given a score to determine a final component score.

RESULTS: The final component score was 4,6±3,9 to PPF group, 7,9±6,6 to ALF group, 10,0±4,5 to LID group and 11,3±5,8 to MID group (p = 0,001).

Table 1—*Variables analyzed during the procedure.*

Component score	PPF n=20	ALF n=20	LID n=20	MID n=20	p
Cardiac dysrhythmia [0 a 4]	0,3±0,4	0,6±0,9	0,4±0,5	0,3±0,4	0,376
Hypoxemia [0 a 4]	0,7±1,1	1,1±1,3	0,5±0,8	1,3±1,4	0,117
Coughing [0 a 6]	1,9±1,6[a]	1,7±1,9[a]	3,4±1,1[b]	3,0±1,8[b]	0,003
Additional lidocaine [0 a 4]	0,6±0,9	0,8±1,0	1,3±1,0	1,3±1,0	0,054
Lidocaine intoxication [0 a 4]	0,0±0,0	0,0±0,0	0,0±0,0	0,0±0,0	—
Restlessness [0 a 6]	0,3±1,0[a]	1,6±1,5[b]	3,3±1,5[c]	1,6±1,9[b]	<0,001
Respiratory depression [0 a 6]	0,2±0,9	0,6±1,5	0,0±0,0	0,8±1,6	0,138
laryngospasm [0 a 1]	0,0±0,0	0,0±0,0	0,0±0,0	0,0±0,0	—
Hypotension [0 a 4]	0,2±0,4	0,5±0,9	0,1±0,3	0,3±0,4	0,287
Dizziness and/or vomiting [0 a 1]	0,0±0,0	0,0±0,0	0,1±0,3	0,0±0,0	0,106
Conscience level [0 a 3]	0,5±0,9[a]	1,2±0,9[b]	0,0±0,0[a]	1,7±1,2[c]	<0,001
Change of the method [0 a 6]	0,0±0,0	0,0±0,0	0,9±2,2	0,9±2,2	0,091

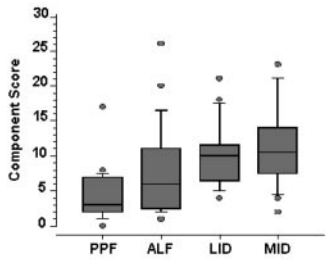
Non-coincident index-letters show significant differences in the Duncan post hoc test. PPF: propofol, ALF: alfentanil, LID: lidocaine, MID: midazolam.

CONCLUSION: The results show the superiority of propofol plus topic lidocaine association use during flexible bronchoscopy when compared with alfentanil, midazolam or lidocaine alone.

CLINICAL IMPLICATIONS: The choice of an effective and low morbidity anesthetic method is basic for the success of a flexible bronchoscopy. This study it demonstrated the superiority of the association of propofol and topic lidocaine in the anesthesia for flexible bronchoscopy.

Advances in Interventional Bronchoscopy, continued

Graphic 1. Final component scores



PPF: propofol, ALF: alfentanil, LID: topic lidocaine, MID: midazolam.

DISCLOSURE: Andre Leite, None.

COMPARISON OF AUTOFLUORESCENCE BRONCHOSCOPY WITH VIDEO WHITE LIGHT AND HIGH MAGNIFICATION VIDEO BRONCHOSCOPY FOR THE DETECTION OF BRONCHIAL DYSPLASIA OR INVASIVE LUNG CANCERS

Johann C. Brandes MD* Loretta Colvin RN Rex Yung MD Johns Hopkins University School of Medicine, Baltimore, MD

PURPOSE: Autofluorescence (AF) Bronchoscopy has been reported to have superior sensitivity in the detection of dysplastic and malignant bronchial epithelium when compared to fiberoptic white light bronchoscopy. This study is designed to compare the quality of fiberoptic autofluorescence bronchoscopy with latest generation white light videobronchoscopy (VB) and high magnification bronchoscopy (HMB).

METHODS: 41 mucosal biopsies were taken from 8 patients with either prior history of lung cancer (#5) or suspected lung cancer (# 3) who underwent diagnostic bronchoscopy. Bronchoscopes used were a Karl-Storz D-light autofluorescence system and the Olympus 160 series videobronchoscope. A prototype Olympus XBF-D160HM (High Magnification) broncosope was used in a subset of patients. Bronchoscopic findings were interpreted by two pulmonologists (JB and RY) and graded on a scale of I (normal), II (inflammation), III (dysplasia) and IV (suggestive of invasive malignancy). Airway biopsies were taken of all grade III and IV lesions, plus major lobar bronchi.

RESULTS: Sensitivity and specificity of the respective bronchoscopic methods were as follows: White light VB including high magnification: sensitivity 30%, specificity 32%, fiberoptic white light: sensitivity: 30%, specificity: 45%, AF: sensitivity: 50%, specificity 37%. False positive results for AF bronchosopy were frequently observed in areas of surgical margins, inflammation and biospsy sites. Lesions missed by AF bronchoscopy were four lesions of squamous metaplasia and one low grade dysplasia. No high grade lesion was missed.

CONCLUSION: Bronchoscopy with AF imaging has superior sensitivity and equal specificity when compared with the newest video white light bronchoscopes and conventional fiberoptic white light bronchoscopy. Video bronchoscopes do not offer additional sensitivity over fiberoptic white light bronchoscopes.

CLINICAL IMPLICATIONS: When diagnostic bronchoscopy with AF was initially compared with fiberoptic white light bronchoscopy, it was suggested that the observed benefit from AF will not persist when compared with the advanced white light video bronchoscopy. Our data confirm a trend towards superiority of AF bronchoscopy over video white light bronchoscopy with or without high magnfication features. Further studies with larger numbers are needed to confirm this trend.

DISCLOSURE: Johann Brandes, None.

Asthma Treatment
10:30 AM - 12:00 PM

EFFECTS OF LONG ACTING BRONCHODILATORS VERSUS LEUKOTRIENE MODIFIERS AS ADD-ON THERAPY TO INHALED CORTICOSTEROIDS IN ASTHMA: A SYSTEMATIC REVIEW

Graeme P. Currie MD* Daniel K. Lee MD Prasima Srivastava MD Aberdeen Royal Infirmary, Aberdeen, United Kingdom

PURPOSE: Despite the widespread use of inhaled corticosteroids, many asthmatic patients experience persistent symptoms. The main alternatives to increasing the inhaled corticosteroid dose are either adding a long acting β2 agonist (LABA) or leukotriene receptor antagonist (LTRA).

METHODS: We performed a comprehensive literature search to highlight the results of all randomised placebo-controlled trials where head-to-head comparisons of both treatments were made in patients using inhaled corticosteroids. We examined their relative effects upon exacerbations, lung function, inflammatory biomarkers and symptoms.

RESULTS: Nine trials were identified which evaluated the effects of LTRAs versus LABAs as add-on therapy to inhaled corticosteroids. Six trials evaluated effects upon exacerbations. In four of these - including the two of longest duration and greatest number of patients - no significant differences were observed between randomised treatments. In most trials (n=8), the addition of a LABA conferred superiority over add-on LTRA in terms of lung function. In the four trials which evaluated effects of treatment upon inflammatory biomarkers, add-on LTRA was significantly superior to LABA. In most trials (n=5) no significant differences were observed between add-on LABA or LTRA in terms of symptoms or quality of life.

CONCLUSION: The addition of a LTRA to an inhaled corticosteroid was generally as effective at reducing exacerbations as adding in a LABA. The addition of a LABA was consistently superior to a LTRA in improving lung function, while the latter treatment conferred significant anti-inflammatory effects to a greater extent.

CLINICAL IMPLICATIONS: In symptomatic asthmatics with impaired airway calibre receiving inhaled corticosteroids, the addition of a LABA would appear appropriate. In those persistent asthmatics with normal airway calibre receiving inhaled corticosteroids, the addition of a LTRA would appear logical in order to attenuate the underlying inflammatory process and relieve symptoms.

DISCLOSURE: Graeme Currie, None.

CONTROL OF AIRWAY INFLAMMATION IS ACHIEVED IN ASTHMA PATIENTS WITH FLUTICASONE PROPIONATE ALONE: ADDING MONTELUKAST PROVIDES NO ADDITIONAL CONTROL OF AIRWAY INFLAMMATION

Paul M. Dorinsky MD* Susan Wilson PhD Steve Yancey MS Donna Reilly BS John Stauffer MD Lisa Edwards PhD Laura Sutton PharmD Ratko Djukanovic MD GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: This randomized, double-blind study evaluated airway inflammation following administration of fluticasone propionate (FP) 100mcg BID or FP 100mcg BID + montelukast (MON) 10mg QD for 12 weeks in 103 subjects with persistent asthma who were symptomatic on short-acting beta2-agonists.

METHODS: Subjects underwent biopsy and BAL at baseline and after 12 weeks of treatment with FP or FP+MON.

RESULTS: Furthermore, clinical asthma control, as assessed by AM and PM PEF, FEV1, albuterol use and rescue-free days was similar with FP+MON compared with FP alone.

CONCLUSION: There was no evidence of incremental improvement in airway inflammation or overall asthma control with the addition of montelukast 10mg QD to FP 100mcg BID.

Median Change at Endpoint	FP 100 mcg BID (n=53)	FP+MON 10mg QD (n=50)	p Value
Eosinophils* Baseline Change	8.93-8.27	7.61-6.88	0.616
Basement membrane thickness (μm) Baseline Change	8.210.92	8.990.74	0.743
Mast cells*† Baseline Change	25.22-5.24	29.27-14.98	0.005
Neutrophils* Baseline Change	21.4319.22	21.8520.92	0.752
CD3+* Baseline Change	53.39-34.09	48.12-49.43	0.303
CD4+* Baseline Change	29.41-21.94	24.30-24.24	0.603
CD8+* Baseline Change	20.59-13.61	17.70-16.50	0.510
CD25+* Baseline Change	0.00-0.47	0.57-0.53	0.266

*Cells in submucosa/mm^2; †mean change

CLINICAL IMPLICATIONS: The common practice of adding a leukotriene modifier to current ICS therapy for broader coverage of inflammation is not supported by this study. The broad anti-inflammatory

effects of ICS adequately control the underlying airway inflammation of asthma. (FPD40014).

DISCLOSURE: Paul Dorinsky, Shareholder shareholder of GSK stock; Employee employee of GSK.

HYDROFLUOROALKANE-134A BECLOMETHASONE DIPROPIONATE IS MORE EFFECTIVE THAN DOUBLE DOSE CHLOROFLUOROCARBON BECLOMETHASONE DIPROPIONATE FOR THE TREATMENT OF SEVERE ASTHMA

Hideto Obata MD* Kenji Ikeda MD Respiratory Division, Saiseikai, Shimonoseki, Japan

PURPOSE: The extent of lung deposition is known to be a major determinant of the therapeutic efficacy of inhaled corticosteroid. The lung deposition of extrafine aerosol of Hydrofluoroalkane-134a Beclomethasone Dipropionate (HFA-BDP) was found to be better compared with the suspension aerosol of chlorofluorocarbon beclomethasone dipropionate (CFC-BDP). The aim of this study is to evaluate pulmonary function in patients with severe asthma when CFC-BDP was changed over to HFA-BDP at half the daily dose.

METHODS: This study enrolled patients (more than 20 years of age) with asthma who used high dose of CFC-BDP and whose symptom were stable with no history of exacerbation for the past year. Twenty-five adult patients with stable asthma and maintained on CFC-BDP, 800 to 2400 μg/day were recruited for this study. In addition, 36% of patients were given oral corticosteroid, 24% anti-leukotriene antagonist, 24% long β2 stimulant , 36% oral xanthine and 100% short acting β2 stimulant . Patients switched from their previous asthma treatment of CFC-BDP to HFA-BDP, at half the daily dose, while all other medications remained unchanged. Pulmonary function test was measured twice at 3 months interval during treatment with CFC-BDP and at3 months after switched over to HFA-BDP.

RESULTS: Switching from CFC-BDP to HFA-BDP significantly improved pulmonary function including predicted FEV1 (from 71.7% to 81.2%), predicted MMF (from 47.0% to 61.0%), predicted V50 (from 39.1% to 50.3%) and predicted V25 (from 38.2% to 48.1%).

CONCLUSION: These data suggest HFA-BDP may improve small airway of patients with severe asthma.

CLINICAL IMPLICATIONS: Asthma therapy. Inhaled corticoteroid. HFA-BDP.

DISCLOSURE: Hideto Obata, None.

LONG-TERM TOLERANCE OF METHOTREXATE ADMINISTERED AS A STEROID SPARING AGENT FOR BRONCHIAL ASTHMA: TWELVE YEARS OF EXPERIENCE

Amalia Moreno MD Christian Domingo MD* Ricard Comet MD Manel Luján MD Miguel Gallego MD Elisa Canturri MD Ana Galera RN Albert Marín MD Corporació Parc Taulí, Sabadell, Spain

PURPOSE: To evaluate the long-term tolerance of methotrexate (MTX) administered in a cohort of steroid-dependent asthmatic patients.

METHODS: Type of study: prospective, observational. Population: patients treated from 1992 to 2004 in our asthma clinic for steroid-dependent asthma (requirement of at least 7.5 mg per day of prednisolone for ≥ than one year). Treatment: 10 mg per week of oral MTX + one weekly dose of folic acid the day after MTX intake. Instrumentation: blood analysis were performed at every three months including leukocyte differential count, CD4 and CD8 level, renal and hepatic function, immunoglobulin level (including IgG subclasses); sputum culture when infection and at the end of the follow-up; hepatic ultrasonography when an accumulated dose of 1,500 mg was reached or whenever hepatic function was altered.

RESULTS: 45 patients have been followed for a mean period of 91.3±39.5 months (range 12-144). The mean accumulated dose of MTX was: 3,499±2,207 mg (range: 470- 7,125). Hematology at entry: Leukocyte: 9,046±2,470/mm3; CD4: 49.3±7.1%; CD8: 25.0±8%; Hct: 40.6±5.2%; Platelet count: 258,543±73,761/mm3; Mean Corpuscular Volume: 89.1±3.9fL; GOT: 19±7 U/L; IgA: 214±113; IgM: 128±90; IgE: 156±331; IgG: 882±344; IgG1: 554±274; IgG2: 279±133; IgG3: 69±58; IgG4: 24±26 (mg/dL). No statistically significant changes were found during the follow-up. Side-effects: 4 patients showed mild elevation of hepatic enzymes that normalized after drug suppression (MTX could be reintroduced and ultrasonography was normal), one alopecia and one asthma. None sputum culture evidenced infection of Aspergillus, Nocardia or Pneumocystis.

CONCLUSION: 1) The concomitant administration of folic acid avoids macrocytic anemia. 2) Liver function should be monitored although seems to be infrequently affected. 3) After liver function recoveries, MTX can be reintroduced safely. 4) Immunity is not affected.

CLINICAL IMPLICATIONS: 1) Long-term administration of a low-weekly dose of MTX is safe. 2) The accumulated dose of 1,500 mg is not a therapeutic limitation.

DISCLOSURE: Christian Domingo, None.

EFFECT OF A RESPIRATORY THERAPIST-DESIGNED ASTHMA MANAGEMENT PROGRAM ON OUTCOMES AND COST OF CARE COMPARED TO A PROGRAM DESIGNED BY NURSES OR STANDARD CARE

Terry S. LeGrand PhD Jay I. Peters MD* David C. Shelledy PhD University of Texas Health Science Center at San Antonio, San Antonio, TX

PURPOSE: To determine if a home asthma management program designed and delivered by respiratory therapists (RTs) is more effective in improving outcomes and reducing cost of care when compared to standard care or a program designed by nurses.

METHODS: Adults treated for asthma exacerbation were offered participation in a three-group (control, nursing, RT), randomized, prospective study. Subjects in the control group (n=60) received standard care. Those in the nursing group (n=58) received home asthma care according to conventional nursing practices over a five week period. Those receiving an RT-designed home asthma management program (n=48) were seen by RTs over five weeks. Each treatment group received education on asthma, equipment use, and medication, as well as training on action to take in the event of an exacerbation. Subjects were followed for 6 months. Quality of life according to SF36 and St. George Respiratory Quotient, hospital and ED admissions, physician office visits, cost of care, asthma episode scores, and patient satisfaction were compared using ANOVA and Chi Square, with $P<0.05$ being considered significant.

RESULTS: Quality of life was improved in the RT group compared to nursing and control. Both nursing and RT groups had fewer ED and physician office visits than control. Cost of care was $3642/subj in the control group and $2324/subj and $2534/subj in the nursing and RT groups, respectively. Asthma episode scores (assessment of subjects' knowledge of what to do during exacerbation) and patient satisfaction scores were higher in the RT group compared to nursing and control.

CONCLUSION: An asthma management program delivered in the home by nurses or RT's results in fewer ED and physician office visits and lower cost of care. Quality of life, asthma episode scores, and patient satisfaction were highest in the RT-designed program.

CLINICAL IMPLICATIONS: A home asthma management program can reduce health care resource utilization and cost of care. An RT-designed asthma management program results in better quality of life, greater knowledge of asthma control, and more satisfaction with asthma care.

DISCLOSURE: Jay Peters, None.

IMPACT OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ON AIRWAY RESPONSIVENESS AND ASTHMA QUALITY OF LIFE IN SUBJECTS WITH ASTHMA AND SLEEP APNEA SYNDROM

Chantal Lafond MD* Frédéric Series MD Catherine Lemière MD Hôpital du Sacré-Coeur, Montréal, PQ, Canada

PURPOSE: CPAP treatment has been inconsistently reported to improve airway responsiveness in asthmatic subjects.The purpose of our research was to determine the effects of nasal CPAP treatment on airway responsiveness and asthma quality of life in asthmatic subjects with obstructive sleep apnea syndrom (OSA).

METHODS: Subjects with stable mild-moderate asthma were recruited following a diagnosis of OSA by polysomnography. They underwent 3 serial methacholine challenge tests and completed baseline specific OSA(QOLAp)and asthma(QOLAs) quality of life questionnaires; then laboratory nasal CPAP titration was performed and CPAP treatment was started. Following 6 weeks of treatment, the questionnaires and 3 serial methacholine challenge tests were repeated, as well as a controlled

polysomnography on CPAP. No change in maintenance anti-asthmatic medication was allowed.

RESULTS: Twenty 49.2 ± 8.9 year old subjects (7F,13M) completed the study. Following 6 weeks of nocturnal CPAP used on the average of 7 hours ± 1, at a pressure of 9 cm H20 ± 3, the apnea-hypopnea index significantly dropped from 48 ± 24 to 3 ± 2 ($p<0.001$). No significant change in FEV1 (80.3 ± 13.6% pred) or PC20 (2.5 ± 1.8 mg/ml) occurred after CPAP treatment compared with baseline (82.2 ± 13.6% pred, 2.2 ± 1.4 mg/ml respectively). QOLAp significantly improved from 4,1 ± 1,4 at baseline to 6,0 ± 1,0 at the end of the study ($p<0.001$) . There was also a significant improvement in QOLAs from 5,0 ± 1,2 at baseline to 5,8 ± 0,9 at the end of the study ($p=0.001$). QOLAs at baseline was inversely correlated with the BMI of the patient (rho=-0.5, $p=0.01$) and the improvement in QOLAs after CPAP treatment was positively correlated with the BMI (rho=0.5, $p=0.03$). There was no correlation between the improvement of QOLAp and QOLAs.

CONCLUSION: Although CPAP treatment does not alter airway responsiveness, it improves asthma quality of life in OSA and asthmatic patients.

CLINICAL IMPLICATIONS: Impact of CPAP treatment on the control of asthma in OSA and asthmatic patients should be assessed on the long term.

DISCLOSURE: Chantal Lafond, None.

Cardiac Issues in Critical Care
10:30 AM - 12:00 PM

DECREASED ANTIOXIDANTS, INCREASED REACTIVE OXIDANTS AND INCREASED LIPID PEROXIDATION IN IRRADIATED TOTAL PARENTERAL SOLUTIONS INCREASE OXIDANT GENERATION IN CRITICALLY ILL PATIENTS

Guy A. Richards MB, BCh* Haden White MB, BCh Heidi Grimmer BSc C. Ramoroka BSc Kalavati Channa BSc Mark Hopley MB, BCh Mary Gulumian PhD University of the Witwatersrand, Johannesburg, South Africa

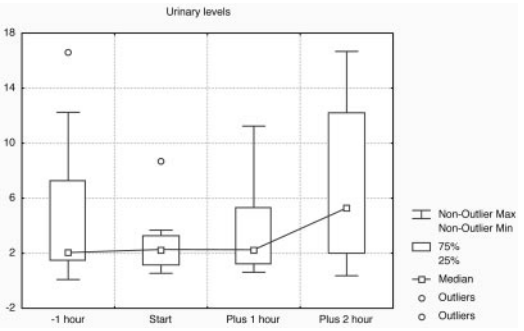
PURPOSE: To assess the effect of irradiation on total parenteral nutrition solutions with reference to reactive oxidant production and decline in antioxidant potential and the effect that these solutions have on critically ill patients.

METHODS: Laboratory investigation utilizing irradiated and non-irradiated, commercially available, total parenteral nutrition (TPN) solutions.Interventions: Measurements of vitamin E and malondialdehyde (MDA) levels. The PBN (α- phenyl-n-test-butylnitrone) spin trap was utilized to measure the presence of free radicals and TEMPOL (2,2,6,6-tetramethyl-4-hydroxy-piperidine-oxyl) was utilized to assess antioxidant capacity. Irradiated TPN was administered to 12 patients and plasma and urinary isoprostanes were measured.

RESULTS: Irradiation reduced Vitamin E levels significantly ($p<0.0025$). MDA products were present in both samples, but were increased significantly ($p<0.0001$) in irradiated samples as were free radicals measured by PBN spin trapping. The irradiated sample had a higher scavenging capacity of TEMPOL free radical which was not initially expected. This was confirmed to be due to depletion of nutrient antioxidants in irradiated samples.Urinary isoprostanes increased by 4.24 units (95% confidence interval: 0.03 to 8.21) 2 hours after administration of irradiated TPN. ($p<0.014$).

CONCLUSION: Lipid hydroperoxides are formed in TPN bags and this is increased by irradiation. This is associated with a significant reduction in Vitamin E. In addition urinary isoprostanes were increased significantly in those that received irradiated TPN. This is relevant in that oxidant stress influences outcome and is associated with development of multiple organ dysfunction. TPN is therefore potentially pro-inflammatory because it is depleted in antioxidants and preformed lipid hydroperoxides are present in the solution.

CLINICAL IMPLICATIONS: Total parenteral nutrition whether irradiated or not, may be pro-inflammatory. Enteral nutrition is preferred, however if not possible, consideration should be given to the co-adminisrtation of additional antioxidant vitamins.



DISCLOSURE: Guy Richards, None.

EFFECT OF TEMPERATURE ON SUPEROXIDE PRODUCTION BY THP1 MONOCYTES

Victor K. Salloum MD* Saikat Chakraborty PhD Akhil Bidani MD UT Health Science Center, Houston, TX

PURPOSE: The respiratory burst of immune cells is an integral part of host defense. In this study, we investigate the effect of temperature (between 25°C and 42°C) on the dynamics of superoxide (O2-) production during the respiratory burst in PMA-activated THP-1 monocytes.

METHODS: The dynamics of superoxide production of PMA-activated monocytes is measured at each temperature (between 25°C and 42°C) as the superoxide dismutase-inhibitable reduction of cytochrome c using the classical spectrophotometric assay.

RESULTS: At each temperature, the cumulative O2- concentration shows a lag period with low O2- production, followed by a period of accelerated production and then a slow saturation to a steady state concentration. Our measurements show that both the dynamics of O2-production and the maximum amount of O2- produced at steady state are affected by temperature, with the latter being affected more profoundly. The steady state O2- concentration shows a triphasic response with respect to temperature – an initial period of gradual increase between 25°C and 32°C is followed by a period of sharp rise in steady state concentration between 32°C and 37°C, and subsequently a fast monotonic decrease when temperature exceeds 37°C.

CONCLUSION: The observed rate of O2- production is proportional to the intracellular concentration of the fully-assembled activated membrane-bound enzyme NADPH oxidase (NOX). Based on our mathematical model, we speculate that between 25°C and 32°C, the assembly of NOX occurs in the transport limited regime, the rate of which increases weakly with temperature. For temperatures between 32°C and 37°C, the activation of NOX occurs in the kinetically controlled regime and thus increases rapidly with temperature. At temperatures above 37°C, the assembled NOX deactivates and/or internalizes rapidly, leading to a fast monotonic decrease of steady state O2-concentration with increasing temperature.

CLINICAL IMPLICATIONS: Hypothermia has been advocated as a means to minimize ischemia reperfusion injury as might occur cerebrovascular accidents and acute myocardial infarction. Our results indicate that hypothermia (as well as fever) could lead to a depression of immune cell function.

DISCLOSURE: Victor Salloum, None.

ELEVATED TROPONIN LEVEL IS NOT SYNONYMOUS WITH MYOCARDIAL INFARCTION

Nitin Mahajan MD* Yatin Mehta MD Malcolm Rose MD Jacob Shani MD Edgar Lichstein MD Maimonides Medical Center, Brooklyn, NY

PURPOSE: Elevated troponins in the absence of angiographically visible coronary lesions are seen in upto 10-15% of those undergoing angiography for suspected coronary artery disease. It is important to identify the cause of myonecrosis in such patients to devise appropriate treatment plans. This retrospective study aims to elucidate the etiology and pathophysiology of elevated cardiac Troponin I (cTnI) in patients with normal coronary arteries on angiography.

METHODS: We retrospectively identified 1551(8.6%) patients with normal coronary arteries from our catheterization database from Jan 2000-Jun 2004. Elevated Troponin levels were found in 217 (14%)

patients. Surgical patients were excluded to form group I (n=144). Group II comprised of age and gender matched patients with myocardial infarction and coronary artery disease.

RESULTS: The etiology of elevated cTnI in group I is shown in table 1. The commonest cause of elevated cTnI was tachycardia followed by myocarditis. Significantly higher prevalence of atherosclerotic risk factors, with the exception of smoking, is seen in group II (Figure 1). Patients in group I have significantly higher left ventricular ejection fractions.

CONCLUSION: This is the largest series on retrospective study of patients with elevated troponin levels. Acute myocardial infarction is a clinical diagnosis. Elevated Troponin reflects myonecrosis as a result of direct myocardial injury and an imbalance between oxygen supply and demand. It does not equate to myocardial infarction. The laboratory is an aide to, not a replacement for,informed decision making.

CLINICAL IMPLICATIONS: Elevated troponin levels do not necessarily imply myocardial infarction. Elevated troponin levels should be interpreted in the underlying clinical context.

Table 1—*The Causes of Elevated Troponin in Group I.*

Event	Number of events Proportion of patients, % (N)
Congestive Heart Failure (Ef<25)	8 (12)
AICD/ Resuscitation/ Defibrillator	3 (4)
Myocarditis	16 (23)
Pericarditis	5 (7)
Cerebrovascular Accident	1 (2)
Sepsis	3 (4)
Collagen Vascular Disease	1 (2)
Severe Aortic Stenosis (Aortic Area < 0.1)	6 (8)
Left Anterior Descending artery bridging	4 (5)
Documented Coronary Spasm	1 (2)
Tachycardia (±hemodynamic compromise)	24 (35)
Hypertensive Emergency	1 (1)
Microvascular Ischemia	2 (3)
Gastro intestinal Bleeding	6 (8)
Myocardial Concussion	1 (1)
Hypercoagulable State	2 (3)
Pulmonary Embolism	1 (2)
Diabetic Ketoacidosis	1 (2)
Chronic Obstructive Pulmonary Disease exacerbation	1 (1)
Left Ventricular Hypertrophy	1 (2)
Septic Shock	4 (5)
Renal Failure	1 (2)
Unknown	7 (10)

DISCLOSURE: Nitin Mahajan, None.

UTILITY OF TRANSESOPHAGEAL ECHOCARDIOGRAPHY DURING INTRAOPERATIVE CARDIAC ARREST

Stavros G. Memtsoudis MD* Peter Rosenberger MD Michaela Noveva MD Holger K. Eltzschig MD Annette Mizuguchi MD Prem Shekar MD Stanton K. Shernan MD John A. Fox MD Brigham and Women's Hospital, Harvard Medical School, Boston, MA

PURPOSE: To examine the usefullness of Transesopahegeal Echocardiography (TEE) during non-cardiac surgery intraoperative cardiac arrest.

METHODS: Patients who suffered an intraoperative cardiac arrest during non-cardiac surgery (1995-2002) were included in the analysis. Surgical operative notes and anesthesia records were reviewed and pertinent data collected. Echocardiogarphy records and review of videotape recordings were used and evaluated for findings. The impact of echocardiographic results on treatment was assessed. Finally, survival data were recorded.

RESULTS: Twenty-two patients (15 male / 7 female) were identified, who suffered an intraoperative cardiac arrest during non-cardiac surgical procedures. Median age was 60.5 years (range 29 – 84 years). In all patients the ACLS protocol was implemented. In 86,4% (19 of 22) of patients a primary diagnosis could be established with TEE. In 81,8% (18 of 22) of patients the TEE findings aided in their further management, and in 54,5% (12 of 22) of patients specific surgical interventions were implemented based on these findings. Diagnosis with TEE revealed signs of myocardial ischemia in 27,3% (6 of 22) of all patients and 3 of these patients underwent emergency coronary artery bypass grafting. In 40,9% (9 of 22) off all patients thromboembolic events of the central vasculature were diagnosed. In 6 patients clots were visualized directly and in 3 indirect signs of pulmonary embolism were identified. Five patients underwent emergency pulmonary embolectomy/thrombectomy. Nine percent (2 of 22) of all patients with pericardial tamponade were treated by pericardiotomy. In 9,1% (2 of 22) of all patients the diagnosis of hypovolemia was made and these patients responded well to fluid resuscitation. Fourteen patients (63%) survived to leave the operating room. Seven (31,8%) of these patients were discharged, while 8 (36,4%) succumbed shortly after the intra operative arrest.

CONCLUSION: TEE was the primary source for diagnosis in 86,4% of all patients. In the majority of patients these findings influenced management.

CLINICAL IMPLICATIONS: Despite limitations of this analysis, we recommend the employment of TEE in a cardiac arrest situation in the operating room whenever possible.

DISCLOSURE: Stavros Memtsoudis, None.

RESUSCITATIVE HYPOTHERMIA AFTER CARDIAC ARREST: PERFORMANCE IN A COMMUNITY HOSPITAL

Cindy Grimes RN Rhonda Anderson MSN Todd Horiuchi MD Mauricio Concha MD Bruce Fleegler MD Kenneth Hurwitz MD* Sarasota Memorial Hospital, Sarasota, FL

PURPOSE: Induced hypothermia improves outcome after cardiac arrest due to ventricular fibrillation. We studied induced hypothermia in a community hospital setting after cardiac arrest due to any cause.

METHODS: A case-control study was conducted in a publicly owned, non-academic, acute care hospital. Thirty-eight patients who underwent induced hypothermia were compared to 103 patients who did not undergo hypothermia. After resuscitation from cardiac arrest, patients underwent hypothermia using an established protocol at the discretion of the treating clinicians. Hypothermia was achieved with either external devices or an intravascular cooling catheter system. Outcome measures included mortality, neurologic recovery, and length of stay (LOS).

RESULTS: The groups were similar in age, sex, APACHE III score, and Glasgow Coma Score (GCS). Hospital mortality in the hypothermia group was 53% versus 71% in the control group (p=0.07). Hospital mortality in 10 patients treated with intravascular cooling was 40%. Compared to Apache III predicted mortality, the hypothermia group mortality ratio was 0.76, versus 1.4 for the control group. Among survivors, the change in GCS from admission to ICU discharge was 7.2 +/- 4.0 (baseline 4.4, discharge 11.7) in the hypothermia group and 6.6 +/- 4.3 (baseline 4.0, discharge 10.6) in the control group (p=0.32). Also among survivors, the ICU LOS was 2.6 +/- 3.5 days less than Apache III predicted in the hypothermia group versus 0.5 +/- 6.8 days less in the control group (p=0.08).

CONCLUSION: Induced hypothermia following cardiac arrest performs well in a community hospital setting. The intravascular cooling catheter was a safe, effective means of inducing hypothermia with a trend towards improved outcomes. Induced hypothermia may be applicable to all cardiac arrest patients regardless of cause.

CLINICAL IMPLICATIONS: Induced hypothermia is safe, simple, and inexpensive. Hospital protocols may help to ensure timely application of this important intervention. Intravascular cooling techniques show promise in terms of ease of use, effectiveness of cooling, and maintaining accessibility to the patient. Further study is needed to determine the optimal patients and techniques for therapeutic hypothermia.

DISCLOSURE: Kenneth Hurwitz, None.

Cardiac Issues in Critical Care, continued

EFFECTS OF VASOPRESSIN ON HEMODYNAMICS IN CARDIOGENIC SHOCK

Walter H. Migotto MD* Francesco Simeone MD Houman Dahi MD Tulane, Kenner, LA

PURPOSE: Assess the effects of vasopressin on hemodynamics of patients with Cardiogenic Shock (CS).

METHODS: Retrospective chart review of 8 patients with CS defined as mean arterial pressure (MAP) < 60 mm Hg, decreased organ perfusion, cardiac index (CI) <2.5 L/min/m2 and pulmonary capillary occlusion pressure >15 mm Hg, who had a pulmonary artery catheter and received a continuous infusion of vasopressin.

RESULTS: The CI, after an infusion of vasopressin at a dose of 0.02 to 0.5 U/min, increased from a baseline of 1.8 to 2.3 L/min/m2 at 12 (+ 4) hours. The MAP increased from 53.3 to 62.75 mm Hg and the urine output from 21.8 to 39.9 ml/hour at 12 (+ 4) hours. Six out of 8 patients had an increased CI within the first 12 hours. Two had a drop in CI within the first 12 hours and one had a drop in CI at 24 hours. Of the 3 patients that had worsening in CI, one had a drop from 2.5 to 1.4 L/min/m2 at 12 hours on a dose of 0.08 U/min. Another had a drop from 2 to 1 L/min/m2 when the dose was increased from 0.1 to 0.2 U/min. A third, who initially had an increase in CI from 2.4 to 2.9 L/min/m2 on 0.1 U/min, had a subsequent drop to 1.3 L/min/m2 at 48 hours when the dose was increased from 0.1 to 0.5 U/min.

CONCLUSION: The use of vasopressin in CS caused, in this case series, an average increase in CI of 27.8 % and an average increase in urine output of 45.7% within the first 12 hours compared to baseline. CI decreased only when higher doses of vasopressin were used (in the range of 0.08 to 0.5 U/min).

CLINICAL IMPLICATIONS: The use of vasopressin in CS should be avoided at higher doses (> 0.08 U/min). The use of "physiologic" doses may deserve furtherinvestigation.

DISCLOSURE: Walter Migotto, None.

Interstitial Lung Disease
10:30 AM - 12:00 PM

SERIAL MEASURES OF PULMONARY ARTERY PRESSURES IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

Steven D. Nathan MD* Shahzad Ahmad MD James Koch MD Scott Barnett PhD Niv Ad MD Nelson Burton MD Inova Heart and Vascular Institute, Falls Church, VA

PURPOSE: Mortality rates are high among patients with idiopathic pulmonary fibrosis (IPF). Pulmonary function studies measures are imprecise at predicting those patients at highest risk of dying. This could partially be explained by the development of pulmonary arterial hypertension (PAH) in some patients that is not appreciated with conventional physiologic measurements. We sought to characterize the prevalence and incidence of PAH by analyzing pulmonary artery (PAP) pressures at two time points in patients disease course.

METHODS: Retrospective review of all patients with IPF who underwent lung transplantation from 2000-2005. PA pressures from the patients transplant evaluation and from the time of their transplant surgery were analyzed and compared. PAH was defined by a mean PAP>25mmHg.Pulmonary function data from their initial evaluation were analyzed for predictors of PAH and progression of PAH.

RESULTS: During the study period, there were 38 patients with IPF who underwent lung transplants and who had serial PAPs available for analysis. The mean PAP at the time of transplant evaluation was 22mmHg. 13/38 patients (34%) qualified as having PAH at this time. The mean PAP at the time of transplant was 33mmHg with 32/38 (84%) of patients qualifying as having PAH. The average time period between PAP measurements was 267 days (range: 33-814). The mean rate of change of PAPs was 3.9mmHg/month. Baseline FVC and Dlco did not predict the presence of PAH or the serial development thereof.

CONCLUSION: The prevalence of PAH is fairly common in patients with advanced IPF who require evaluation and listing for transplant. Based on serial measures of PAPs, it appears inevitable that most patients will develop PAH during their disease course.

CLINICAL IMPLICATIONS: PAH might be a significant contributor to the morbidity and mortality of patients with IPF.

DISCLOSURE: Steven Nathan, None.

COMPLICATIONS OF VIDEO ASSISTED THORACOSCOPIC LUNG BIOPSY IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

Mary E. Kreider MD* Nadia Ahmad MD John Hansen-Flaschen MD Larry Kaiser MD Milton Rossman MD John Kucharczuk MD Joseph Shrager MD University of Pennsylvania School of Medicine, Philadelphia, PA

PURPOSE: Current practice guidelines recommend video assisted thoracoscopic lung biopsy (VATSLB) for patients with interstitial lung diseases (ILDs) who do not have diagnostic CT scans. However, VATSLB in this population carries risk. The reported incidence of death after biopsy in patients with idiopathic pulmonary fibrosis (IPF) is up to 17%. We examined the morbidity and mortality associated with VATSLB in a group of outpatients with undefined ILD.

METHODS: A retrospective cohort study of 68 outpatients referred for VATSLB of undefined ILD over a ten-year period. Information on post-operative mortality, prolonged air leaks (≥ 4 days or readmission for pneumothorax), pneumonias, worsening oxygenation, and re-admissions was abstracted from charts to calculate the incidence of these outcomes.

RESULTS: Average age was 57.9 years (range 38-84). The median length of stay was 2 (range 1-43) days and the median duration of chest tube therapy was 1 (range 1-11) day. Incidence of outcomes (95% CI): post-operative mortality 4.4% (3 of 68 patients) (0.9%-12.4%), prolonged air leak 11.8% (5.2%-21.9%), post-operative pneumonia 2.9% (0.4%-10.2%), worsening oxygenation 14.8% (6.6%-27.1%), readmission within one month 9.0% (3.4%-18.5%). Subsequent pathologic diagnoses included usual interstitial pneumonitis (UIP) (34%), non-specific interstitial pneumonitis (6%), desquamative interstitial pneumonitis/ respiratory bronchiolitis associated interstitial lung disease (4%), chronic hypersensitivity (8%), sarcoidosis (9%), honeycomb lung (9%), normal (3%), acute interstitial pneumonitis (2%), bronchiolitis (2%), emphysema (2%), and unclassifiable (22%). All three subjects who died had UIP. These patients were intubated for hypoxemic respiratory failure on post-operative days 2-8. Each had pulmonary embolus and congestive heart failure (CHF) excluded with appropriate clinical testing, and was treated with antibiotics and high dose steroids. One other subject was re-intubated post-operatively; she responded to diuresis for newly identified CHF.

CONCLUSION: VATSLB for outpatient subjects with undefined ILD is associated with appreciable surgical mortality/morbidity. The risks may be greatest in those who are subsequently diagnosed with IPF.

CLINICAL IMPLICATIONS: Further investigation is needed to better define both the exact incidence of these outcomes and risk factors for their development.

DISCLOSURE: Mary Kreider, None.

BASAL LEVELS OF NERVE GROWTH FACTOR ARE HIGHER IN CO-CULTURED HUMAN A-549 TYPE II ALVEOLAR EPITHELIAL CELLS WITH HUMAN FIBROBLASTS THAN IN EITHER CELL LINE CULTURED ALONE

Susan M. Rohr DO* Art Heires BS Anthony Floreani MD University of Nebraska Medical Center, Omaha, NE

PURPOSE: To illustrate that nerve growth factor plays a significant role in the cellular millieu of human A-549 type II alveolar epithelial cells and human fibroblasts in vitro.

METHODS: Human A-549 type II alveolar epithelial cells and human fibroblasts were cultured alone and in a co-culture transwell membrane insert system with LHC-9 media. Basal nerve growth factor levels were measured for all conditions using a commercially available direct immunoassay system with a detection range of 7.8 to 500 pg/ml.

RESULTS: The basal levels measured in single cell culture systems was 0-20 pg/ml for both the fibroblasts and A-549 type II alveolar epithelial cells in isolated culture. Nerve growth factor levels in the co-culture system were consistently higher at 50-100 pg/ml.

CONCLUSION: Basal nerve growth factor levels are influenced by local cellular interaction between human fibroblasts and human A-549 type II alveolar epithelial cells in a co-cultured system. The levels obtained in the co-culture system are significantly higher than basal levels obtained from either cell line alone.

Interstitial Lung Disease, continued

CLINICAL IMPLICATIONS: Nerve growth factor may serve as an important immunoregulator promoting the T-helper 2 (TH2) cell cytokine response observed in patients with asthma and idiopathic pulmonary fibrosis. Nerve growth factor may play a key role in regulating cell survival and cell death by interacting with Tyrosine kinase A and p75 neurotrophin receptors. The elevation of nerve growth factor in the co-cultured system supports the theory that there are important interactions between human fibroblasts and A-549 type II alveolar epithelial cells in vitro that influence nerve growth factor secretion. This interaction likely translates to an important in vivo relationship between alveolar and airway epithelial cells and lung fibroblasts that influences autocrine and paracrine secretion of nerve growth factor. We suggest there is a disruption in this balance that promotes surges in nerve growth factor resulting in a TH2 cell inflammatory response, fibroblast transformation, proliferation, and cell survival that contributes to the airway remodeling and fibrosis observed in patients with asthma and idiopathic pumonary fibrosis.

DISCLOSURE: Susan Rohr, None.

INFLAMMATORY MARKERS IN BRONCHOALVEOLAR LAVAGE FLUID OF PATIENTS WITH IDIOPATHIC PULMONARY ALVEOLAR PROTEINOSIS

Shi-Chuan Chang PhD Fang-Chi Lin MD* Yi-Chu Chen BS Department of Medicine, Yuan-Shan Veteran Hospital, I-Lan, Taiwan ROC

PURPOSE: Idiopathic pulmonary alveolar proteionsis (iPAP) is regarded as an autoimmune disease since anti-GM-CSF antibodies could be detected in blood and bronchoalveolar lavage fluid (BALF) of the patients. However, inflammation, the cardinal feature of autoimmune disease, is rarely demonstrated in lung parenchyma of the patients with iPAP. In this study, we measured inflammatory markers and compared the differences between patients with iPAP and inflammatory lung diseases.

METHODS: Tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, IL-8, surfactant protein D (SP-D) and KL-6 were measured in BALF using enzyme-linked immunosorbent assays in 12 iPAP, 13 idiopathic pulmonary fibrosis (IPF), and 17 patients with connective tissue disease (CVD), and 17 controls without lung diseases.

RESULTS: Compared with controls, iPAP patients had higher values of TNF-α, IL-6, IL-8, SP-D and KL-6 in BALF. The patients with iPAP had significantly higher levels of BALF TNF-α, SP-D and KL-6 than did those with IPF and CVD. BALF values of IL-8 were comparable between the patients with iPAP and IPF, but significantly higher in patients with iPAP than in those with CVD. In iPAP patients, the levels of BALF IL-8 were highly correlated with the values of serum LDH; however, the levels of BALF KL-6 were negatively correlated with the value of PaO2.

CONCLUSION: Increased inflammatory cytokines, chemokines and markers of lung injury in BALF of the patients with iPAP highly suggested that inflammation of lung parenchyma might occur in iPAP. The reasons why inflammation of the lung has not yet been demonstrated in iPAP remain unknown. Further studies are needed to verify the issues.

CLINICAL IMPLICATIONS: Lung inflammation may play a relevant role in pathogenesis of iPAP.

DISCLOSURE: Fang-Chi Lin, None.

PIRFENIDONE MEDIATES DIFFERENTIAL EFFECTS ON LIPOPOLYSACCHARIDE-INDUCED CYTOKINE EXPRESSION IN HUMAN PERIPHERAL MONONUCLEAR CELLS

Roderick Phillips PhD* Tony Wang MD Lawrence M. Blatt PhD Scott Seiwert PhD InterMune, Inc., Brisbane, CA

PURPOSE: Idiopathic pulmonary fibrosis (IPF) is a fatal, progressive disorder for which there is no FDA-approved therapy. Although the etiology is unknown, augmented proinflammatory mediator production (such as tumor necrosis factor [TNF]–α and interleukin [IL]-1β), coupled with increased proinflammatory cell recruitment and deposition of extracellular matrix (ECM) proteins, are thought to be crucial steps in disease development. One promising treatment for IPF is pirfenidone (PFD). To support ongoing clinical studies we investigated the biological basis of pirfenidone activity.

METHODS: Human peripheral blood mononuclear cells (PBMCs; 100,000 cells per well in triplicate) were pretreated with PFD (5 mM to 5 μM) for 1 h and then stimulated with lipopolysaccharide (LPS; 1 μg/mL to 0.01 ng/mL) for 1, 2, 4, 8, or 24 h. Supernatants were then collected and assayed for protein expression using a multiplex cytokine platform (Bio-Rad, Inc.).

RESULTS: PFD had differential effects on cytokine expression in PBMCs following LPS stimulation. We find that half-maximal inhibition of TNF-α secretion (TNF-α EC50) occurred with between 720 μM and 962 μM PFD, depending on the concentration of LPS. Given that the maximal human serum concentration of PFD is 88 μM following 800 mg TID, these data indicate TNF-α levels would maximally be reduced by 8.6% in patients receiving this regimen. Simultaneous monitoring of 16 other cytokines demonstrated that PFD additionally inhibited expression of GM-CSF, IFN-γ, IL-1β, IL-2, and IL-4, but augmented expression of IL-10, and MCP-1.

CONCLUSION: The effects of PFD on LPS-induced cytokine expression in PBMCs are likely more complex than initially thought. Pirfenidone reduces expression of TNF-α and therefore may reduce expression of ECM components. Since IL-10 pretreatment in mouse models of liver, lung, and pancreatic fibrosis reduced the severity of fibrosis by down-regulating chronic inflammatory responses, our observation that PFD increases IL-10 expression suggests that PFD may modulate the onset of fibrosis by more than one mechanism.

CLINICAL IMPLICATIONS: Pirfenidone may prove beneficial for the treatment of IPF; further clinical trials are warranted.

DISCLOSURE: Roderick Phillips, Shareholder; Employee All authors are employees of InterMune, Inc.

CD8+ T LYMPHOCYTES AND NEUTROPHILS IN BRONCHOALVEOLAR LAVAGE FROM PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS ARE ASSOCIATED WITH CLINICAL AND FUNCTIONAL PARAMETERS

Spyros A. Papiris MD Androniki Kolintza MD Effrosyni D. Manali MD* Marilena Karatza PhD Josef Milic-Emili MD Charis Roussos MD Zoe Daniil MD Attikon University Hospital, Athens, Greece

PURPOSE: To investigate the relationship between BAL cells, including macrophages, neutrophils, eosinophils, T lymphocytes (TLs) (CD3+) and their subpopulations (CD4+, CD8+, CD4+/CD8+ ratio and CD8+38+) with lung function indices and grade of dyspnoea, in IPF patients.

METHODS: Twenty six patients with IPF were studied, 17 males age of 63 ± 9 years (mean ± SD). Differential BAL cell counts were evaluated on May-Gr_nwald-Giemsa stained cytospins and expressed as percentages of total cells. BAL lymphocyte subsets were evaluated by flow cytometry and expressed as percentages of lymphocytes. FEV1, FVC, TLC, DLCO, PaO2, PaCO2 and P(A-a)O2 were measured in all. The level of dyspnoea was assessed by the Medical Research Council (MRC) chronic dyspnoea scale.

RESULTS: CD8+ TLs showed a positive correlation with the MRC (r=0.462, p=0.023), the CD4+/CD8+ ratio an inverse (r=-0.537, p=0.006). Activated CD8+ TLs, identified by the expression of the activation marker CD38+, were inversely related to the FEV1 and FVC (r=-0.533, p=0.032 and r=-0.592, p=0.02, respectively). The neutrophils showed a significant positive correlation with the MRC (r=0.421, p=0.032), and negative correlations with the DLCO (r=-0.535, p=0.005), PaO2 (r=-0.436, p=0.033), and PaCO2 (r=-0.516, p=0.010). No other significant correlations could be identified.

CONCLUSION: In IPF BAL neutrophils and CD8+ TLs are associated with the grade of dyspnoea and functional parameters of disease severity.

CLINICAL IMPLICATIONS: Both BAL neutrophils and CD8+ TLs might play a role in IPF pathogenesis.

DISCLOSURE: Effrosyni Manali, None.

Lung Cancer: Cell Type, Gender and Preoperative Assessment
10:30 AM - 12:00 PM

THE RELATIONSHIP BETWEEN LUNG FUNCTION AND NON-SMALL CELL LUNG CANCER IN MEN AND WOMEN

Samir Malhotra MD* Stephen Lam MD S.F. P. Man MD Wei Q. Gan MD Don D. Sin MD Department of Medicine (Respiatory Division), University of British Columbia & T, Vancouver, BC, Canada

PURPOSE: Reduced forced expiratory volume in one second (FEV1) has been linked to non small cell lung cancer (NSCLC). However, it is

Lung Cancer: Cell Type, Gender and Preoperative Assessment, continued

unclear what NSCLC histologic subtypes are associated with FEV1. Moreover, there is little information on whether sex modifies this relationship. We investigated the relationship between FEV1 and subtypes of NSCLC, and if it is modified by sex.

METHODS: We used data, including FEV1, from patients who underwent tumor resection for NSCLC at a teaching hospital in Vancouver. We divided the cohort into quartiles of predicted FEV1. Using logistic and linear regression we determined whether FEV1 was related to the occurrence of adeno or squamous cell carcinoma in men and women.

RESULTS: There were 610 patients in the study (36% females). Women were more likely to have adenocarcinoma than men (72% vs. 40% respectively; $p<0.001$). In women, there was no significant relationship between FEV1 and risk of any histological subtypes of NSCLC. At all FEV1 values, 70% of all NSCLC were adenocarcinoma in women. However, in men there was an inverse relationship between the risk of adenocarcinoma and FEV1. The lowest quartile of FEV1 was 47% less likely to have adenocarcinoma compared with the highest FEV1 quartile (adjusted odds ratio, 0.52; 0.28 to 0.98; p for trend 0.028). The reverse was observed for squamous cell carcinoma.

CONCLUSION: In individuals undergoing resection for NSCLC, the risk of adenocarcinoma and squamous cell carcinoma of the lung varies as a function of FEV1, independent of smoking intensity in men but not in women. In women, adenocarcinoma predominates across all levels of FEV1.

CLINICAL IMPLICATIONS: Women and men may differ in their airway biology, which may be responsible for the differential susceptibility to histologic subtypes of NSCLC. Animal models suggest that the females airway inflammatory response to cigarette smoke is increased. Further research into the role of inflammation in adenocarcinoma as well as hormonal, molecular and genetic differences will aid in the understanding of disease modifying effects of gender in individuals with NSCLC.

DISCLOSURE: Samir Malhotra, Grant monies (from sources other than industry) Dr. Don Sin: Canada Research Chair (Respiration) and a Michael Smith/St. Paul's Hospital Foundation Professorship in COPD.

GENDER DIFFERENCES IN SURVIVAL OF PATIENTS WITH NON-SMALL CELL LUNG CANCER: DO TUMORS BEHAVE DIFFERENTLY IN WOMEN?

Juan P. Wisnivesky MD* Michael Iannuzzi MD Thomas G. McGinn MD Ethan A. Halm MD Mount Sinai School of Medicine, New York, NY

PURPOSE: Women with lung cancer appear to have better survival compared to men. Whether this is due to differences in treatment, tumor biology, or due to a longer life expectancy is not clearly understood. This study sought to evaluate whether there are gender differences in lung cancer survival after controlling for competing causes of death and type of treatment.

METHODS: This study included 18,967 cases of histologically confirmed, Stage I and II non-small-cell lung cancer diagnosed between 1991 and 1999 from the Surveillance, Epidemiology and End Results registry linked to Medicare records. Patients were grouped in three categories according to the treatment received: surgery, radiation or chemotherapy but no surgery, and untreated cases. We used stratified analyses and multivariate models to identify gender differences in survival among these groups using three methods to control for competing causes of death: lung cancer specific survival, overall survival adjusting for comorbidities, and relative survival calculated by the life-table method.

RESULTS: Women in the three treatment groups had better cancer specific, overall, and relative survival than men ($p<0.0001$ for all comparisons). Lung cancer specific 5-year survival for women was 54% compared to 40% for men ($p<0.0001$). Among untreated patients, women had approximately a 25% decreased risk of death compared to men. Stratified and multivariate analyses showed that women had significantly better survival than men after controlling for age, race, stage at diagnosis, histology, median income, geographic area, access to care, and type of treatment.

CONCLUSION: In this national, population-based sample, women with non-small cell lung cancer had better risk-adjusted survival rates compared to men in all treatment groups. That this gender difference was observed among untreated patients suggests that lung cancer in women has a different intrinsic biologic behavior and natural history that in men.

CLINICAL IMPLICATIONS: These gender difference in survival have implications in the design and interpretation of lung cancer trials and could be incorporated in the current prognostic classification.

DISCLOSURE: Juan Wisnivesky, None.

COMPARING ALGORITHMS FOR THE PREOPERATIVE FUNCTIONAL ASSESSMENT OF PATIENTS WITH LUNG CANCER

M. Y. Ersoy MD* Leendert Keus Other Sevin Baser MD Carlos A. Jimenez MD Georgie A. Eapen MD Rodolfo C. Morice MD The University of Texas Health Science Center Houston, Houston, TX

PURPOSE: A review of the literature and British Thoracic Society guidelines state that an FEV1 ≥2L is a safe lower limit for pneumonectomy in patients with lung cancer. Others have utilized FEV1 based on % of predicted normal ranging between ≥60% and ≥80% to indicate a patient suitable for pneumonectomy. There is an apparent lack of congruency between various methods for preoperative patient selection.

METHODS: To develop a more reliable algorithm for the preoperative selection criteria we compared FEV1 in absolute values(L) and as % of predicted normal to quantitative radionuclide estimates of predicted postoperative FEV1(ppo%FEV1) for all patients with unilateral lung cancer referred to our pulmonary laboratory for preoperative evaluation between January 2002 and May 2005.

RESULTS: A total of 1,334 patients (M=774,F=560), mean age=64yrs±12 (range=19-93) were studied. Patients' mean FEV1=2.04L±0.72(70.4%±19.7). Six hundred and thirty one patients (47%) had an FEV1 ≥2L (mean=2.64L±0.54). Of these, 309(49%) had an FEV1<80%. Among patients with a baseline FEV1≥2L, the ppo%FEV1was<40% in 189(30%) and it was <35% in 84(13%). Four hundred and seventeen patients(31%) had a baseline FEV1≥80%. Of these, 95(23%) had an FEV1<2L. For patients with a baseline FEV1≥80%, the ppo%FEV1 was <40% in 47(11%) and it was <35% in 9(2%).There were 552(41%) patients with FEV1≥60% and ≤79%. For these, the ppo%FEV1was<40% in 227(41%) and it was <35% in 141(26%).

CONCLUSION: There is a significant discrepancy between preoperative selection criteria that use FEV1 as absolute value (L) and as % of predicted. Almost one-half of patients with an FEV1 ≥2L had an FEV1 <80% of predicted. Approximately one-third of patients an FEV1 ≥2L would have been deemed inoperable based on ppo%FEV1 of <40%.

CLINICAL IMPLICATIONS: Algorithms for preoperative functional assessment for patients with lung cancer that use values of FEV1 ≥80% for pneumonectomy or ppo%FEV1≥35% are better than predictions for resection using absolute values of FEV1 (L). This approach is more reliable and reduces bias caused by variations in patients' age, gender, race, and height.

DISCLOSURE: M. Ersoy, None.

HURRY UP AND WAIT: THE EFFECT OF WAIT TIME ON SURVIVAL IN NON-SMALL CELL LUNG CANCER

Michael K. Gould MD* Sharfun Ghaus MD VA Palo Alto Health Care System, Palo Alto, CA

PURPOSE: Prior studies of the effect of wait time (time to diagnosis or treatment) on survival in patients with non-small-cell lung cancer (NSCLC) yielded results that were mixed and confounded by several sources of bias. We aimed to describe variation in wait times, identify predictors of longer wait times, and examine the effect of wait time on survival.

METHODS: We performed a retrospective cohort study by reviewing the records of consecutive patients who were diagnosed with NSCLC between 1/1/02 and 12/31/03 at VA Palo Alto Health Care System. We used multivariable statistical methods to identify independent predictors of longer wait times, and to examine the effect of wait time on survival.

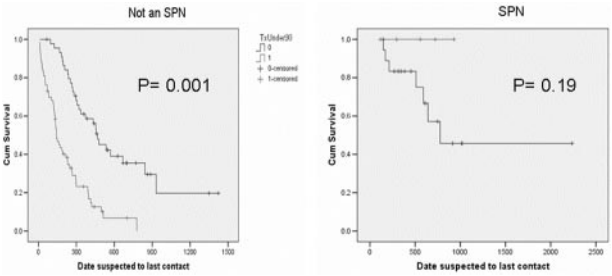
RESULTS: We identified 129 veterans with NSCLC (mean age 67 years, 98% men, 83% white), most with adenocarcinoma (51%) or squamous cell carcinoma (30%). A minority (18%) presented with a solitary pulmonary nodule (SPN). Median time from initial suspicion to treatment was 85 days (range 3 to 1355 days). Independent predictors of longer wait times (>90 days) were hospitalization within 7 days of initial suspicion (OR 6.0, 95% CI 2.2 to 16.2), tumor size >3 cm (OR 5.4, CI 2.1 to 14.1), chest x-ray findings other than the primary tumor (OR 2.6, CI 0.9

Lung Cancer: Cell Type, Gender and Preoperative Assessment, continued

to 7.5), and any symptom (OR 2.5, CI 1.0 to 6.0). In multivariable analyses, wait time was not associated with survival (HR 1.5, CI 0.9 to 2.5). In patients with SPN, there was a trend toward improved survival when wait time was <90 days (figure).

CONCLUSION: Wait times for our patients with NSCLC were often longer than recommended. Patients with more severe presentations of NSCLC had shorter wait times, confounding the relationship between wait time and survival. Our results suggest the hypothesis that in patients with malignant SPN, survival may be better in patients treated within 90 days.

CLINICAL IMPLICATIONS: If confirmed, our results suggest that quality improvement efforts should focus on reducing wait times in patients with solitary nodules and others with potentially resectable NSCLC.



DISCLOSURE: Michael Gould, None.

ENDOSCOPIC ULTRASOUND IS MORE ACCURATE THAN POSITRON EMISSION TOMOGRAPHY IN THE STAGING OF NONSMALL CELL LUNG CANCER

Rosemary F. Kelly MD* Vita V. Sullivan MD Douglas B. Nelson MD Amy M. Holmstrom RN Frank A. Lederle MD Mandeep S. Sawhney MBBS VA Medical Center, Minneapolis, MN

PURPOSE: Accurate assessment of mediastinal lymph nodes (MLN) is vital to optimizing treatment of lung cancer patients. Often currently available strategies fail to identify patients with advanced mediastinal disease. Accurate diagnosis of advanced nonsmall cell lung cancer (NSCLC) is critical to appropriate treatment with neoadjuvant therapy. We prospectively compared two promising new modalities, positron emission tomography (PET) and endoscopic ultrasound (EUS), for staging MLN in NSCLC.

METHODS: From May 2004 to January 2005, Minneapolis VA Medical Center patients with known or suspected NSCLC, who were considered suitable candidates for surgical resection, were enrolled in the study. Prospectively, data was collected for subjects who underwent both PET and EUS as part of the preoperative evaluation. Outcomes were analyzed by tissue confirmation of diagnosis or serial imaging follow-up.

RESULTS: 56 eligible patients were enrolled, with complete data available for 53. Final diagnosis was based on tissue in 47 subjects and on serial imaging in 6 subjects. PET imaging correctly diagnosed MLN status in 75% of subjects, while EUS guided fine-needle-aspiration was correct in 94% of subjects (difference 18.7%, p = 0.012, 95% CI 4.8% - 31.6%). Over all sensitivity, specificity and accuracy of PET were 60%, 92% and 75%; compared with 89%, 100% and 94% for EUS. We estimated that EUS obviated a surgical procedure in 54% (95% CI, 41.20% - 73.08%) of patients with enlarged MLN, and in 28% (95% CI, 10.37 % - 46.77%) of patients without suspicious nodes on imaging studies.

CONCLUSION: EUS guided fine-needle-aspiration was more accurate than positron emission tomography in staging MLN in lung cancer patients. EUS offers histologic confirmation of NSCLC involvement of MLN and allows a more appropriate utilitzation of neoadjuvant therapies.

CLINICAL IMPLICATIONS: The inclusion of EUS for preoperative staging of NSCLC allows for neoadjuvant therapy to be instituted without a surgical procedure being performed in the mediastinum. Mediastinoscopy can then be used for restaging patients following adjuvant treatment and reserve surgical resection for those patients that truly have a significant response to treatment.

DISCLOSURE: Rosemary Kelly, None.

ROLE OF BRAIN MR IN STAGING OF ADENOCARCINOMA OF THE LUNG IN NEUROLOGICALLY ASYMPTOMATIC PATIENTS

Eun H. Kang MD* Hojoong Kim MD O. Jung Kwon MD Samsung Medical Center, Seoul, South Korea

PURPOSE: Routine brain MRI as a staging work-up of non-small cell lung cancer remains controversial, although adenocarcinoma of the lung has a high frequency of brain metastasis. To estimate the incidence of brain metastasis in patients with neurologically asymptomatic adenocarcinoma of the lung and to determine the usefulness of routine brain MRI, this study was designed prospectively.

METHODS: From May 1999 to April 2004, we performed routine brain MRI in all patients with newly diagnosed adenocarcinoma of the lung in Samsung Medical Center. The patients with any neurologic signs and/or symptoms were excluded. Brain MRI consisted of pre- and post-contrast image. The radiographically positive findings were acceptable only when two experienced neuroradiologists readed the same findings independently.

RESULTS: Total 782 (median age 61 years, M:F=1.52:1) patients were enrolled. Overall positive rate on brain MR was 23.0%(180/782). The incidence of asymptomatic brain metastasis was presented to the table.

CONCLUSION: Brain MRI could be helpful for the diagnosis of occult brain metastasis in patients with adenocarcinoma of the lung.

CLINICAL IMPLICATIONS: Lung cancer, brain metastasis.

DISCLOSURE: Eun Kang, None.

Pulmonary Function: Beyond Spirometry 10:30 AM - 12:00 PM

EFFECT OF BODY MASS INDEX ON PULMONARY FUNCTION TESTS

Boris I. Medarov MD* Paul Strachan MD Rubin Cohen MD Long Island Jewish Medical Center, New Hyde Park, NY

PURPOSE: It is well recognized that obesity affects the mechanics and physiology of the respiratory system. However, the specifics of that relationship have not been clearly established. This study examines the impact of body mass index (BMI) on Pulmonary Function Tests (PFT).

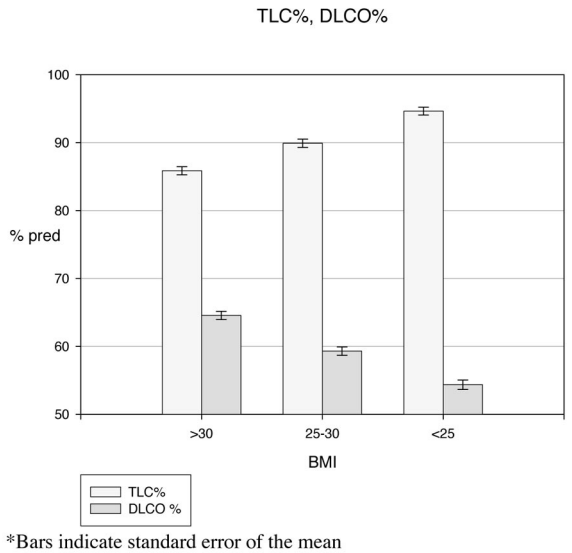
METHODS: 4610 complete pulmonary function tests were included. The study subjects were divided into three groups- BMI>30 (N=1345), BMI 25-30 (N=1572) and BMI<25 (N=1693). The mean forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF), total lung capacity (TLC), expiratory reserve volume (ERV), inspiratory capacity (IC), residual volume (RV), diffusing capacity (DLCO) values were entered for each of the 3 groups along with the percentage of predicted values for FEV1, TLC, DLCO and RV. Analysis of variance (ANOVA) was performed for each variable with subsequent pair-wise comparisons.

RESULTS: FEV1 was not affected and had no relationship to BMI. However, the impact of BMI on TLC, RV, DLCO and ERV was substantial (Figure 1, 2). DLCO showed a direct proportional relationship to BMI- the higher BMI, the higher DLCO- a fact suggested by other studies but not universally accepted. Pearson correlation performed on TLC and BMI showed the highest coefficient in the group with BMI>30 (correlation coefficient -0.13). Linear regression demonstrated that for each increase of BMI by 1, TLC% decreases by 0.42 points.

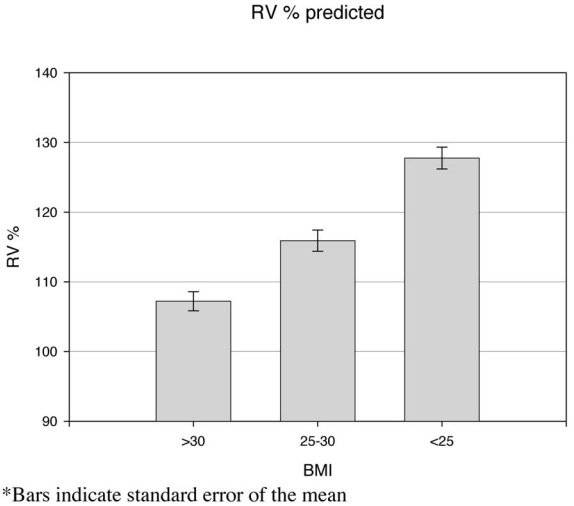
CONCLUSION: Increased BMI impacts on TLC, RV and ERV, but not on FEV1. DLCO increases as BMI rises.

CLINICAL IMPLICATIONS: Awareness of the effects of BMI on lung function testing will result in better interpretation of the results and hopefully avert unnecessary pulmonary work up.

Pulmonary Function: Beyond Spirometry, continued



*Bars indicate standard error of the mean



*Bars indicate standard error of the mean

DISCLOSURE: Boris Medarov, None.

FORCED EXPIRATORY VOLUME IN 1 SECOND/FORCED EXPIRATORY VOLUME IN 6 SECONDS (FEV1/FEV6) IS A SUBOPTIMAL SURROGATE FOR FEV1/FORCED VITAL CAPACITY (FEV1/FVC) IN THE SPIROMETRIC DIAGNOSIS OF AIRFLOW OBSTRUCTION IN A DIVERSE URBAN POPULATION

Mayuko Fukunaga MD* Eugene J. Kim MD Shobharani C. Sundaram MD James Sullivan BA Patricia Friedmann MS Steve H. Salzman MD Beth Israel Medical Center, New York, NY

PURPOSE: Spirometry can be difficult to perform due to the requirement for complete exhalation to measure FVC. Some have suggested that a 6-second expiratory time may be sufficient for diagnostic spirometry. Swanney and colleagues (AJRCCM 2000;162: 917–919) studied whites in New Zealand and found that FEV1/FEV6 had a sensitivity of 95.0% and specificity of 97.4% for the diagnosis of airway obstruction defined by FEV1/FVC. We evaluated the utility of FEV1/FEV6 in a diverse urban population and factors that may influence the sensitivity of this parameter.

METHODS: We reviewed all spirometric studies performed at Beth Israel Medical Center during 2003-2004. Tests were excluded if they did not meet American Thoracic Society criteria for acceptability and reproducibility, had exhalation times under six seconds, or were done in Asian subjects (the NHANES III reference set provides equations only for white, black and Hispanic subjects). Tests were independently categorized as obstructive or non-obstructive using both FEV1/FEV6 and FEV1/FVC. Sensitivity and specificity of FEV1/FEV6 for diagnosis of obstruction were calculated using FEV1/FVC as the gold standard.

RESULTS: In the 1926 tests that met all study criteria, the sensitivity of FEV1/FEV6 for defining airflow obstruction was 85.6%(95%CI:83.0-88.2) and specificity was 97.1%(95%CI:96.1-98.0). Sensitivity in whites was 88.7%(95%CI:85.3-91.4), in blacks, 78.2%(95%CI:70.2-84.6) and in Hispanics, 83.2%(95%CI:76.7-88.2)($p<0.001$ for blacks vs. whites). Sensitivity varied from 100%(95%CI:100) in severe obstruction to 73.7%(95%CI:68.2-79.2) in mild obstruction ($p<0.001$ for all grades of severity). Sensitivity was inversely related to expiratory time: 100%(95%CI:100) for 6-8 seconds, to 78.0%(95%CI:72.0-84.0) for $>$ 16 seconds ($p< 0.001$ for all expiratory times).

CONCLUSION: The overall sensitivity of FEV1/FEV6 in the diagnosis of obstructive airways disease is lower in our diverse urban population (85.6%) compared to the study by Swanney and co-workers of white New Zealanders (95.0%). In our study, factors associated with a lower sensitivity of FEV1/FEV6 included mild airflow obstruction, tests with longer expiratory times and black race.

CLINICAL IMPLICATIONS: Practioners should be cautious about using FEV1/FEV6 as a replacement for FEV1/FVC without assessing its use in their patient population.

DISCLOSURE: Mayuko Fukunaga, None.

AIRWAY RESPONSIVENESS TO INHALED MANNITOL IS INCREASED IN SMOKERS AND DECREASES AFTER SHORT-TERM SMOKING CESSATION

Daiana Stolz MD* Christian Gysin David Miedinger MD Ryan Tandjung Christian Surber PhD Michael Tamm MD Jörg Leuppi MD University Hospital Basel, Pneumology, Basel, Switzerland

PURPOSE: To determine the prevalence of airway hyperresponsiveness to inhaled mannitol in healthy smokers compared to nonsmokers and COPD patients and to longitudinally assess whether airway hyperresponsiveness to mannitol improves after smoking cessation.

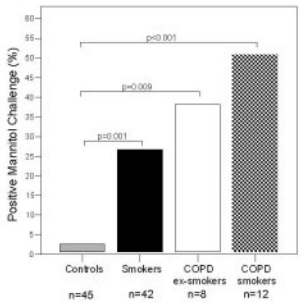
METHODS: Airway hyperresponsiveness to inhaled mannitol was determined in smokers (n=42), COPD patients (n=20) and healthy controls (n=45). In smokers, mannitol test was repeated three months after smoking cessation. Demographics including age, lung function and atopy status were similar for smokers and controls (p=ns).

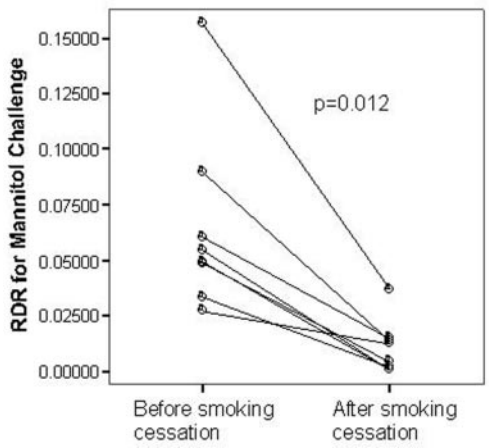
RESULTS: Airway hyperresponsiveness to mannitol (= 15% fall in FEV1) was significantly more common among smokers (26.2%) and COPD-patients (45%) as compared to controls (2,2%) ($p<0.01$ for both)(see figure 1). The response-dose-ratio (% fall in FEV1/cumulative dose) was significantly higher in smokers (0.0231 ± 0.293) as compared to controls (0.0085 ± 0.234), respectively ($p<0.01$). After successful smoking cessation, response to mannitol became negative in all but one patient ($p=0.021$) and response-dose-ratio decreased in all cases ($p=0.012$)(see figure 2). None of the patients with a negative mannitol test turned positive, irrespective of the outcome of smoking cessation.

CONCLUSION: Bronchial hyperresponsiveness to mannitol is markedly increased in smokers and in COPD patients as compared to controls. Airway hyperresponsiveness positivity rate and response-dose-ratio to mannitol significantly decrease after short-term smoking cessation.

CLINICAL IMPLICATIONS: As increased AHR affects survival in COPD, particularly in smokers, early diagnose of AHR in smokers could have prognostic implications concerning COPD development. Moreover, evidence of AHR may act as a further motivation for asymptomatic smokers to quit, specially if this finding is likely to be influenced by giving up smoking.

Pulmonary Function: Beyond Spirometry, continued





DISCLOSURE: Daiana Stolz, None.

A LOGARITHMIC MODEL OF PREDICTING FVC BASED ON FEV1, FEV2, AND FEV3

Octavian C. Ioachimescu MD* Kevin McCarthy RRT Mani Kavuru MD James Stoller MD Cleveland Clinic Foundation, Cleveland, OH

PURPOSE: Accurate measurement of forced vital capacity (FVC) is important in pulmonary function testing. Since the rate of achieving spirometric end-of-test criteria is usually less than optimal, with resultant under-recording of the FVC, the current analysis proposes a logarithmic model of predicting FVC based on FEV1, FEV2, and FEV3, especially when end of test criteria are not met (i.e., no expiratory plateau or short exhalation time).

METHODS: Estimated logFVC and exp(Estimated logFVC) were derived after multivariate analysis and construction of a logarithmic regression model from volume measurements within the first 3 seconds of exhalation (based on FEV1, FEV2, and FEV3). We developed the model on a large derivation cohort and subsequently evaluated it on a distinct validation cohort of patients.

RESULTS: The derivation group consisted of 35,885 consecutive spirometric tests performed in the Cleveland Clinic Foundation Pulmonary Function Laboratory. The equation derived was as follows: Estimated logFVC = – 0.04 – 0.416×logFEV1 – 1.612×logFEV2 + 2.991×logFEV3 (R2 = 0.95, $p < 0.0001$, RMSE = 0.087). The equation was applied to an independent validation set of 61,290 spirometric measurements on as many consecutive, different patients. Based on the above equation, Exp (Estimated logFVC) = 0.10 + 0.963×FVC (R2 = 0.97, $p < 0.0001$, RMSE = 0.241). In the validation cohort, the prevalence of obstruction was 66% (based on values of the measured FEV1/FVC compared to NHANES III values). In the same cohort, the mean residual, i.e. the difference between estimated and measured FVC (± standard deviation) was 6.9 (± 238) mL.

CONCLUSION: Our predictive model based on logarithmic values of the spirometric measurements had a good diagnostic performance and behaved reasonably accurate in situations of short exhalation time and/or when no expiratory plateau is achieved.

CLINICAL IMPLICATIONS: Since FVC is frequently under-recorded with resultant over-estimation of FEV1/FVC and under-diagnosis of airflow obstruction, we showed that estimating FVC from FEV1, FEV2 and FEV3 using a logarithmic model can improve the precision of the estimation and offer practical diagnostic advantages.

DISCLOSURE: Octavian Ioachimescu, None.

SEASONAL VARIATION IN LUNG FUNCTION

Paul Strachan MD* Boris I. Medarov MD Long Island Jewish Medical Center, New Hyde Park, NY

PURPOSE: Many patients report a subjective feeling of worsening respiratory status during different times of the year, attributed to changes in weather. There is very little objective data to confirm the presence or absence of a seasonal variation in lung function. This study aims to examine the seasonal effect on the major indices of pulmonary function tests.

METHODS: In a New York City pulmonary function laboratory of an academic medical center, 4486 pulmonary function tests (PFT) were performed during the period of 3/1997-5/2002. We divided the tests into four groupings, based on three month intervals corresponding to the respective seasons: Winter: January-March (N=1118), Spring: April-June (N=1281), Summer: July-September (N=1080), Autumn: October-December (N=1007). The mean forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), total lung capacity (TLC) and diffusing capacity for carbon monoxide (DLCO) values were entered for each of the 4 groups along with the FEV1/FVC ratio and the percentage of predicted values for FEV1, TLC and DLCO.

RESULTS: There was a significant decrease in the absolute and predicted FEV1 in the July to September grouping (Fig 1). This was accompanied by a decrease in the FEV1/FVC ratio (Fig 2) and the predicted DLCO during the same period. No significant change in TLC was found.

CONCLUSION: The data shows FEV1 and DLCO are significantly decreased during the summer months of July to September. This may explain some of the changes in symptoms experienced by patients.

CLINICAL IMPLICATIONS: This study demonstrates that in areas with four distinct seasons, lung function declines during the summer months. Further research into the reasons for the reduction in lung function seen in the PFT results may be indicated.

DISCLOSURE: Paul Strachan, None.

CHANGES IN EXERCISE CAPACITY OF MEDICAL INTERNS OVER THEIR FIRST YEAR OF TRAINING

Eduardo Velez Calderon MD* Marta Zulik MD Naim Aoun MD Victor M. Pinto-Plata MD Bartolome R. Celli MD St. Elizabeth's Medical Center, Boston, MA

PURPOSE: To determine if cardiorespiratory fitness decreases in medical interns during their first year of training.

METHODS: Incoming medical interns at Caritas St. Elizabeth's hospital were asked to participate in this prospective cohort study. Informed consent was obtained from all subjects prior to enrollment. Medical history, height and weight were recorded. Spirometry and Maximal Voluntary ventilation were performed on a volume displacement, water-sealed spirometer (SensorMedics, Yorba Linda, CA) according to published guidelines (12). Symptom-limited cardiopulmonary exercise test with an incremental ramp protocol was completed on a cycle ergometer (Vmax 29, SensorMedics), while breathing room air. Breath by breath oxygen uptake and carbon dioxide output, pulse oxymetry, and 12-lead ECG were recorded continuously. Maximal work rate (watts), oxygen uptake (VO2) and anaerobic threshold (AT), were measured according to published guidelines (13). After 6 months of internship, we repeated the cardiopulmonary exercise using the same protocol. Results were compared at both times using paired Student's t-test.

Pulmonary Function: Beyond Spirometry, continued

RESULTS: 14 subjects (10 male, 4 female) agreed to participate. Repeated measurements were available in 10 subjects (7 male, 3 female). All subjects terminated the test because of muscular fatigue. Significant reductions were observed in maximal work rate (216± 51 vs. 197±52, $p<0.007$), and in Anaerobic Threshold (1.34±0.33 vs. 1.09±0.24, $p<0.0008$). No significant differences were seen in peak heart rate, maximal oxygen uptake (VO2), O2-pulse, VO2/WR and HR/VO2 ratios.

CONCLUSION: 6 months after enrolling in a medical internship, normal subjects had a decrease in maximal work rate and anaerobic threshold.

CLINICAL IMPLICATIONS: These findings suggest the development of progressive physical deconditioning in normal subjects during medical training. Although this may result from the demanding schedule that is associated with medical training, adequate planning for regular physical activity may prevent the occurrence of such event.

DISCLOSURE: Eduardo Velez Calderon, None.

Pulmonary Hypertension Therapy
10:30 AM - 12:00 PM

SITAXSENTAN THERAPY IN PULMONARY ARTERIAL HYPERTENSION RESULTS IN SIGNIFICANTLY FEWER LIVER FUNCTION ABNORMALITIES THAN BOSENTAN

Terrance Coyne MD* Richard Dixon PhD Encysive Pharmaceuticals, Houston, TX

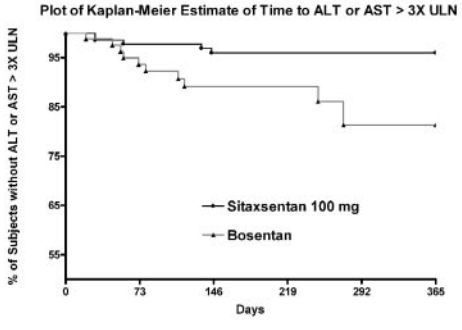
PURPOSE: The first approved endothelin receptor antagonist (ETRA) for the treatment of pulmonary arterial hypertension (PAH) is bosentan (BOS), an oral, twice-daily, non-selective ETA/ETB ETRA. While a significant advance for PAH, BOS therapy has been complicated by abnormal liver function tests [>3X upper limit of normal (abLFT)] in a controlled trial setting (12% at the labeled dose) and in clinical practice, a finding that has been subsequently seen at varying rates with all ETRAs studied in PAH. Sitaxsentan (SITAX), is an oral, once-daily, highly selective (>6500:1) ETA ETRA in development for PAH which demonstrated lower abLFT rates with 100mg QD in STRIDE-1. These lower abLFT rates were confirmed in STRIDE-2: 6.5% of patients randomized to placebo, 3.2% for SITAX 100mg, 4.9% for SITAX 50mg, and 11.5% for BOS. Here, we report on the long-term LFT rates observed for patients (pts) treated for up to one year with BOS, in accordance with the product label, or SITAX.

METHODS: STRIDE-2 was an 18 week, multi-center, placebo-controlled study that randomized 246 patients (pts) 1:1:1:1 to PBO, SITAX 100 mg, SITAX 50 mg or open label, efficacy-rater blinded, BOS followed by an extension with pts receiving either BOS or SITAX 100 mg. During the extension, pts on PBO in STRIDE-2 were randomized to SITAX 100mg or BOS; pts on SITAX 50mg received SITAX 100mg and pts on SITAX 100mg or BOS were continued on those treatments.

RESULTS: Kaplan-Meier estimates of time to abLFT at 1 year of exposure are 4.0% for SITAX 100mg and 18.7% for BOS ($p = 0.0086$).

CONCLUSION: Long-term treatment with SITAX 100mg QD results in significantly fewer liver function abnormalities than bosentan.

CLINICAL IMPLICATIONS: Sitaxsentan 100mg QD has been shown to be safe and effective in the treatment of PAH, with a lower rate of liver function abnormalities than bosentan.



DISCLOSURE: Terrance Coyne, Shareholder Encysive Pharmaceuticals; Employee Encysive Pharmaceuticals; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Sitaxsentan.

THE USE OF SILDENAFIL IN THE ACUTE TREATMENT OF PATIENTS WITH SEVERE PULMONARY ARTERIAL HYPERTENSION AND RIGHT HEART FAILURE

Lalaine M. Corate MD* Patricio Escalante MD Glenna Traiger MSN Wendy Hill MSN Rory Hachomavich MD Shelley Shapiro MD University of Southern California, Los Angeles, CA

PURPOSE: The acute treatment of severe Pulmonary Arterial Hypertension (PAH) poses a therapeutic challenge. Immediate access to agents such as prostacyclin and endothelin receptor blockers (ERBs) is limited. Sildenafil has been shown to have a direct vasodilator effect in the pulmonary circulation. The goal of this study is to describe the treatment response to Sildenafil for unstable, WHO Class IV PAH patients.

METHODS: We performed a retrospective, cohort review of 14 consecutive patients with WHO Class IV PAH admitted to the hospital in severe right heart failure (RHF) and treated with Sildenafil. Treatment also included digoxin, diuretics and inhaled nitric oxide. Sildenafil was initiated at 50 mg TID and increased to 100 mg TID after 24 hours. Outpatient follow-up data and outcome measurements included periodic 6-minute walks (6MW), supplemental oxygen requirements, WHO classification status, need for additional PAH therapy, hospitalizations and death.

RESULTS: All patients were discharged on Sildenafil without concomitant prostacyclin or ERBs. After ≥ 4 weeks of therapy with Sildenafil, the mean increase in 6MW (compared to pre-discharge 6MW) was 122.4 meters (95%CI:50.5-194.3, $p=0.004$). The mean reduction in oxygen supplementation by nasal cannula was 2.1L (95%CI:3.53-0.75, $p=0.005$). The degree of improvement in 6MW distance, oxygen requirements, and WHO classification status was statistically associated with the time of treatment on Sildenafil. At 6 months, the average 6MW distance was 351M (n=5). Four patients had additional therapy added ≥ 5 months. One patient died and 3 patients required re-hospitalization prior to 1 year for progressive PAH and RHF. At 1 year, 13 patients remained on Sildenafil and were WHO Class II-III, without signs of RHF. No significant side effects were noted.

CONCLUSION: Sildenafil 100 mg TID can be used in the acute setting to stabilize patients with WHO Class IV PAH. Long-term therapy with Sildenafil was associated with good clinical outcomes, including improvement in WHO classification and 6MW distance.

CLINICAL IMPLICATIONS: This study proposes a treatment strategy for decompensated PAH that circumvents problems of delayed access to prostacyclins and ERBs therapy.

DISCLOSURE: Lalaine Corate, None.

SILDENAFIL IN ACUTELY DECOMPENSATED RIGHT HEART FAILURE SECONDARY TO PULMONARY ARTERIAL HYPERTENSION

Namita Sood MB, BCh* Gretchen Whitby RN The Ohio State University, Columbus, OH

PURPOSE: Pulmonary arterial hypertension (PAH) is a devastating disease. The natural progression of the disease is characterized by sustained increase in pulmonary artery pressure resulting in right ventricular failure(RHF). The mortality in acutely decompenated right heart failure patients is high. Significant progress has been made in the treatment of patients with PAH with improved survival. However management of acutely decompensated patients remains a challenge. The management usually entails intravenous diuretics which may not be tolerated because of systemic hypotension and renal insufficiency, IV epoprostenol which is not easy to prescribe at short notice.

METHODS: Case series of 7 patients with newly diagnosed severe pulmonary arterial hypertension and decompensated right heart failure-.All patients had evidence of RHF and acute respiratory failure and failed to improve with diuresis and were treated with oral sildenafil starting at 12.mg and then increased to 25mg every 8 hrs and 5omg every eight hours as tolerated.

RESULTS: All 7 patients had severe PAH with mean pulmonary artery pressure was 61 + 15.6 mmHg (mean + SD) and Pulmonary vascular resistance 13 + 5.4 woods units CI 2 + .63 L /min/sq meter.All patients demonstrated dramatic improvement with Sildenafil.(table 1)There were no adverse events.

CONCLUSION: We conclude that sildenafil is safe and effective in decompensated right heart failure.

CLINICAL IMPLICATIONS: Sildenafil should be considered in these critically ill patients .

Pulmonary Hypertension Therapy, continued

Patient	mRA	mPA	CI	PVR	Outcome
1	10	47	1.7	16	Extubated and off all pressors 72 hrs later
2	11	58	3	8.7	Resolution RHF discharged 72 hrs later
3	12	41	1.22	12.4	PaO2 58mm Hg on 100% NRB to off O2 72 hrs later
4	26	75	2.4	9.5	Resolved RHF and improved saturations with activity discharged 72 hrs later
5	7	86	2.3	21	PaO2 70 mmHg on 100%NRB to PaO2 64mmHg on 6L NC
6	20	65	1.5	8	Resolution of right heart failure discharged 72hrs later
7	19	55	2.5	20	PaO2 80mm Hg on 100% NRB to 88mmHg on 6L 72hr later

DISCLOSURE: Namita Sood, None.

LEVELS OF HYDROGEN PEROXIDE IN EXHALED BREATH CONDENSATE ARE ELEVATED IN PULMONARY ARTERIAL HYPERTENSION COMPARED TO HEALTHY CONTROLS AND CYSTIC FIBROSIS PATIENTS

Eduardo J. Vasquez MD* Mark S. Scheetz MS Peter Murphy MD Austin B. Thompson MD University of Nebraska Medical Center, Omaha, NE

PURPOSE: Patients with pulmonary arterial hypertension (PAH) have complex vascular lessions that include inflammatory cells. Investigation of surgical specimens from patients with PAH demonstrate evidence of oxidative stress reflected by upregulation of cellular antioxidant defenses. The levels of hydrogen peroxide (H2O2) in exhaled breath condensate (EBC) have been found to be elevated in a variety of inflammatory diseases of the lower respiratory tract including asthma, COPD, cystic fibrosis and ARDS. H2O2 levels correlate with airway inflammation, lung neutrophilic activation and oxidative stress. It was hypothesised that H2O2 levels could be used to non-invasively evaluate the state of airway inflammation and oxidative stress in PAH.

METHODS: Subjects with PAH (n=17), healthy controls (n=30) and cystic fibrosis as positive controls (n=13) were recruited for sample collection. Subjects with PAH and the healthy controls were age matched. Smokers or subjects with an upper respiratory infection were excluded. EBC was collected using the Jaeger ECoScreen device for fifteen minutes wearing a nose clip. H2O2 was measured using a method described by Ruch based on reaction with homovanillic acid producing a highly fluorescent dimer. Demographics and clinical data were collected from the medical record.

RESULTS: Average volume of EBC was 2.5 ml after 15 minutes. Patients with PAH were found to have higher levels of H2O2 (1.093 nm/ml ± 1.165) compared to CF (0.733 nm/ml ± 0.723) and healthy controls (0.355 ± 0.244, p =0.0322). The levels were not correlated with the PA pressure obtained by 2D echo (r2=.028), sex or age of the subjects.

CONCLUSION: Levels of hydrogen peroxide in EBC were higher in patients with pulmonary hypertension compared to healthy controls. No correlation between sex, age or pulmonary artery pressure of PAH subjects were found.

CLINICAL IMPLICATIONS: EBC is an easily performed, non-invasive method for sampling lung contents. In PAH, levels of H2O2 and other markers of inflammation and oxidative stress may provide a target to monitor therapeutic responses that reflect the underlying cellular pathophysiology.

DISCLOSURE: Eduardo Vasquez, None.

VASOACTIVE THERAPY CAN HELP IMPROVE FUNCTIONAL CAPACITY IN PATIENTS WITH FIBROTIC LUNG DISEASE AND PULMONARY HYPERTENSION

Omar A. Minai MD* Debasis Sahoo MBBS Alejandro C. Arroliga MD Kevin McCarthy RRT Atul C. Mehta MD Cleveland Clinic Foundation, Cleveland, OH

PURPOSE: Interstitial lung disease (ILD) may be associated with hypoxia and pulmonary hypertension (PH). The coexistence of these diseases may produce severe and progressive functional limitation which may be ameliorated by the use of vasoactive therapy. Traditionally vasoactive therapy is not used in such patients due to a perceived lack of benefit and fear of worsening hypoxia.

METHODS: We reviewed records of patients with ILD who had received vasoactive therapy for PH on a compassionate basis. Data retrieved included demographics, PFTs, radiographic findings, echocardiographic findings, six-minute walk (6MW) results, BNP, and NYHA functional class assessment.

RESULTS: We identified 11 patients with ILD who had received therapy for PH [age 54±8 yrs (mean±SD); 3M/8F; 6Caucasian/5AA]. Baseline characteristics included BMI 26±7 (mean±SD), FVC 50±16% (mean±SD), FEV1 47±17% (mean±SD), DLCO 23±16 (mean±SD). All patients had a restrictive ventilatory defect, mild (N=2), moderate (N=2), severe (N=7) and resting hypoxia 83±9 (mean±SD) %. Patients received epoprostenol (N=7), remodulin (N=3), or bosentan (N=4) over a mean of 29 (range 5-84) months. Over the first three months of therapy NYHA functional class improved from 3.3± 0.6 (mean±SD) to 2.6±0.5 (mean±SD) (p=0.048) and by 1 functional class in 60% of patients. 6MW distance improved from 845± 288 (mean±SD) to 1063±449 (p=NS) (mean±SD) and BNP declined from 521±284 (mean±SD) to 311±430 (mean±SD) (p=NS). Oxygen requirements, RVSP, and Hb did not show any significant change. The patients with severe disease also showed an improvement in 6MW and BNP when analyzed separately.

CONCLUSION: Our group of patients with combined ILD and PH benefited from vasoactive therapy in terms of improvement in NYHA functional class, 6MW distance, and BNP. Larger, prospective studies are needed to identify the patients most likely to benefit from such intervention.

CLINICAL IMPLICATIONS: Vasoactive therapy may help improve functional capacity in selected patients with fibrotic lung disease and PH.

DISCLOSURE: Omar Minai, None.

PULMONARY HYPERTENSION IN THE ELDERLY: DEMOGRAPHICS AND OUTCOMES FOLLOWING THERAPY WITH BOSENTAN

Maria Carrillo MD* Hector Cajigas MD Adam Greenbaum MD Kevin M. Chan MD Henry Ford Health Systems, Detroit, MI

PURPOSE: Pulmonary hypertension (PH) is typically a disease of young women. The use of screening echocardiograms has increased the detection of PH in the elderly. We describe the demographics, and outcomes of bosentan treated PH patients(pts) ≥ 60 years of age.

METHODS: Retrospective chart review of patients referred to the Henry Ford Hospital PH program over two years. Demographics, hemodynamics, 6 minute walk test (6MW), WHO class were recorded. Pts who completed at least 6 months of bosentan therapy followed by repeat right heart catheterization were included. Pts ≥ 60 years old were compared to pts < 60 years old. Paired Student t-test was used for comparisons.

RESULTS: 62 pts ≥ 60 (Grp 1)and 60 pts < 60 (Grp 2)had PH. Diastolic dysfunction(DD)(31%), connective tissue disease(CTD) (15%), IPAH(15%), CTEPH(13%), and pulmonary disease(PD)(13%)were causes of PH in Grp 1. CTD(19%), IPAH(17%), portopulmonary(13%), DD(12%), PD(7%)and CTEPH(10%)predominated in Grp 2. Bosentan was initiated in 19 pts(Age 71±7)in Grp 1 and 10 pts(Age 47±5)in Grp 2. 4 discontinuations(1 nausea, 3 refractory edema)occurred in Grp 1 while 1 discontinuation(transaminitis)happened in Grp 2. 9 pts in grp 1 and 6 pts in grp 2 qualified for analysis. Overall 6MW increased from 249m to 307m and the change in 6MW distance between the groups was no different(69.8±132 vs 41±73m). WHO class fell significantly following treatment from 3.5±0.6 to 2.4±1.2(p=0.0016)which was most affected by grp 1 with a fall from 3.8±0.4 to 2.2±1.1(p=0.0017). Grp 2 was without change in WHO class(3.2±0.8 to 2.7±1.5). Hemodynamic measurements revealed overall improvement in mPAP(52±12 to 47±13mmHg)(p=0.04) and PVR(12.2±7 to 9.4±4 WU)(p=0.049).

CONCLUSION: Awareness of PH as a cause of dyspnea is increasing in the elderly. DD is the predominant cause, but IPAH, CTD and CTEPH represent 43% of PH patients ≥60. Bosentan is effective in lowering WHO class, and is equivalent in changing pulmonary hemodynamics and walking distance when compared to younger pts.

CLINICAL IMPLICATIONS: IPAH, CTD and CTEPH should be suspected in the elderly PH patient. Bosentan is effective in this population.

Pulmonary Hypertension Therapy, continued

	6MW (m)	Δ6MW after bosentan (m)	WHO Class	WHO Class after bosentan	MPAP (mmHg)	MPAP after bosentan (mmHg)	PVR (WU)	PVR after bosentan (WU)
Grp 1 (N=9)	232±122	69.8±132	3.8±0.4	2.2±1.1*	50.8±10	45.0±3.8	11.9±5.6	9.2±2.7
Grp 2 (N=6)	275.8±101	41±73	3.2±0.8	2.7±1.5	55±16	50±22	12.9±8.9	9.8±6.9
Total	249±112	58±110	3.5±0.6	2.4±1.2*	52±12	47±13*	12.2±7	9.4±4*

*p≤0.05 compared to baseline

DISCLOSURE: Maria Carrillo, Consultant fee, speaker bureau, advisory committee, etc. Actelion

Tuberculosis Treatment Issues
10:30 AM - 12:00 PM

CLINICAL EFFICACY OF LINEZOLID, CLARITHROMYCIN AND CAPREOMYCIN IN THE TREATMENT OF MULTI-DRUG RESISTANT PULMONARY TUBERCULOSIS

Sudhir K. Agarwal MD* Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

PURPOSE: Objective of the study was to see the clinical efficacy of a combination therapy with linezolid (L), azithromycin (AZ), capreomycin (CPM) and other second-line anti-tuberculosis drugs in the treatment of multi-drug resistant pulmonary tuberculosis (MDR-TB).

METHODS: Ninety-one patients with MDR-TB were assigned to a study group (46 cases), treated with L, AZ, CPM, pyrazinamide (Z) , ethambutol (E) and ethionamide(Et); or a control group (45 cases), treated with streptomycin (S), Z , E and Et. The course of treatment was 18 months. Linezolid was given for 6 months and aminoglycosides (capreomycin/streptomycin) for 10 weeks.

RESULTS: 42 cases in the study group and 41 in the control group completed the treatment. The sputum negative conversion in the study group (81%) was significantly higher than in the control group (55%). The radiological improvement rate was 46% in the study group, significantly higher than that in the control group (27%) ($P<0.01$). The closure rate of the lung cavities in the study group (65%) was higher than in the control group (44%) ($P<0.05$). No significant difference was found in the side-effects between the two groups.

CONCLUSION: The regimen including linezolid, clarithromycin, capreomycin and other second-line anti-TB drugs was effective and safe for the patients with MDR-TB.

CLINICAL IMPLICATIONS: Linezolid, clarithromycin and capreomycin combination may be used along with other anti-tuberculosis drugs for the management of MDR TB.

DISCLOSURE: Sudhir Agarwal, None.

SOME OBSERVATIONS ON USE OF RESERVED DRUGS IN RE-TREATMENT OF DRUG FAILURE PULMONARY TUBERCULOSIS PATIENTS

Nirmal Chand MD* M. S. Parhar PhD Bharat Bhushan MD Satish Duggal MD Sandeep Gupta MD Jorawar Singh MBBS Dept. of TB. & Chest, Medical College Amritsar, Amritsar, India

PURPOSE: To evaluate results of treatment given to drug failure pulmonary tuberculosis patients, for formulating treatment in newer patients.

METHODS: Hospital record of past 7 years was analyzed. In all 60 such patients were encountered.

RESULTS: It is difficult to treat drug failure patients of pulmonary tuberculosis patients. Majority 50 (83%)of these patients were males.All the patients had taken anti tubercular as streptomycin, isoniazid, rifampicin, ethambutol pyrazinamide, regularly in previous years regularly in various combinations for 4-6 months. All had sputum positive at the start of the treatment. They were retreated with regimens containing cycloserine, ethionamide, isoniazid, pas and oflaxacin / sparfoxacin for one year, at least, along with kanamycin injection for 3 months. Patients were advised / motivated to continue treatment for one year after sputum conversion.It was observed that only 30 (50%) completed chemotherapy. Among them 28 (84%) achieved bacteriological quiscence. On follow for 12 to 24 months (average 14 months) 6 patients (20%) of these patients relapsed bacteriologically. Among 30 patients who took incomplete treatment (average 6 months) 6 patients (20%) achieved sputum convertion. On the whole drugs were well tolerated in most of the patients. Almost all the patients complained of high cost of treatment. The cost factor was the most common reason sited for discontinuation of treatment by patients.

CONCLUSION: Therapy with reserve drugs is very costly due to high cost of drugs and longer duration of treatment.So chances of defaults are very high. To counter this, these patients should be fully motivated to complete the course of treatment so as to stop further spread of multi drug resistant tuberculosis in the community.

CLINICAL IMPLICATIONS: Proper record keeping in treatment of pulmonary tuberculsis patients is must. Patients failing on 1st line drugs need to be treated promptly so as to prevent the further spread of resistant tuberculosis. These drugs need to be supplied free of cost to achieve this goal.

DISCLOSURE: Nirmal Chand, None.

EXPERIENCE USING THREE REGIMENS TO TREAT LATENT TUBERCULOSIS INFECTION IN A TARGETED TESTING PROGRAM, 2000-2004

Lewis R. Mooney MD* Margaret J. Oxtoby MD John C. Grabau PhD Edwin M. Rodriguez Suffolk County, New York, Department of Health Services, Brentwood, NY

PURPOSE: Groups targeted for the Targeted Testing Program (TTP) were foreign-born persons recently arrived from high TB prevalence countries. These individuals were deemed unlikely to complete the Centers for Disease Control and Prevention (CDC) preferred nine-month regimen of isoniazid (9-INH) to treat Latent Tuberculosis Infection (LTBI) due to their seasonal jobs. Use of a shorter course regimen to treat LTBI was initiated to help improve completion of therapy rates in this population.

METHODS: The TTP began using a four-month course of Rifampin 4-RIF to treat LTBI after reports of fatal and severe liver injuries associated with the use of a 2-month course rifampin and pyrazinamide (2-RZ). Individuals deemed to be unsuitable candidates for Rifampin-containing drug regimens (e.g. patients on oral contraception or those using medications with potential for interaction with RIF) were placed on 9-INH. All groups had similar demographics and received identical follow-up care.

RESULTS: Completion of therapy rates were as follows: 2-RZ 77% (106 completed therapy/138 started therapy), 4-RIF 79% (166 completed therapy/209 started therapy), 9-INH 62% (41 completed therapy/66 started therapy). Statistical comparison: 4-RIF vs. 9-INH $p < 0.01$; 2-RZ vs. 9-INH $p < 0.05$; 4-RIF vs. 2-RZ-not significant. There were no significant adverse drug effects or deaths in any group.

CONCLUSION: In this mobile population, the shorter LTBI treatment course of 4-RIF was well accepted, demonstrated no hepatic toxicity and contributed to a higher completion of therapy rate then the preferred 9-INH.

CLINICAL IMPLICATIONS: Shorter course regimens contribute to improved completion of therapy rates in foreign-born persons recently arrived from high TB prevalence countries who have LTBI.

DISCLOSURE: Lewis Mooney, None.

EFFICACY AND SAFETY OF KANAMYCIN, ETHIONAMIDE, PAS AND CYCLOSERRINE IN MULTI DRUG RESISTANT PULMONARY TUBERCULOSIS PATIENTS

Rajendra Prasad MD* S.K. Verma MD A. Jain MD King George Medical University, Lucknow, India

PURPOSE: We carried out this study to determine the efficacy and safety of a regimen containing Kanamycin, Ethionamide, PAS and Cycloserine in Multi-drug resistant pulmonary tuberculosis patients.

METHODS: A prospective, uncontrolled study of 45 pulmonary tuberculosis patients, who had received adequate first-line anti-tuberculosis treatment including supervised category II retreatment regimen, and were still sputum smear positive for acid fast bacill and resistant to at least Isoniazide and Rifampicin. They were planed to give Kanamycin (initial 4-6 months), Ethionamide, PAS and Cycloserine for a minimum period of two years.

RESULTS: Out of 45 patients, 35 (77.7%) achieved sputum conversion with in 6 months and 34 (75.5%) remained so at the end of two years. 2 (4.4%) patients expired, 6 (13.3%) patients were lost to follow up, and 3

Tuberculosis Treatment Issues, continued

(6.6%) patients remained sputum smear positive for AFB through out the period of study. 34 patients, declared cured, were followed for an average period of 17.4 months (3-60 months), during which 2 (5.7%) patients relapsed , 6 (17.6%) patients were lost to follow-up and rest 26 (76.4%) remained sputum smear for AFB negative. 8 (17.7%) patients developed major side effects which required stoppage/change of drugs.

CONCLUSION: In MDR-TB patients, regimen consisting of Ethionomide, PAS and Cycloserine with injection Kanamycin in initial 4-6 months appears to be effective and safe.

CLINICAL IMPLICATIONS: MDR TB can be cured successfully with appropriate combination of drugs for an adequate duration and requires much effort from both the patients and health care workers.

DISCLOSURE: Rajendra Prasad, None.

SURGICAL MANAGEMENT OF PULMONARY TUBERCULOSIS-INDICATIONS AND RESULTS

Velappan S. Jayaraman MBBS* Rajiv Santosham MBBS Roy Santosham MD Sasankh MBBS Ravi Santosham MD Rajan Santosham MBBS Santosham Chest Hospital, Chennai, India

PURPOSE: Our objective was to evaluate the role of surgery in pulmonary tuberculosis and the results achieved in the management of these patients.

METHODS: A total of 1327 patients (male-823, female-504)underwent surgery for pulmonary tuberculosis in our centre from 1970 to 2004. Pulmonary resections performed in 1115 patients included pneumonectomy in 102 patients (7.6%), lobectomy in 897 patients (67.9%), and segmental resections in 118 patients (8.8%). Bilateral lung resections were performed in 17 patients. Decortication accompanied lung resections in 354 patients and was done as an isolated procedure in 212 patients (15.9%). Thoracoplasty was done in 151 patients. Video Assisted Thoracosopic Surgery was done only in early empyema cases for decortication and to assess the size and site of bronchopleural fistula preoperatively. Surgery was indicated for massive hemoptysis in 562 patients (42.4%), destroyed lung in 82 patients (6.1%) and other causes like persistent fibrocavity with active disease, localized bronchiectasis and chronic suppurative lung lesions. Twelve patients underwent bronchopleural fistula repair with omental patches. Sixteen patients had multidrug resistant tuberculosis and surgery was done for localized lesions in these patients. Clagett's procedure was done in 10 patients with persistent empyema.

RESULTS: The duration of hospital stay ranged from 7 to 60 days. Overall, 32 patients had recurrence of hemoptysis(5.7%). Emergency re-exploration for postoperative bleeding was performed in 42 patients(3.2%). The other major postoperative complications were wound infection in 89 patients(6.7%), bronchopleural fistula in 64 patients(4.8%), empyema in 31 patients(2.3%) and prolonged air leak in 76 patients(5.6%). Respiratory failuire occured in 6 patients(0.45%). A total of 16 patients(1.2%) died.

CONCLUSION: Though anti-tuberculous chemotherapy resolved pulmonary tuberculosis in a majority of patients, there are still definite indications in which surgical management plays a vital role.

CLINICAL IMPLICATIONS: Surgical management of pulmonary tuberculosis is adjuvant in multidrug resistant thick walled cavitary tuberculosis and life saving in localised cavity causing life threatening massive hemoptysis and fastens the recovery of patients with mulctiloculated complicated pleural efusions.

DISCLOSURE: Velappan Jayaraman, None.

Benefits of the Newest Treatments for COPD
12:30 PM - 2:00 PM

THE EFFECT OF ROFLUMILAST ON HUMAN INFLAMMATORY CELLS RELEVANT TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASTHMA

Herrmann Tenor MD Armin Hatzelmann PhD Shahin Sanjar PhD* Christian Schudt PhD ALTANA Pharma AG, Florham Park, NJ

PURPOSE: Chronic airway inflammation is the key characteristic common to COPD and asthma. However, different cellular mechanisms are involved in the pathophysiology of both airway diseases. In COPD, prominent pro-inflammatory effector cells are CD8+ T-cells, neutrophils, and macrophages, whereas in asthma, CD4+ T-cells, eosinophils, and dendritic cells are relevant to the inflammatory process. Phosphodiesterase 4 (PDE4) is expressed in all inflammatory cells and degrades cAMP, an intracellular modulator of various pro-inflammatory responses. Thus, PDE4 inhibition represents a key target for anti-inflammatory therapies. We examined the in vitro effects of roflumilast, an investigational PDE4 inhibitor, on human inflammatory cells.

METHODS: Cells were isolated from human peripheral blood of healthy donors. Release of cytokines was determined using ELISA. Reactive oxygen species (ROS) were measured using a luminol-enhanced chemiluminescence assay. Leukotrienes were analyzed by HPLC. Cell proliferation was determined by incorporation of [^{3}H] thymidine.

RESULTS: In CD8+ T-cells, roflumilast reduced the anti-CD3 induced release of granzyme B and interleukin (IL)-2 in the presence of a PDE3-selective inhibitor with IC50 values of 2.7nM and 8.5nM, respectively. Roflumilast almost completely inhibited leukotriene B4 synthesis in neutrophils (IC50=2nM) whereas ROS formation was reduced up to 70% with an IC35 value of 4nM. Additionally, roflumilast inhibited TNFα release from monocyte-derived macrophages by about 70% (IC35=13nM) when tested in the presence of a PDE3-selective inhibitor and 1nM PGE2. In CD4+ T-cells, roflumilast inhibited cell proliferation by about 60% (IC30=7nM) as well as IL-2, IL-4, and IL-5 synthesis (IC values ranged from 1 to 13nM). Further, roflumilast suppressed fMLP-induced ROS release from eosinophils by about 70% (IC35=7nM). Lipopolysaccharide-induced release of TNFα from monocyte-derived dendritic cells was partially inhibited by roflumilast (IC20=5nM).

CONCLUSION: Roflumilast has shown effective inhibition of human inflammatory cell functions in vitro, which are involved in the pathogenesis of COPD and asthma.

CLINICAL IMPLICATIONS: The PDE4 inhibitor roflumilast may provide anti-inflammatory treatment for patients with chronic inflammatory airway diseases such as COPD and asthma.

DISCLOSURE: Shahin Sanjar, Employee The presenting author S Sanjar is employee of ALTANA Pharma AG, Florham Park, NJ, USA. The authors H Tenor, A Hatzelmann, and C Schudt are employees of ALTANA Pharma AG, Konstanz, Germany.; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. The authors have been involved in the presented research on the investigational product roflumilast, which is in clinical development and sponsored by ALTANA Pharma AG.

COMBINATION THERAPY OF TIOTROPIUM PLUS SALMETEROL (T+S) SUPERIOR TO SINGLE AGENT THERAPY (TIO OR SALM) IN TERMS OF DYSPNEA IMPROVEMENT IN COPD

JA Van Noord MD* J-L Aumann MD E Janssens MD JJ Smeets A Mueller PJG Cornelissen PhD Atrium Medical Center, Heerlen, Netherlands

PURPOSE: Guidelines recommend combination therapy of long-acting bronchodilators in moderate to severe COPD.

METHODS: Baseline and Transition Dyspnea Indices (BDI and TDI) were assessed at the end of 6-week treatment periods in a 4-way, double-blind, crossover study of Tio 18 mcg (qd), Salm 50 mcg (bid), T (qd) + S (qd) or T (qd) + S (bid). In addition, bronchodilator-mediated symptom benefit was evaluated by the need for reliever medication (puffs of salbutamol during last 3 weeks of each period).

RESULTS: Mean screening FEV1 of the study population (N=97; 77 m/20 f, aged 65 yrs) was 1.09 L (39 % pred). The BDI was 6.9. A TDI (focal score) $\geq$ 1 unit is considered clinically relevant.

CONCLUSION: This is the first study with crossover design using BDI/TDI to assess dyspnea. Combination therapy was superior to single agent therapies in perceived dyspnea; no difference was found between once- or twice-daily Salm add-on therapy to Tio. Symptom benefit of combination regimens over the single agents was also reflected in less need for reliever medication.

CLINICAL IMPLICATIONS: In conclusion, combination therapy of T+S provided superior and clinically relevant improvement in dyspnea and less need for reliever medication compared to single agent therapies in moderate to severe COPD.

DISCLOSURE: JA Van Noord, Grant monies (from industry related sources) First three authors received honorarium to conduct clinical research.

Benefits of the Newest Treatments for COPD, continued

EFFECT OF FLUTICASONE PROPIONATE/SALMETEROL 250/50 ON LUNG HYPERINFLATION AND EXERCISE ENDURANCE IN PATIENTS WITH COPD

D.E. O'Donnell MD* F. Sciurba MD B. Celli MD D.A. Mahler MD K. Webb MS C. Kalberg PhD G. Crater MD K. Knobil MD Queen's University, Kingston, ON, Canada

PURPOSE: To evaluate the effect of fluticasone propionate (FP)/salmeterol Diskus (FSC) 250/50 BID and placebo (PLA) on lung hyperinflation and exercise endurance. A preliminary comparison of FSC and salmeterol (SAL) was included, allowing for initial evaluation of the contribution of FP to FSC.

METHODS: A randomized, double-blind, parallel-group, multicenter study was conducted in 185 COPD patients with hyperinflation at rest (mean FEV1=41%, FRC=156% pred). Pre- and 3 hr post-dose spirometry, body plethysmography and constant-load cycle cardiopulmonary exercise tests (at 75% of maximum work rate) were performed at Day 1 (first dose) and Week 8. Post-dose evaluations were used for comparisons of FSC (n=62) and PLA (n=64), pre-dose for FSC and SAL (n=59).

RESULTS: At a standardized time across exercise tests: inspiratory capacity (IC), tidal volume and ventilation were significantly ($p \leq 0.02$) greater with FSC than PLA (Week 8 post-dose); and IC was greater ($p=0.031$) with FSC than SAL (Week 8 pre-dose). No significant safety concerns were associated with the cardiopulmonary exercise tests.

CONCLUSION: FSC significantly reduced lung hyperinflation at rest and during exercise and increased exercise endurance time compared to PLA. Preliminary comparisons between FSC and SAL suggest superiority of FSC in patients with COPD.

CLINICAL IMPLICATIONS: FSC is effective at improving exercise tolerance, a key goal in the management of stable COPD.

	Treatment Difference at Week 8	
	FSC-PLA (post-dose)	FSC-SAL (pre-dose)
FEV_1, L	0.24±0.04*	0.09±0.04†
FRC, L	-0.35±0.12 *	-0.14±0.12
RV, L	-0.35±0.13 *	-0.10±0.14
IC, L	0.33±0.06*	0.12±0.06†
Exercise endurance time, sec	132±45*	66±44
Peak ventilation, L/min	4.2±1.0*	0.7±1.0

Mean±se; *$p \leq 0.005$; †$p \leq 0.029$.

DISCLOSURE: D.E. O'Donnell, Grant monies (from industry related sources) Received research grants from GlaxoSmithKline; Consultant fee, speaker bureau, advisory committee, etc. Received consultant fees from GlaxoSmithKline.

OBSERVATIONAL STUDY OF THE RISK OF ED VISIT OR HOSPITALIZATION IN COPD PATIENTS RECEIVING MAINTENANCE THERAPIES: A TIME-DEPENDENT ANALYSIS

Thomas Delea MS* May Hagiwara PhD Rohit Borker PhD Richard Stanford PharmD Policy Analysis Inc. (PAI), Brookline, MA

PURPOSE: Evidence from controlled trials in patients with COPD suggest that maintenance therapy with fluticasone/salmeterol combination (FS) may improve lung function and symptoms compared with inhaled corticosteroids alone (IC), salmeterol alone (SL), or ipratropium with albuterol (IA). The objective of this study was to compare risk of COPD related emergency department (ED) visit or hospitalization in COPD patients receiving different initial maintenance therapies.

METHODS: Data from a large US health-insurance claims database was used to identify patients with diagnoses of COPD (ICD-9-CM 491.xx, 492.xx, 496.xx) who initiated inhaled maintenance therapy with FS, IC, SL, ipratropium (IP), or IA between 1/98-12/04. Risk of COPD-related ED/hospitalization was analyzed using repeated-measures logistic regression analysis with exposure to study therapies and other characteristics (age, sex, emphysema diagnosis, Charlson comorbidity index, use of short-acting beta agonists, oral corticosteroids, antibiotics, or oxygen therapy, and ED visit/hospitalization in the previous year) included as time-dependent covariates.

RESULTS: 36,076 subjects were identified with 41,268 person years of follow-up. 3,425 experienced a COPD-related ED visit/hospitalization during follow-up (8.1 per 100 person years). The unadjusted rate of ED visit/hospitalization per 100 person years of exposure to study therapy was 6.8 for FS, 11.0 for IC, 9.1 for SL, 30.2 for IP, 21.9 for IA, and 18.1 for combinations of two or more study therapies. In multivariate analysis, exposure to FS was associated with lower risk of COPD-related ED visit/hospitalization compared with IC (adjusted odds ratio [OR] 0.68, 95% confidence interval [CI] 0.55-0.83), IP (OR 0.41, 95%CI 0.34-0.50), IA (OR 0.39, 95%CI 0.33-0.46), and combinations of two or more study therapies (OR 0.46, 95%CI 0.38-0.54). Results were similar when patients with an asthma diagnosis were excluded, as well as for all-cause ED visit/hospitalization.

CONCLUSION: Therapy with FS is associated with reduced risk of COPD-related ED visit/hospitalization compared with IC, IP, or IA.

CLINICAL IMPLICATIONS: Although results of observational studies alone are insufficient to establish causality, these findings provide further evidence of clinical benefits for FS as initial therapy in patients with COPD.

DISCLOSURE: Thomas Delea, Employee R Borker and R Borker are employees of GSK.; Grant monies (from industry related sources) This study was funded by GSK.; Consultant fee, speaker bureau, advisory committee, etc. T Delea and M Hagiwara are employees of PAI which has received research funding and consulting fees from GSK.

LUNG VOLUME REDUCTION SURGERY IMPROVES THE BODE INDEX

David J. Lederer MD* Patricia A. Jellen MSN Joshua R. Sonett MD John H. Austin MD Frances L. Brogan MSN Mark E. Ginsburg MD Byron M. Thomashow MD New York Presbyterian Hospital LVRS Program, New York, NY

PURPOSE: The National Emphysema Treatment Trial (NETT) found that lung volume reduction surgery (LVRS) improves survival, exercise capacity, and quality-of-life in a subset of patients with severe emphysema. We report our experience with LVRS following publication of the NETT.

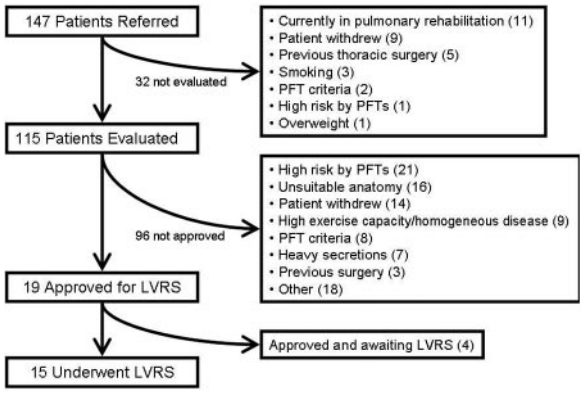
METHODS: We prospectively collected demographic and clinical data of patients referred for LVRS. All evaluations were performed according to NETT protocols. The Wilcoxon signed-rank test was used to compare paired continuous variables.

RESULTS: We evaluated 115 patients for LVRS between January 1, 2004 and April 29, 2005 (Figure). Fifteen patients (13%) underwent LVRS after completing pulmonary rehabilitation. The average age was 62.9 ± 5.1 years and 7 (47%) were male. All 15 patients had upper lobe predominant emphysema and met NETT inclusion criteria. Six (40%) had low exercise capacity and 9 (60%) had high exercise capacity, as defined by the NETT. Seven underwent video-assisted thoracoscopic surgery and 8 underwent median sternotomy. No deaths occurred during the study period. Median intensive care unit (ICU) and hospital lengths of stay (LOS) were 2 (interquartile range 2-3) and 9 (interquartile range 7-9.5) days, respectively. Postoperative complications included prolonged air leak (>7 days) in 6 of 15 (40%) and 1 each of blood transfusion > 2 units, arrhythmia, and Clostridium difficile diarrhea. Seven patients have returned for 6 month follow-up; no patient was lost to follow-up. Pulmonary function, exercise capacity, Medical Research Council dyspnea score, and the BODE index improved significantly compared to post-rehabilitation values (Table). Three (43%) had an improvement in maximal exercise capacity of >10 Watts.

CONCLUSION: Utilizing NETT criteria no mortality was seen. Complications and hospital and ICU LOS were minimal. Improvements in the BODE index, lung function, exercise capacity, and dyspnea can be achieved with LVRS in patients with severe upper lobe emphysema. Larger studies should determine if decrements in the BODE index predict improved survival.

CLINICAL IMPLICATIONS: LVRS improves BODE index, a predictor of mortality in patients with COPD. Utilizing NETT criteria may minimize mortality and morbidity in patients undergoing LVRS.

Benefits of the Newest Treatments for COPD, continued



Table—*Six Month Outcomes After Lung Volume Reduction Surgery*

Variable	Pre-LVRS*	Post-LVRS	p Value
BODE index	5.7±1.4	2.9±1.7	0.02
FVC % predicted	52.7± 12	69.6± 18	0.03
FEV_1 % predicted	27.9± 7	37.1± 13	0.02
TLC % predicted	114.3± 11	99.6± 13	0.02
DLCO % predicted	26.1± 11	29.4± 11	0.46
PaO_2, mm Hg	63.3± 13	68.7± 11	0.15
Maximal workload during CPET, Watts	34 ± 15	46 ± 15	0.03
Distance walked in 6 minutes, meters	374 ± 48	431 ± 63	0.02
MRC Dyspnea score	2.7±1.4	0.7±0.8	0.03

*Data are mean ± standard deviation.

DISCLOSURE: David Lederer, None.

THE QUALITY OF HEALTH CARE DELIVERED TO AMERICANS WITH OBSTRUCTIVE LUNG DISEASE

Richard A. Mularski MD* Steven M. Asch MD William H. Shrank MD Eve A. Kerr MD Claude Setodji PhD John Adams PhD Joan Keesey BS Elizabeth A. McGlynn PhD VA Greater Los Angeles Healthcare System, Los Angeles, CA

PURPOSE: Adherence to recommended processes of health care for obstructive lung disease is unknown. We measured the quality of care delivered to participants in a community-based sample of the U.S. population with asthma and chronic obstructive lung disease (COPD).

METHODS: We performed a medical record review on randomly selected individuals from a pool of 20,158 from 12 communities representative of the national population in cities > 200,000. We requested medical records from all providers of consenting participants for the previous two years; 20 trained nurses abstracted performance on 45 indicators of obstructive lung disease quality derived from RAND's Quality Assessment Tools System. Multivariate logistic regression evaluated effects of patient demographics, insurance, health status, and comorbidity on the quality of health care.

RESULTS: 429 participants out of 6712 consenting respondents were eligible for quality evaluation for 3672 episodes of care in obstructive lung disease. Overall, participants received 53.5 % (95% C.I.) [50.0, 57.0] of recommended care for asthma (n=260) and 58.9 % [51.7, 64.4] of recommended care for COPD (n=169). We detected significant variation in the quality of care across the 12 sites (COPD scores highest 64 % in one community vs. low 48 %, $p < 0.001$). Logistic modeling identified few characteristics related to the quality of obstructive lung disease care provided to patients. In multivariate analysis, African Americans received better care than whites (adjusted scores 62% vs. 53% for asthma, $p = 0.02$; 67% vs. 56% for COPD, $p < 0.01$); lower income participants and those without insurance received lower quality of care.

CONCLUSION: Overall, Americans with asthma and COPD received < 57% of recommended care. There was wide variation across communities in the quality of care delivered.

CLINICAL IMPLICATIONS: Obstructive lung disease affects 8.5% of Americans and chronic lower respiratory disease ranks as the number four cause of death. The deficits in processes of care for asthma and COPD present ample opportunity for improvement in the health of Americans. Chest physicians should take the lead in quality improvement initiatives.

DISCLOSURE: Richard Mularski, Grant monies (from sources other than industry) Supported by the Robert Wood Johnson Foundation; grants from AHRQ, NCI, NINR, CMS.

Cardiac Surgery Variables Affecting Outcomes
12:30 PM - 2:00 PM

IMPACT OF PREVIOUS PERCUTANEOUS CORONARY INTERVENTION ON SYMPTOM RECURRENCE AND ADVERSE CARDIAC EVENTS FOLLOWING CORONARY ARTERY BYPASS GRAFT SURGERY

Ahmet T. Gurbuz MD* Ayhan A. Zia MD Gursel Ates MD Ahmet Sasmazel MD Haiyan Cui PhD Tucson Medical Center, Tucson, AZ

PURPOSE: The number of percutaneous coronary interventions is increasing with improving technology. There is limited outcome data on patients who had undergone a percutaneous coronary intervention and subsequently require surgical revascularization.

METHODS: 634 Patients underwent coronary artery bypass graft surgery (CABG) between 2001 and 2005. Mean follow-up was 29.4 ± 11.3 months and was complete in 611 patients. The effect of preoperative percutaneous coronary intervention as a risk factor for symptom recurrence and adverse cardiovascular events during follow up period was determined using multivariate Cox Regression Analysis.

Table 1—*Evaluation of Cardiovascular End Points According to PCI History.*

	PCI (n=190)	No PCI (n=421)	p
Angina	22 (11.6%)	12 (2.9%)	0.0001
CHF	5 (2.6%)	4 (1.0%)	0.110
MI	9 (4.7%)	4 (10.0%)	0.003
Reintervention	23 (12.1%)	9 (2.1%)	0.0001
CVA	6 (3.2%)	2 (0.5%)	0.007
Sudden Cardiac Death	5 (2.6%)	2 (0.5%)	0.033
Death	19 (10.0%)	15 (3.6%)	0.0001

CVA: Cerebrovascular event, CHF: Congestive Heart Failure, MI: Myocardial Infarction

RESULTS: There were no differences in the cardiovascular risk factors and intraoperative variables between patients in either group except for lower incidence of diabetes in percutaneous coronary intervention group. Preoperative percutaneous coronary intervention was an independent risk factor for symptom recurrence ($p<0.0001$), combined adverse cardiac events ($p<0.0001$) and slightly increased overall mortality (p 0.04) in the multivariate analysis. Comparison of patients with and without a prior percutaneous coronary intervention showed that former was significantly more prone to develop symptom recurrence, combined adverse cardiac events and overall mortality (Table 1). Among the patients with a history of percutaneous coronary intervention, the ones who developed restenosis following percutaneous coronary intervention had worse outcomes after CABG compared to the ones who did not (Table 2).

CONCLUSION: In this study, patients with previous percutaneous coronary intervention were more likely to develop symptom recurrence and adverse cardiovascular events following CABG. This difference was

Cardiac Surgery Variables Affecting Outcomes, continued

more pronounced in patients who had at least one recurrent stenosis after a percutaneous coronary intervention prior to CABG.

CLINICAL IMPLICATIONS: History of percutaneous coronary intervention and restenosis may act as an adverse prognostic factor following CABG.

Table 2—*Evaluation of Individual End Points According to History of Failed PCI.*

Failed PCI	P	Yes (n=69)	No (n=121)
Angina	20 (29.0%)	2 (1.7%)	0.0001
CHF	5 (7.2%)	0	0.003
MI	8 (11.6%)	1 (0.8%)	0.0001
Reintervention	21 (30.4%)	2 (1.7%)	0.0001
CVA	2 (2.9%)	4 (3.3%)	0.87
	5 (7.2%)	0	0.003
Death	18 (26.1%)	1 (0.8%)	0.0001

CHF: Congestive Heart Failure, CVA: Cerebrovascular accident, MI: Myocardial Infarction

DISCLOSURE: Ahmet Gurbuz, None.

PROGNOSTIC VALUE OF PREOPERATIVE CARDIAC TROPONIN I IN PATIENTS UNDERGOING EMERGENCY CORONARY ARTERY BYPASS GRAFTING DUE TO NON-ST VERSUS ST-ELEVATION ACUTE CORONARY SYNDROMES

Matthias Thielmann MD* Parwis Massoudy MD Markus Neuhäuser PhD Stephan Knipp MD Ivan Aleksic MD Jarowit Piotrowski MD Raimund Erbel MD Heinz Jakob MD Thoracic and Cardiovascular Surgery, West-German Heart Center Essen, University, Essen, Germany

PURPOSE: Cardiac troponin I (cTnI) is a highly sensitive and specific marker for myocardial damage, which has been shown to predict patients outcome pre- and postoperatively following elective coronary artery bypass surgery (CABG). Wether preoperatively elevated cTnI levels similarly predict the outcome in patients undergoing emergency CABG due to acute coronary syndromes (ACS) is currently unknown.

METHODS: A possible correlation between preoperative cTnI levels and in-hospital mortality and major adverse cardiac events (MACE) were investigated in 57 patients with ST-elevation ACS (STE-ACS) in group 1 and 197 with Non-ST-elevation ACS (NSTE-ACS) in group 2 with 12 hours between onset of symptoms and revascularization. Primary study endpoint was all-cause in-hospital mortality. Secondary endpoints were low cardiac output syndrome (LCOS) and hospital course.

RESULTS: CTnI levels on admission were significantly higher in group 1 compared to group 2 (7.1±1.8 vs. 1.4±1.8 ng/mL; $P<0.001$). LCOS with subsequent IABP-support occurred in 16/57 (28.1%), and 18/197 (9.1%) patients, respectively (Odds ratio [OR]: 3.9, 95% confidence interval [CI]: 1.7-8.8; $P<0.001$). Overall in-hospital mortality was significantly higher in group 1 compared to group 2 (14.3 vs. 4.1%; OR: 3.9, 95% CI: 1.3-12.3; $P<0.01$). Postoperative ventilation time, intensive care and hospital stay were significantly longer in group 1 compared to group 2. Univariate and multivariate logistic regression analyses of preoperative cTnI levels strongly correlated with in-hospital mortality and LCOS in patients with STE-ACS ($P<0.01$) and NSTE-ACS ($P<0.001$).

CONCLUSION: Preoperative cTnI measurement before emergency CABG appears as a powerful and independent determinant of short-term surgical risk like in-hospital mortality and MACE in STE-ACS and NSTE-ACS.

CLINICAL IMPLICATIONS: Preoperative cTnI measurement in patients undergoing emergency CABG due to STE-ACS or NSTE-ACS can serve as an incremental variable of risk for in-hospital mortality and MACE. Whether the time point for surgery should be postponed or rather accelerated due to the information of a single preoperative cTnI level remains uncertain and has to be elucidated in further studies.

DISCLOSURE: Matthias Thielmann, None.

STROKE AFTER AORTIC SURGERY: HISTORY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IS A SIGNIFICANT AND INDEPENDENT RISK FACTOR

Zhandong Zhou MD* Syed Raza MD Joginder Bhayana MD Irfan Rizvi MD Adit Suresh BS St. Joseph Hospital, Syracuse, NY

PURPOSE: Stroke is a known complication after aortic surgery. The contributing factors for this complication are not well defined.

METHODS: Between the years 1990 and 2000, 267 patients underwent aortic surgery at our institution. Prospectively collected data (for reporting to the New York State Cardiac Surgery Registry) were used to analyze risk factors for stroke.

RESULTS: Mean age was 60±13 years. Surgery type includes replacement of: ascending aorta 35.2%, aortic root and ascending aorta (Bentall procedure) 41.6%, aortic arch 2.8%, and descending aorta 20.2%. Twenty one percent patients had concomitant procedures on the heart, and 18.7% patients had previous heart surgery. Hypothermic circulatory arrest (HCA) was used in 37.8% patients. Overall 22 patients had post-operative stroke (8.2%). Fifteen patients had stroke within 24 hours of surgery while 7 patients had stroke 24 hours after surgery. Of 30 pre-operative and intra-operative risk factors, we identified 6 to be independent predictors of stroke: history of Chronic obstructive pulmonary disease (COPD, $p<0.005$), cerebral vascular disease (CVD, $p<0.015$), peripheral vascular disease (PVD, $p<0.048$), chronic renal failure (CRF, $p<0.019$), congestive heart failure (CHF, $p<0.038$) and smoking ($p<0.044$).

CONCLUSION: Although CVD, PVD, CRF, CHF, and smoking are known to be risk factors for stroke after aortic surgery, COPD is the most significant predictor for stroke in our series. This relationship has not been addressed in the literature. For strokes occurring after 24 hours, peripheral vascular disease including diseased aorta is the only independent risk factor.

CLINICAL IMPLICATIONS: This study suggests that optimizing patients with COPD in peri-operative period may reduce the risk of stroke from aortic surgery.

DISCLOSURE: Zhandong Zhou, None.

PERIOPERATIVE USE OF AMIODARONE IN CARDIAC SURGERY PATIENTS TO ACHIEVE NORMAL SINUS RHYTHM UPON DISCHARGE

Charles E. Oribabor MD* Naim Mansuroglu MD Althea Tinker Allan Mariano Ralph Slepian MD Frew Gebreab MD Larry H. Bernstein MD Leonard Lee MD Anthony J. Tortolani MD NY Methodist Hospital, Weill Medical College of Cornell University, Brooklyn, NY

PURPOSE: To use Amiodarone to achieve (1)a high rate of normal sinus rhythm at discharge in open-heart surgery patients.2-To reduce morbidity and resource utilization for postoperative atrial fibrillation in open-heart surgery patients.(3)To reduce length of stay.

METHODS: 156 patients studied prospectively.STUDY DURATION: April 1st 2004 to March 30th 2005. INCLUSION CRITERIA:(1)Age greater than 70 years old(2)Patients with an Ejection Fraction less than 30%(3)Preoperative mitral valve surgery patients(4)-Preoperative Aortic valve surgery patients(5)Preoperative Combined CABG and valve surgery patients(6)Postoperative Stanford A Aneurysm surgery patients TARGET LOAD FOR AMIODARONE LOAD: 1700mg to 2000mg(A)-Preoperative patients began there load orally. (B)-Same day patients began their load intravenously started intraoperatively.DOSING SCHEDULE: (1)Amiodarone 400mg orally twice a day for Preoperative patients(2)Amiodarone IV: 150 mg over 10 minutes,then infusion at 1mg/minute for 6 hours followed by 0.5 mg/minute over42 hours for same day patients.DISCHARGE CRITERIA(1)Amiodarone was discontinued on discharge for all patients who remained in normal sinus rhythm during their postoperative course(2)Amiodarone was continued for 2 weeks post discharge for all patients who developed postoperative atrial fibrillation but had converted to normal sinus rhythm by the time of discharge. Re-admissions for Atrial fibrillation over a 4 week period was tracked.

RESULTS: (1)Preoperative Atrial fibrillation rate 11 %(2)Postoperative atrial fibrillation rate: 32%(2)-Discharge rate in Normal sinus rhythm: 93.78%(3)-Actual Risk reduction 61.78 %: (4)Numbers needed treat: 1.61 patients (5)Readmissions for atrial fibrillation : zero (6)Length of stay reduced to 4.9 days.

CONCLUSION: (1)Perioperative Amiodarone use in high risk cardiac surgery patients leads to 93.78 percent discharge rate in normal sinus rhythm.(2)-No readmissions for atrial fibrillation were encountered at post discharge follow up (3)-The incidence of postoperative atrial fibril-

Cardiac Surgery Variables Affecting Outcomes, continued

lation remains relatively high because of the length of time required to fully load patients with 1.7 to 2mg of Amiodarone.

CLINICAL IMPLICATIONS: The attainment and maintenance of normal sinus rhythm postoperatively in open heart surgery patients with the perioperative use of Amiodarone has lead to(1)-Reduced resource utilization for the treatment of postoperative atrial fibrillation.(2)-Reduced length of stay .(3)Reduced risk of bleeding from anticoagulation.

DISCLOSURE: Charles Oribabor, None.

DOES ADJUNCTIVE TRANSMYOCARDIAL LASER REVASCULARIZATION (TMR) REDUCE POSTOPERATIVE ATRIAL FIBRILLATION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING?

Gary S. Allen MD* Osceola Regional Medical Center, Kissimmee, FL

PURPOSE: Postoperative atrial fibrillation (AF) after coronary artery bypass grafting (CABG) may occur in as many as 30% of cases. Medical management of this problem is often ineffective. While the etiology for postoperative AF remains unclear, increased cardiac sympathetic nervous activity is a likely factor. Previous animal studies have shown that TMR with a Holmium:YAG laser can sympathectomize the regional myocardium. The purpose of this study is to examine the effect of TMR on the incidence of postoperative AF.

METHODS: Fourteen U.S. centers participated in a nonrandomized study during the period from January 1, 2002 to March 31, 2005. Patients with diffuse multi – small vessel coronary artery disease (CAD) who could not be completely revascularized by CABG alone compromise the study population. Patients were followed in-hospital and through 30 days.

RESULTS: A total of 739 (men 72%) patients with a mean age of 64±11 years and a mean ejection fraction of 51%±10% underwent CABG + TMR. Among comorbidities (hyperlipidemia:83%; hypertension:78%; prior myocardial infarction:36%; smoking:59%), only diabetes (47%) occurred more frequently compared to the Society of Thoracic Surgeons (STS) database for primary CABG ($p<0.05$). An on pump technique was used in 643 (87%) operations. Patients received an average of 3.0±1.1 bypass grafts and 22±9 TMR channels. At 30 days, all-cause mortality was 2.4%. The incidence of postoperative AF was 5.3%, and significantly lower ($p<0.001$) than that reported for CABG alone in a multicenter (32%) experience.

CONCLUSION: Postoperative AF in the CABG patient increases CVA risk, length of stay and complicates patient management. While TMR has proven itself valuable in angina reduction for patients with diffuse CAD it's effect on postoperative AF has not been previously described. Study patients undergoing CABG + TMR demonstrated a significantly lower incidence of postoperative AF compared to historical controls. This striking difference warrants further investigation.

CLINICAL IMPLICATIONS: TMR with a Holmium:YAG laser may have a place in the prevention of AF in the post CABG patient.

DISCLOSURE: Gary Allen, None.

PREDICTORS OF POSTOPERATIVE PNEUMONIA FOLLOWING CARDIOPULMONARY BYPASS

Rochelle M. Wynne RN * Mari Botti PhD Donald Esmore MBBS Deakin University, Melbourne, Australia

PURPOSE: The purpose of this study was to determine which pre and/or peri-operative factors predicted the development of pneumonia following surgery with cardiopulmonary bypass for coronary artery bypass grafting with or without valvular or other concomitant cardiothoracic surgery.

METHODS: Data from July 1996 until December 2002 were retrieved from a single University affiliated, tertiary teaching hospital database. Pneumonia was diagnosed by one of the following: positive cultures of sputum, blood, pleural fluid, empyema fluid, transtracheal fluid or transthoracic fluid; consistent with clinical findings that included chest x-ray evidence of pulmonary infiltrate, elevated temperature, new productive cough or purulent sputum. Predictor selection was guided by previous studies examining pulmonary complications following cardiac surgery. The effect of 16 preoperative and 10 peri-operative variables on pneumonia was examined using direct entry multivariate logistic regression.

RESULTS: Of 5364 cases, 342 (6.4%) patients were diagnosed with pneumonia. Patients were on average 63.5 + 12.6 years of age, with a body mass index of 26.9 + 4.5 kg/m2 and 27.8% (n = 1491) of the sample were female. Significant predictors of pneumonia from the preoperative context were gender (OR 1.3, 95%CI:1.014-1.653, $p<.05$), New York Heart Association Class III (OR 0.753, 95%CI:0.572-0.992, $p<.05$) and emergency surgical status (OR 0.645, 95%CI:0.432-0.962, $p<.05$). From the peri-operative context perfusion time greater than 120 minutes (OR 0.606, 95%CI:0.473-0.777, $p<.001$), the need for mechanical support (OR 0.380, 95%CI:0.268-0.539, $p<.001$), peri-operative myocardial infarction (OR 0.302, 95%CI:0.110-0.831, $p<.05$) and peri-operative stroke (OR 0.281, 95%CI:0.171-0.461, $p<.001$) predicted postoperative pneumonia. While this model correctly classified 93.6% of cases it only explained 4.9% (R2) of the variation in pneumonia outcome.

CONCLUSION: Pre and peri-operative factors make a minimal contribution to predicting the risk of postoperative pneumonia in cardiac surgical candidates.

CLINICAL IMPLICATIONS: Patient and process factors from the postoperative context require exploration and inclusion in multivariate models in order to develop reliable risk prediction strategies for pneumonia.

DISCLOSURE: Rochelle Wynne, None.

Critical Care: Rapid Response in Delivery of Care
12:30 PM - 2:00 PM

S.E.P.S.I.S: SEPSIS EDUCATION PLUS SUCCESSFUL IMPLEMENTATION AND SUSTAINABILITY IN THE ABSENCE OF A RAPID RESPONSE TEAM

Avelino Verceles MD* R. M. Schwarcz MD Paul Birnbaum MD Praveen Mannam MD Herbert Patrick MD Drexel University College of Medicine, Philadelphia, PA

PURPOSE: Although institutions worldwide are acknowledging the decrease in mortality from therapies presented within the Surviving Sepsis campaign, many have encountered major obstacles in implementation. At our tertiary care, University Hospital facility we devised a "hospital-centric" sepsis pathway using a multi-format educational approach. We believe an educational program emphasizing ways to identify patient signs and symptoms is a more efficient way to improve outcomes, rather than appropriating resources to a specialized team, such as a Rapid Response Team.

METHODS: As an institution-wide performance improvement project, we introduced a sepsis protocol in our institution's Medical, Cardiac, Cardiothoracic, Surgical, and Neurological Critical Care Units, to be implemented in the immediate resuscitation of patients in severe sepsis (SS). The S.E.P.S.I.S. program was entitled "The Need For Speed". A simple one page flow diagram was distributed as the sepsis pathway in every bedside nursing folder, together with a three page companion outlining current evidence-based-therapies in treating SS. After introducing the sepsis pathway to the house staff and nursing staff, we collected performance improvement data from May 2004-August 2004 focusing on protocol milestone goals and mortality. Our "bundle" was time to antibiotics, CVP ≥8, MAP ≥65, and SvO2 ≥70 (Chest 2004,126:863S). During that time we educated all workers involved in patient care, with regards to our Educational Program. This included weekly educational sessions, focused on the sepsis protocol and the reasoning behind milestone goals. Also, bedside teaching regarding therapy for SS was conducted during ICU rounds. During a second period, September 2004 – October 2004, we again assessed milestone and mortality data. Our results were presented to our institution's Performance Improvement committee. This project was approved by our Institutional Review Board.

RESULTS: See Tables.

CONCLUSION: We achieved a significant reduction in mortality of patients using our multi-format educational approach without a Rapid Response Team.

CLINICAL IMPLICATIONS: Others may wish to incorporate all or part of our multi-format, "hospital-centric" educational approach. We believe that we will sustain our decreased mortality of patients with SS through this approach.

Critical Care: Rapid Response in Delivery of Care, continued

Mortality and Apache II Scores Across Education Program Implementation

	Mortality	Mean Apache II
Initiation of S.E.P.S.I.S. (5/04-8/04)	47%	28±6
Completion S.E.P.S.I.S. (9/04-10/04)	31%	27±6

Achievement of Therapeutic Milestones With Education Integration

	Time to Abx	Time to CVP	Time to MAP	Time to SvO2
Initiation of S.E.P.S.I.S	2.67	4.11	3.77	6.97
Completion of S.E.P.S.I.S	0.41	2.95	1.29	3.28

DISCLOSURE: Avelino Verceles, None.

IMPROVED HOSPITAL MORTALITY BY INSTITUTION OF A RAPID RESPONSE TEAM IN A UNIVERSITY HOSPITAL

Alexis Meredith MD* Steven Q. Simpson MD Carol Cleek MSN Timothy Williamson MD Amy O'Brien-Ladner MD University of Kansas, Kansas City, KS

PURPOSE: Our hospital sought to decrease unwitnessed arrests and their attendant morbidity and mortality by implementing a rapid response team (RRT) to intervene earlier in the course of a patient's declining clinical status. A challenge to the implementation of RRTs in the setting of teaching hospitals has been coping with the multiple layers and skill levels of physician caregivers involved in responding to patient care needs. We describe our experience with initiating an RRT under such circumstances.

METHODS: An RRT committee consisting of medical and surgical critical care physicians, hospitalists, critical care nurses, and respiratory therapists developed guidelines for triggering a rapid response event. Any caregiver may activate the RRT via a specific pager. Initial responders include a critical care nurse and respiratory therapist. Simultaneously, the on call resident and the patient's attending physician are notified. Attending physicians may also request the presence of an intensivist.

RESULTS: In the first quarter of the program there were 77 RRT deployments involving 69 patients. The RRT was deployed to all units and areas of the hospital, including the lobby. The majority of events were triggered by respiratory symptoms (45%),diminished level of consciousness (33%), and hypotension (17%). 55 episodes (71%) resulted in moving the patient to an increased level of care, 7(13%) to telemetry and 48(87%) to ICU. 4 patients remain in hospital; 3 were not admitted; 62 were discharged or died. Of the latter group, 48(77%) survived to discharge. 6 patients progressed to arrest during RRT deployment; 4(67%) survived to discharge (vs. 27% overall arrest survival to discharge in preceding year). Crude overall weekly hospital mortality decreased from 3.8% to 1.9% during the quarter (p=0.029).

CONCLUSION: Assuring attending physician involvement with a multidisciplinary approach allowed the RRT to efficiently care for patients with deteriorating clinical status in a university teaching hospital.

CLINICAL IMPLICATIONS: The RRT potentially identifies critically ill patients at an earlier stage of their course when intervention can have significant impact on survival. As a result, crude hospital mortality may improve.

DISCLOSURE: Alexis Meredith, None.

IN-HOSPITAL CARDIOPULMONARY RESUSCITATION (IHCPR): RESULTS OF A PROGRAM TO IMPROVE TEAM LEADER SKILLS USING A COMPUTERIZED PATIENT SIMULATOR (CPS)

Mari Adachi MD* Vanessa Ribaudo MD Marnie Rosenthal DO Adey Tsegaye MD Roslyn Schneider MD Paul H. Mayo MD Beth Israel Medical Center, New York, NY

PURPOSE: IHCPR is a low frequency high risk event that requires a well organized team response. We observed specific problems in team leader function during IHCPR in our hospital. We have investigated whether CPS scenario training might improve team leader skills.

METHODS: In July 2004, 31 medicine residents (PGY-3) were divided into 14 groups.(2-3 residents per group) Each group of residents was tested and scored for leader function using a standardized inpatient cardiac arrest scenario. In addition to the residents, 6 other medical housestaff served as actors during each session. Following testing, each resident ran 3 additional arrest scenarios and was debriefed extensively after each scenario. They achieved perfect checklist score (11 essential steps) before the end of training. For 10 months following training, we scored actual IHCPR events to observe for code leader competencies.

RESULTS: Before training, code leader skills were poor when tested with the CPS. For example, only 14% of the residents identified themselves as code leader. None established a "no-go zone" around the patient, and few assigned or monitored function of the airway team and cardiac compression. During actual clinical IHCPR events, code leaders were very effective in achieving many components of the assigned checklist, but we identified several problematic issues; team leaders were not effective in "crowd control"; large numbers of observers/unauthorized personnel were not cleared from around the patient. Also, training was not completely successful in establishing effective behavioral patterns, i.e., some residents could not assume command presence/voice during IHCPR.

CONCLUSION: CPS training for IHCPR leader skill is effective in training certain aspects of task orientated function. However, our future training methods will have to address the challenges of "crowd control" and behavioral patterns which are critical elements of IHCPR.

CLINICAL IMPLICATIONS: Scenario based CPS training seems to be effective in team leader training for well defined tasks during IHCPR. It is less clear that CPS methods can address intrinsic behavioral patterns during combined team training.

DISCLOSURE: Mari Adachi, None.

IMPACT OF A MULTIDISCIPLINARY TEAM ON INTENSIVE CARE UNIT CLINICAL OUTCOMES IN A COMMUNITY HOSPITAL

Ian J. Morales MD* Carlos E. Baleeiro MD David J. Henson MD Meharry Medical College, Nashville, TN

PURPOSE: To determine the impact on clinical outcomes of a team approach to the care of patients admitted to an adult intensive care unit (ICU).

METHODS: We designed and implemented a multidisciplinary team approach to provide recommendations and assistance in the care of patients admitted to a 16-bed medical/surgical ICU at Cookeville Regional Medical Center, a 176-bed community hospital. The team consisted of a critical care physician, a nurse supervisor, a clinical pharmacist, a respiratory therapist and other allied health personnel. We compared all patients admitted after implementation (1/1/2004 to 9/30/04) with historical controls (patients admitted between 1/1/2003 and 9/30/2003). Values are expressed as mean ± SD (median).

RESULTS: Before implementation, 1102 patients were admitted to the ICU, 278 of them requiring mechanical ventilation. After implementation, 1145 were admitted, 282 requiring MV (NS). Mechanical ventilation length was shorter after implementation of the team, 3.4 ± 3.8 (median 2.0) days compared with 5.2 ± 4.6 (median 4.0) days in the control group, p=0.0438. Mortality and ICU length of stay (LOS) outcomes for patients requiring and not requiring MV can be seen in tables 1 and 2.

CONCLUSION: In patients not requiring MV, ICU LOS was shorter for patients admitted after implementation of the team compared with controls. For patients requiring MV, ICU LOS was the same but length of MV was shorter in patients admitted after implementation. Mortality was unchanged by our intervention.

CLINICAL IMPLICATIONS: A multidisciplinary ICU team approach appears to improve some patient outcome measures in a community hospital ICU setting. Similar findings had been previously reported only in large centers.

Critical Care: Rapid Response in Delivery of Care, continued

Table1—*Clinical Outcomes of Patients Requiring Mechanical Ventilation*

	Before Implementation N=278	After Implementation N=284	p Value
Mortality	71 (25.5%)	72 (25.4%)	p>0.9999
ICU LOS (days)	5.4 ± 7.0 (median 2.75)	4.9 ± 4.7 (median 3.25)	p=0.3066

Table 2. Clinical outcomes of patient not requiring mechanical ventilation

	Before Implementation N=824	After Implementation N=861	P value
Mortality	67 (8.1%)	69 (8.0%)	p>0.9999
ICU LOS (days)	5.2 ± 4.6 (median 4.0)	3.4 ± 3.8 (median 2.0)	**p<0.001**

DISCLOSURE: Ian Morales, None.

BIODEFENSE TRAINING FOR INTERNAL MEDICINE RESIDENTS

Sally Stipho MD* Andrew Artenstein MD Susan Potter MSN Marc Shapiro MD Liudvikas Jagminas MD Patricia Russo-Magno MD Eleanor Summerhill MD Memorial Hospital of RI/Brown Medical School, Pawtucket, RI

PURPOSE: In this era of increased national bioterrorism awareness, training physicians to recognize and respond to potential biological and chemical events has not yet been well integrated into the curriculum of Internal Medicine residency and fellowship programs. Given that victims of bioterrorism may present to community-based primary care physicians, hospitalists, or Critical Care specialists as well as Emergency Medicine providers, programs must address this deficit. This project was a collaborative effort between members of the divisions of Pulmonary and Critical Care Medicine, Infectious Diseases, and Emergency Medicine at Brown Medical School, and was designed to develop a Biodefense curriculum for Internal Medicine residents at one of the major teaching affiliates.

METHODS: The curriculum consisted of a series of 3 lectures pertaining to biological, chemical, and radiologic agents, as well as public health emergency infrastructure. A manual of selected reading was also provided. All residents in the program subsequently participated in a 4 hour training seminar. Instruction included the use of personal protective equipment (PPE), and participation in simulated Emergency Department and Intensive Care Unit scenarios utilizing sophisticated mannequins with monitoring and interactive capability on whom a number of invasive procedures may be performed. These sessions were videotaped and followed by constructive feedback.

RESULTS: Pre and post self-assessments of knowledge and skill level were performed, as well as objective medical knowledge testing. 22 of 30 participating residents responded to the questionnaire and performed the examination (73%). All respondents agreed that the experience was beneficial. Major findings were as follows:.

CONCLUSION: Our curriculum had a positive effect on level of awareness, skills, and knowledge base in Biodefense. Future goals include achieving a higher level of competence among trainees attending these sessions and assessment of long term retention of knowledge and skill sets.

Self-assessment: Knowledge of biologic agents	PRE (% of residents)	POST (% of residents)
None	31.8	4.5
Minimal	63.6	45.5
Some	0	40.1
Moderate	0	0
Excellent	0	0
n/a	4.5	9.1

CLINICAL IMPLICATIONS: The addition of a curriculum in Biodefense to Internal Medicine residency and fellowship training programs will better enable future primary care and subspecialist physicians, in particular intensivists, to recognize and respond appropriately to potential biologic and chemical events.

DISCLOSURE: Sally Stipho, None.

THE USE OF A NEW PRESENTATION FORMAT IMPROVES PATIENT CARE AND TEACHING IN THE ICU

Javid Kamali MD* Eleana Zamora MD Betty Chang MD University of New Mexico, Albuquerque, NM

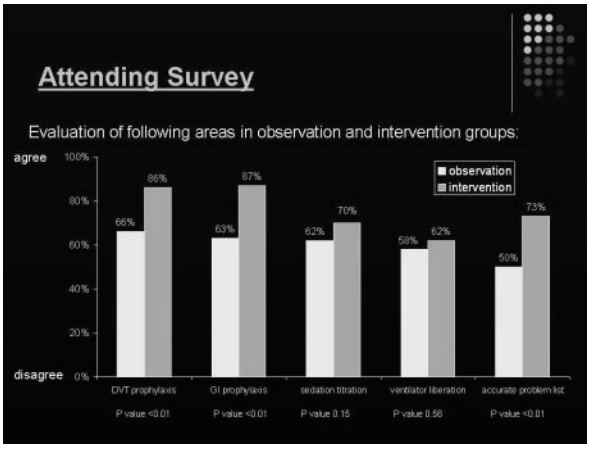
PURPOSE: ICU patients require a detailed, accurate daily assessment and plan for optimal care. We conducted a study to determine how a well organized, daily progress note can help the Housestaff understand the complex ICU issues, improve documentation, and optimize application of standard of care.

METHODS: Residents in two affiliated institutions, a University hospital and a VA hospital, were observed for four months. During the first two months residents used their own or institution's progress notes and presentation format. After two months a new standardized progress note was introduced and Housestaff was asked to present and document using the new format. Housestaff and Intensivists completed questionnaires assessing several areas during observation and intervention months. The survey included documentation of relevant data, application of ICU standards of care (daily discontinuation of sedation, GI and DVT prophylaxis), and presentation of problem list and plan.

RESULTS: Subjective evaluation by the Housestaff did not change in either arm, ranking themselves high regardless of intervention. Intensivists however, noticed significant improvement in identification and documentation of relevant data, presentation of assessment and plan, and application of certain ICU standards in patient care with the standardized progress note (Graph 1). Documentation and presentation areas which did not improve were the daily discontinuation of sedation and ventilator weaning.

CONCLUSION: Based on Intensivists' evaluations, a standardized presentation format improves patient care in several areas. The poor performance and lack of improvement in some areas, such as daily discontinuation of sedation, highlights the need for additional attention from the intensivists, fellows and senior residents. A larger study with evaluation of objective data is needed to more accurately confirm these results.

CLINICAL IMPLICATIONS: We believe this is the first study assessing the impact of a standardized presentation format in applying well established ICU standards in patient care. We demonstrated that such a format improves documentation, presentation, and therefore likely patient care and teaching.



DISCLOSURE: Javid Kamali, None.

Nosocomial/Immunocompromised/Fungal Pneumonia
12:30 PM - 2:00 PM

NOSOCOMIAL PNEUMONIA IN ELDERLY PATIENTS FOLLOWING CARDIAC SURGERY

Ali A. El Solh MD* Milapchand Bhora MD Lilibeth Pineda MD Rajwinder Dhillon MD University at Buffalo, Buffalo, NY

PURPOSE: Age > 65, broad spectrum antibiotics, female sex, duration of mechanical ventilation, and a high acute physiology and APACHE II have all been related to the development of NP post CABG. Yet, none of these investigations has examined the reasons for the increased risk of NP post cardiac surgery in the elderly. The purpose of this study is to identify modifiable risk factors of nosocomial pneumonia (NP) in elderly patients post cardiac surgery.

METHODS: We conducted a case-control study in a postoperative intensive care unit of a University affiliated hospital.Seventy three case-control pairs were identified. Controls subjects were matched for age, gender, type of surgery, forced expiratory volume in one second (FEV1), and ejection fraction.Baseline sociodemograpahic information, Charlson Comorbidity Index, intra-and postoperative data were collected. When suspected, the presence of NP was confirmed by quantitative culture of protected bronchoalveolar lavage fluid ≥103 colony forming unit/ml or positive blood/pleural fluid culture identical to that recovered from respiratory samples.

RESULTS: The incidence of NP in elderly post heart surgery was 8.3%. The mean duration after heart surgery to the occurrence of pneumonia was 7.2+/- 4.9 days. Four variables were found to be significantly related to the development of NP by multivariate analysis: Charlson Index > 2 (adjusted odds ratio [AOR] 4.7; 95% confidence interval [CI], 1.9-11.4; $p < 0.001$), reintubation (AOR 6.2; 95% CI, 1.1-36.1; $p=0.04$), transfusion ≥ 4 units of PRBC (AOR 2.8; 95% CI, 1.2-6.3; $p=0.01$), and the mean equivalent daily dose of morphine (AOR 4.6; 95% CI, 1.4-14.6; $p=0.01$).

CONCLUSION: This study has identified three potentially modifiable risk factors that are responsible for the occurrence of NP in the elderly population post cardiac surgery: reintubation, PRBC transfusion, and excessive use of narcotics.

CLINICAL IMPLICATIONS: Although there are limited effective measures to lessen the burden of comorbidities, avoiding reintubation, finding a substitute to allogenic blood transfusion, and improved assessment of pain management could reduce the rate of NP in the post operative period of cardiac surgery in the elderly population.

DISCLOSURE: Ali El Solh, None.

EARLY INFECTIOUS PULMONARY COMPLICATIONS IN AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) RECIPIENTS

Ahmed A. Mahmoud MD* Mark R. Litzow MD Steve G. Peters MD Angela Dispenzieri MD Ayalew Tefferi MD Bekele Afessa MD Mayo Clinic College of Medicine, Rochester, MN

PURPOSE: To describe the infectious pulmonary complications that develop in autologous HSCT recipients during the first 30 days after transplant.

METHODS: In this prospective, observational study, we included all adults who had autologous HSCT in Mayo Medical Center. Confirmed bacterial pneumonia was defined by the growth of bacteria from respiratory specimen or pleural fluid in the appropriate clinical setting. If there was no growth of bacterial pathogen in the presence of the clinical criteria, the pneumonia was considered presumed. Fungal pneumonias were diagnosed according to International Consensus criteria described by Ascioglu et al.

RESULTS: Four hundred seventy HSCT recipients were enrolled in the study. Patients mean (SD) age was 54.6 (11.4) years; 61.5% were male and 93.4% were Caucasian. All but 7 patients had underlying hematologic malignancies. The source of stem cell was peripheral blood in 450 (95.7%). Pulmonary infections developed in 65 (13.8%) during the first 30 days following HSCT. These infections included presumed pneumonia (62), confirmed bacterial pneumonia (2), possible fungal pneumonia (2), probable fungal pneumonia (1) and probable pulmonary aspergillosis (1). The mean (SD) age of HSCT recipients with infection 58.1 (9.9) compared to 54.2 (11.3) of those without infection ($P = 0.0094$). There were no statistically significant differences in gender, ethnicity, graft source, and neutrophil engraftment period between patients with and without pulmonary infections.

CONCLUSION: Infectious pulmonary complications occur in about 14% of autologous HSCT recipients during the first month following transplant. The most common infectious pulmonary complication is presumed pneumonia. Fungal and viral pulmonary infections are uncommon during the first month after transplant. Old age appears to be a risk factor for the development of pulmonary infection.

CLINICAL IMPLICATIONS: Since fungal and viral pulmonary infections are uncommon during the first 30 days following HSCT, clinicians should focus on preventing and treating bacterial pulmonary complications.

DISCLOSURE: Ahmed Mahmoud, None.

DIAGNOSIS OF INVASIVE PULMONARY ASPERGILLOSIS WITH MULTISLICE CT-ANGIOGRAPHY

Stefan Sonnet MD Carlos Buitrago MD Jakob Passweg MD Michael Tamm MD* University Hospital Basel, Basel, Switzerland

PURPOSE: Invasive pulmonary aspergillosis (IPA) is a frequent infectious complication in neutropenic patients which is associated with a high mortality. IPA is suspected if antibiotic resistant-fever and infiltrates develop in neutropenic patients. The diagnostic yield of bronchoscopy with BAL for IPA is only 30% due to the fact that aspergillus is usually found intravascular. Typical signs on CT scan include the halo sign and consolidations with central necrosis. This study was undertaken to analyze the diagnostic value of CT angiography and to define whether signs of angio-invasiveness are more specific than other CT-signs for IPA.

METHODS: Consecutive immunocompromised patients with antibiotic resistant fever (n=30) underwent pulmonary CT angiographies (16 detector multislice CT) (n=41). CT scans were analyzed for infiltrate, consolidations and the halo sign. CTA were examined for vessel occlusion. CTA was considered positive if signs of vessel occlusion were detected.

RESULTS: A total of 47 lesions were noticed in 23 CTs (56%). Conversely, in 18 CTs no lesions were found. Histological examination was performed in 33 lesions (12 patients) and not available in 14 lesions (11 patients). In cases with histological examination, CTA was positive (vessel occlusion) in 13 of 16 histologically proven IPA lesions and in 2 non-fungal infiltrates. CTA was negative in 15 lesions with non-fungal etiology and in 3 lesions with documented IPA. In cases without histological confirmation (11 patients, 14 lesions) final diagnosis was based on clinical outcome and CT follow-up. CTA was positive in 6 cases with possible IPA (defined according to guidelines) and negative in 8 lesions without evidence of IPA (hematoma; fibrosing alveolitis; bacterial pneumonia). The overall sensitivity of the CTA sign was 86.4% and the specificity 92.0%. In comparison, the classical halo sign had a sensitivity of only 36.4% and a specificity of 84.0% to detect IPA.

CONCLUSION: CT angiography has a higher sensitivity than the classical CT-signs to detect IPA in neutropenic patients.

CLINICAL IMPLICATIONS: Multislice CT angiography seems to be an excellent diagnostic method to diagnose invasive pulmonary aspergillosis.

DISCLOSURE: Michael Tamm, None.

CT-GUIDED FINE NEEDLE ASPIRATION FOR DIAGNOSIS OF PULMONARY ASPERGILLOSIS

Masateru Kawabata MD* Hisafumi Takaya MD Atsushi Miyamoto MD Keishi Sugino MD Susumu Sakamoto MD Kazuma Kishi MD Eiyasu Tsuboi MD Sakae Homma MD Kunihiko Yoshimura MD Toranomon Hospital, Tokyo, Japan

PURPOSE: The prevalence of pulmonary aspergillosis is increasing because of the growing aged population and the diversity of medical treatments. However, it is not easy to diagnose aspergillosis microbiologically or pathologically. Although we frequently utilize CT-guided fine-needle aspiration (CT-FNA) for diagnosis of pulmonary aspergillosis, the usefulness and safety of the procedure is not well established. In this context, we have conducted a study to clarify the value of CT-FNA for making diagnosis of pulmonary aspergillosis.

METHODS: We retrospectively reviewed the medical records of the individuals with pulmonary aspergillosis who underwent CT-FNA from April 2003 to March 2005, and analyzed the accuracy and complications of the procedure. We percutaneously punctured the cavitary lesions or infiltrations with chest CT guiding by using 21 or 23 gauges-needle. If no specimen was obtained, small amount of saline (two to five ml) was infused into the lesions and recollected. The specimens were examined microbiologically and cytologically.

Nosocomial/Immunocompromised/Fungal Pneumonia, continued

RESULTS: Thirteen patients (8 males and 5 females) were enrolled and the mean age was 60.7 years old (41-77 years old). Six patients had been performed thoracic surgery previously and five had sequelae of tuberculosis. Diabetes mellitus and nontuberculous mycobacteriosis were associated with respective three cases. Two had been under medication with corticosteroid or immunosuppressive agents. Before CT-FNA, serial sputum cultures were negative in all cases, and bronchoscopic examinations were not conclusively diagnostic for aspergillosis in three. All patients were punctured successfully and sufficient specimens for the examinations were obtained. Aspergillus was isolated from six cases and five specimens were cytologically positive for Aspergillus. In total, eight of thirteen (61.5%) could be diagnosed pulmonary aspergillosis definitely by CT-FNA. In all patients, CT-FNA were performed without any serious complications such as pneumothorax or bleeding.

CONCLUSION: CT-FNA is an useful technique in defining diagnosis of pulmonary aspergillosis which could be conducted safely and less invasively.

CLINICAL IMPLICATIONS: If pulmonary aspergillosis is clinically suspected but the diagnosis is undetermined, CT-FNA should be considered as the next diagnostic approach.

DISCLOSURE: Masateru Kawabata, None.

SEROLOGIC STUDIES IN PATIENTS WITH PULMONARY COCCIDIOIDAL NODULES OR MASSES

Sammy C. Campbell MD* Michael P. Habib MD University of Arizona, Tucson, AZ

PURPOSE: To determine the use of coccidioidal serology in evaluating the cause of pulmonary masses or nodules.

METHODS: At the Tucson VA hospital, we retrospectively reviewed 142 needle biopsies or aspirations (FNA) of pulmonary nodules or masses from July 2001 through June 2003 and concomitant serologic studies (within 3 months) of the FNA. The serologic studies were immunodiffusion tube precipitin antibody (IDTP), immunodiffusion complement fixation antibody (IDCF) and complement fixation titers to Coccidioides antigen. We also reviewed all 86 additional persons diagnosed with pulmonary coccidioidomycosis during the same period.

RESULTS: Of the 142 persons with FNA, all had negative serology. Eighteen had coccidioidomycosis, 92 had cancer, 40 had non-diagnostic FNA and one had histoplasmosis. Of the 86 other persons with pulmonary coccidioidomycosis all were positive by IDCF testing except three who had positive IDTP. Eighteen had a mass or nodule, 38 had pneumonia, 3 had hilar adenopathy, 8 had single cavities, 9 had diffuse disease, and 10 had chronic fibrocavitary disease. Of the 18 persons with a coccidioidal mass or nodule (and positive serology), 9 were know to be post-primary coccidioidal pneumonia. For the other 9, the nodule or mass was of unknown cause. The positive serologic test was evidence that the lesion was due to coccidioidal infection. With over one year follow-up, there was no indication of growth or other evidence of neoplastic disease in these 9 individuals.

CONCLUSION: Coccidioidal serology is used to evaluate patients with lung nodules or masses in an endemic area. Persons with negative serology are often referred for lung FNA when there is suspicion of cancer. Persons with a positive serology are presumed to have coccidioidal infection as the etiology of the mass or nodule. Although patients with coccidioidal nodules may have negative serology, no patient with cancer had positive serology.

CLINICAL IMPLICATIONS: Coccidioidal serology is useful in evaluating lung nodules and masses where coccidioidomycosis is endemic. A positive serologic test for antiboidy is used to help diagnose coccidioidal etiology and to exclude cancer.

DISCLOSURE: Sammy Campbell, None.

NEUTROPHILS IN A PATIENT WITH JOB'S SYNDROME ARE LESS VISCOELASTIC THAN THOSE IN NORMAL SUBJECTS

Masaru Yanai MD* Tomoko Suzuki MD Hiroshi Kubo MD Hidetada Sasaki MD James P. Butler PhD Ishinomaki Red Cross Hospital, Ishinomaki, Japan

PURPOSE: To investigate the regional viscoelasticity of locomoting neutrophils in a patient with Job's syndrome, in both a stable condition and in a condition with severe infection.

METHODS: We measured regional rheological properties in the leading, body, and trailing regions of spontaneously locomoting neutrophils in a patient with Job's syndrome (27yo, male) in a stable condition and in a condition with pneumonia and meningitis, and compared the results with those of normal subjects. We optically trapped intracellular granules and measured their displacement for 500ms following a 100nm step change in the trap position. Results were analyzed in terms of a simple viscoelasticity model, and using the structural damping model (stress relaxation follows a power law in time).

RESULTS: Regional viscoelastic stiffness and viscosity or structural damping storage and loss moduli were all significantly lower in leading regions compared to pooled body/trailing regions (the latter were not significantly different); leading regions were significantly more fluid-like than body/trailing regions in both the patient and normals. The rheology of leading region and body/trailing regions of neutrophils in the stable patient is ~50% less elastic and less viscous than that in normals. Neutrophils obtained when the patient suffered from pneumonia and meningitis were not significantly different rheologically from those obtained when the patient was in a stable condition.

CONCLUSION: 1) The significantly more fluid-like behavior of the leading edge supports the idea that intracellular pressure may be the origin of motive force in neutrophil locomotion. 2) In a patient with Job's syndrome, neutrophils are less viscoelastic than those in normals. Moreover, neutrophils failed to show any significant stiffening when the patient suffered from severe infection. These results may account in part for neutrophil dysfunction in Job's syndrome.

CLINICAL IMPLICATIONS: Intervention to make neutrophils stiffer may be helpful in improving neutrophil function in patients with Job's syndrome.

DISCLOSURE: Masaru Yanai, Grant monies (from sources other than industry) From the Ministry of Education and Science, Japan.

Palliative and End of Life Care
12:30 PM - 2:00 PM

THE UNMET NEEDS OF CRITICAL CARE FAMILIES AS PERCEIVED BY THE ICU TEAM

Antara Mallampalli MD* Jane Dowling PhD Marilyn Lederer Kalpalatha K. Guntupalli MD Baylor College of Medicine, Houston, TX

PURPOSE: The families of critically ill patients are under a great deal of stress for a variety of reasons. To assess the needs of families as perceived by critical care caregivers, we reviewed the applications to an RFP from the CHEST foundation for the "Critical Care Family Assistance Program" grant.

METHODS: We retrospectively analyzed proposals over a 2 year cycle (2004-2005). Information was extracted regarding the perceived unmet needs of the families of ICU patients in each institution, as elaborated by the institution's critical care team based on a variety of assessment methods including surveys of families, focus groups, staff surveys, and direct observations by team members. Information from a total of 52 ICUs from the following categories was available: Group I: Tertiary referral center of academic program (n=32); Group II: Urban hospital of community >100,000 (n=16); Group III: Pediatric ICUs (n=4).

RESULTS: The following were the most frequently cited unmet needs of families of ICU patients: more secure and comfortable waiting areas (33/52); better, more frequent, and/or more systematic communication with the ICU team (29/52); better education materials regarding the ICU and illnesses of the family member (27/52); financial assistance with lodging and board for low-income families (21/52); more liberal and/or consistent visiting hours (2/52). Other needs cited included more interpreter services and language-diverse educational resources, a dedicated ICU social worker, and activities for children of patients/families. The perceived needs did not differ significantly between the three groups of ICUs.

CONCLUSION: There is increasing awareness of the importance of improving family satisfaction with, and understanding of, the care of loved ones who are critically ill. Evidence suggests that a satisfied family affects the outcome of the ICU patient positively. Regardless of the type of ICU, geographic location, or number of beds, certain common needs seem to be of importance to the families of critically ill patients.

CLINICAL IMPLICATIONS: Hospital and ICU administrations should be cognizant of these needs in order to better serve the families of their critically ill patients.

DISCLOSURE: Antara Mallampalli, None.

IMPROVING MEDICAL STUDENT INTENSIVE CARE UNIT COMMUNICATION SKILLS: A NOVEL EDUCATIONAL INITIATIVE

Scott M. Lorin MD* David M. Nierman MD Mount Sinai School of Medicine, New York, NY

PURPOSE: To determine whether Intensive Care Unit (ICU) communication skills of fourth year medical students could be improved by an educational intervention.

METHODS: Prospective study conducted from August, 2003 to May, 2004. Tertiary care university teaching hospital. All fourth year students were eligible to participate during their mandatory four-week CCM clerkship. The educational intervention included formal teaching of a communication framework for the initial meeting with the family member of an ICU patient, followed by a practice session with an actor playing the role of a standardized family member (SFM) of a fictional patient. At the beginning of the CCM rotation, the intervention group received the educational session, while students in the control group did not. At the end of each CCM rotation, all students interacted with a different SFM portraying a different fictional scenario. Sessions were videotaped, and were scored by both investigators together using a standardized grading tool across four major domains: Introduction, Gathering Information, Imparting Information, Setting Goals and Expectations. Ten study subjects were chosen at random six months later, and their videotapes again reviewed and scored by both investigators blinded to the initial scoring results.

RESULTS: A total of 106 (97%) medical students agreed to participate in the study. The total mean score as well as the scores for the four domains for the intervention group were significantly higher than for the control group ($p < 0.0001$). These differences remained statistically different after adjusting for multiple comparisons. The observed intra-rater agreement for the communication assessment instrument was good ($\kappa = 0.69$).

CONCLUSION: The communication skills of fourth year medical students can be improved by teaching and then practicing a framework for an initial ICU communication episode with a SFM.

CLINICAL IMPLICATIONS: This educational initiative has important implications regarding teaching and assessing core critical care communication skills in the medical school curriculum.

DISCLOSURE: Scott Lorin, None.

CASE-BASED, FACILITATED SMALL GROUP DISCUSSIONS TO TEACH END-OF-LIFE CARE FOR PATIENTS WITH ADVANCED CHRONIC (RESPIRATORY) DISEASE

Ronald W. Damant MD* Justin Weinkauf MD Brendan Leier PhD Barbara Russel PhD Paul Byrne MD University of Alberta, Edmonton, AB, Canada

PURPOSE: Chronic respiratory conditions like Chronic Obstructive Pulmonary Disease (COPD) are a common cause of death in many countries. Further "graying" of the population will result in an increasing prevalence of and mortality from these so-called "non-malignant" conditions. End-of-life care for patients with chronic (respiratory) disease is an important aspect of health care delivery. Those caring for patients nearing the end-of-life must be proficient in the principles and practice of palliative care. Our study was designed to evaluate the use of facilitated, small group discussions focusing on illustrative cases (cognitive simulation) to teach/learn this essential knowledge.

METHODS: Consenting medical students (all from the University of Alberta) and resident physicians (from medical schools across Canada) were given a "primer" reviewing the principles of end-of-life care (numerous guidelines exist). They then participated in two small group sessions during which they were asked to manage a hypothetical but plausible patient dying from advanced COPD. Finally, a questionnaire regarding their experience was completed.

RESULTS: 100% of participants disagreed with the statement, "end-of-life care is well-represented in the training programs in which I have been enrolled". 100% of participants, however, agreed or strongly agreed that "end-of-life management is an important part of health care", and that it would be an "important part of (their) future duties". 57% and 43% strongly agreed or agreed that "small group discussions are an excellent way to learn end-of-life care", and all either agreed or strongly agreed that they would "recommend the experience to a colleague". An analysis of the intervention's effect on both general (conceptual) and specific (recall of practical details) learning outcomes indicates that participants perceived an improved understanding in several dimensions of end-of-life care.

CONCLUSION: End-of-life care is likely underrepresented in medical training programs across Canada. Case-based, facilitated small group discussions appear to be a highly acceptable method with which to teach and learn end-of-life care.

CLINICAL IMPLICATIONS: The potential exists to improve end-of-life patient care through standardized, case-based, small group discussions/simulations.

DISCLOSURE: Ronald Damant, None.

CORRELATION OF THE QUALITY OF DYING AND DEATH QUESTIONNAIRE AND THE CRITICAL CARE FAMILY SATISFACTION SURVEY IN A MULTI-SPECIALTY INTENSIVE CARE UNIT

Daniel E. Ray MD* Cathy Fuhrman RN Darryl Arnold Tamara Masiado Jack Geracci Thomas Wasser PhD Robert Kruklitis MD Lynn Deitrick PhD Lehigh Valley Hospital and Health Network, Allentown, PA

PURPOSE: Instruments to evaluate patient/family care and satisfaction at the end-of-life in an intensive care unit (ICU) are limited. The Quality of Dying and Death Questionnaire (QODD) and the Critical Care Family Satisfaction Survey (CCFSS) are tools that have been validated in different populations. The goal of this study was to correlate the results of the Family and Nurse QODD and CCFSS for patients who died in a multi-specialty ICU.

METHODS: This study took place in a 28-bed medical, surgical, and trauma ICU of a 610-bed community-based, tertiary referral center. As part of ongoing quality improvement, the CCFSS is given to families upon discharge from the ICU while the QODD is distributed within two weeks of discharge to families of patients who die in our ICU. Using Pearson's correlation, total scores for the Family and Nurse QODD were compared to the total score and subscales of the CCFSS. Correlation was significant at the 2-tailed, 0.01 level.

RESULTS: Between 3/1/04 and 4/30/04, 182 deaths occurred in the ICU's of which 159 (87%) of the families and nurses received the QODD and 180 (99%) received the CCFSS. Return rates were variable (19.4%, CCFSS; 51.9% Family QODD; 63.5% Nurse QODD). There were 26 matching sets of QODD and CCFSS. There was poor correlation between the Family and Nurse QODD ($r = 0.422$, $p = 0.05$). The Family QODD correlated well with the CCFSS information subscale ($r = 0.598$, $p = 0.019$), but in general the Family QODD and Nurse QODD did not correlate with the CCFSS total score ($r = -0.086$ and $r = 0.006$, respectively).

CONCLUSION: (1) Incompleteness and low return rates make survey methodology as part of quality improvement in ICU challenging (2) the Family and Nurse QODD may not be interchangeable as quality indicators for the end-of-life care, and (3) family perception of quality care during the dying process is associated with satisfaction with information.

CLINICAL IMPLICATIONS: Continued validation of the QODD and CCFSS is needed.

DISCLOSURE: Daniel Ray, None.

OUTCOME OF NURSING HOME PATIENTS PRESENTING TO AN EMERGENCY DEPARTMENT IN RESPIRATORY FAILURE

Jason L. Moore MD* Rajika Munasinghe MD Lawrence MacDonald MD Sinai-Grace Hospital, Detroit, MI

PURPOSE: There is limited information regarding the outcome and survival of institutionalized patients who present with acute respiratory failure. We investigated the inpatient outcome and one year mortality of nursing home patients intubated in an emergency department.

METHODS: We performed a retrospective analysis of medical records of nursing home patients who presented to our Emergency Department with acute respiratory failure from 2000-03. Cause of acute respiratory failure, severity of illness, length of stay, hospital survival and cost of admission were noted. Multivariate analysis of admission patient characteristics was performed to determine which were associated with outcome. One-year mortality data were collected from hospital records and the Michigan Department of Vital Statistics. For hospital outcome analysis each admission was analyzed. One-year mortality analysis was performed per patient.

RESULTS: 354 episodes of acute respiratory failure in 277 patients were studied. Overall hospital mortality was 48%. Mean hospital length of stay was 4.27 [$\pm$ 6.051 standard deviation (SD)] days in patients who expired and 10.78 ($\pm$ 6.107 SD) days for survivors. Mean total charges of admission were $30,032 for all patients. Fifteen clinical factors at presentation were significantly associated with hospital mortality. Most predictive were: presence of

Palliative and End of Life Care, continued

cardiopulmonary resuscitation (CPR) [89% mortality; odds ratio (OR) 8.397; p< 0.0001], vasopressor use in the ED (70% mortality; OR 2.586; p< 0.0001), history of cancer of any type (70% mortality; OR 2.543; p<0.005) and cardiovascular failure (65% mortality; OR 2.018; p<0.0001). For the 277 patients studied the one-year mortality was 87%.

CONCLUSION: The occurrence of acute respiratory failure in nursing home patients is associated with significant hospital mortality and charges. Less than 15% survive for one year after the intubation episode. Hospital mortality was especially pronounced in patients with a history of cancer, vasopressor use in the ED, who present in cardiovascular failure or who have undergone CPR.

CLINICAL IMPLICATIONS: End-of-life-care discussions in the nursing home population should include consideration of acute respiratory failure as a harbinger of death.

DISCLOSURE: Jason Moore, None.

PALLIATIVE MEDICINE IN CRITICAL CARE IN AN ACUTE CARE COMMUNITY HOSPITAL

Paul A. Selecky MD* Debbie Lepman MPH Molly Hewett RN Kirsten Pyle RN Herbert Rogove DO Cheryl Steffen Kristyn Sparks Don Oliver PhD Hoag Hospital, Newport Beach, CA

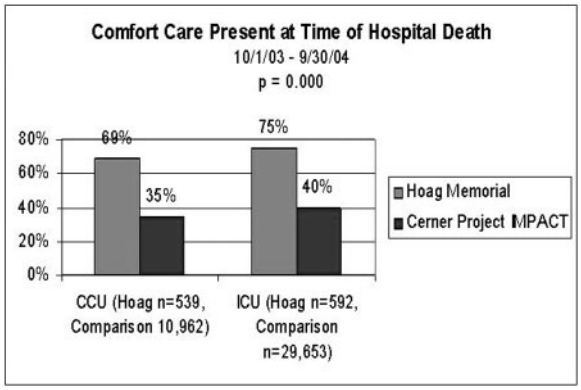
PURPOSE: The daily practice in critical care units is to treat life-threatening illness and prolong life, often at significant burden. What happens when the patient/family/healthcare team decides that the treatment is futile and not in the patient's best interests, and says "No more"? A multidisciplinary program was developed in this 400-bed community hospital to provide palliative care in this critical care setting.

METHODS: A team of intensivisits and other physicians, nurses, social workers and chaplains created a program of providing palliative care, including a hospital-wide program in advance care planning, multidisciplinary patient care rounds, a daily Patient Goals Sheet that includes palliative care as an option, family conferences, a Comfort Care Pathway, a full-time hospital Palliative Care Coordinator, and pre-printed order set for ventilator withdrawal of the dying patient. Data were collected using a critical care software that compared results to a national database of like hospital beds, as well as to published literature.

RESULTS: Analysis revealed that 87% of CCU admissions had a written Advance Directive compared to 29% of the national database. In the ICU, it was 79% vs. 30% in the comparative database. Patients died on comfort care orders 69% of the time in ICU compared to 35% of the database. In the ICU, it was 75% vs. 40% (see graph). In addition, requests for ethics consults decreased from weekly to once monthly or less. Compared to published literature, palliative end-of-life care was initiated sooner in patients with global cerebral ischemia or sepsis.

CONCLUSION: An multidisciplinary team effort in palliative care can improve the care of critically ill patients for whom aggressive life-sustaining treatment is no longer productive for the patient.

CLINICAL IMPLICATIONS: The burden of aggressive life-sustaining treatment in critical care units can be relieved by an organized multidisciplinary approach to providing palliative care for selected patients for whom aggressive care is thought not to be in the patient's best interests, and thus reduce prolonged suffering of terminally-ill patients and the inappropriate use of critical care resources.



DISCLOSURE: Paul Selecky, None.

Pediatric Asthma
12:30 PM - 2:00 PM

REMOVAL OF FINANCIAL AND ACCESS BARRIERS DOES NOT GUARANTEE ADHERENCE TO ASTHMA CONTROLLER THERAPY

Lynn B. Gerald PhD* Leslie McClure PhD Joan Mangan PhD Linda Gibson RN Roni Grad MD University of Alabama at Birmingham, Birmingham, AL

PURPOSE: Inhaled corticosteroids offer considerable protection against asthma exacerbations. However, few patients take their inhaled steroids as prescribed. Underuse of inhaled steroids is common among inner-city children. Commonly cited barriers to adherence include lack of access to medication, cost of medication, and ease of access to refills. Therefore, we are collaborating with inner-city school districts to examine the effect of school based supervised asthma therapy on asthma morbidity.

METHODS: Two hundred and ninety six children (ages 6-13) with persistent asthma who have enrolled in the study were examined. Children are currently in the baseline data collection phase of the study. In this phase, rescue and controller medication are provided at no charge to participants but medication use is not yet supervised. To obtain refills of medications, parents are instructed to call the study coordinator and request that medication be mailed to them. We examined the number of children who had rescue medication at school at the time of enrollment and the number of children who have refilled their controller medication on schedule since the time of enrollment.

RESULTS: Ninety-two percent of children in the sample are black, 7% are white and 44% are female. Of the 296 children, 36 (8%) had rescue medication at school at the time of enrollment. On average, children had approximately 1.4 fewer refills than were expected (p<0.0001). To date, two hundred thirteen children have been due to refill their controller medication. Of these 213, 148 (69%) have never refilled their controller medication and 36 (17%) have refilled their medication at the expected rate. The remaining 29 (14%) have refilled their medication at less than the expected rate. Refill rates did not differ by race, gender or age of the child.

CONCLUSION: These data indicate that even when commonly cited barriers to adherence are removed, refill rates are much lower than expected.

CLINICAL IMPLICATIONS: There is a need to consider other social and behavioral factors which may influence patients' decisions to adhere to medication regimens.

DISCLOSURE: Lynn Gerald, None.

AREA UNDER THE MAXIMUM EXPIRATORY FLOW-VOLUME CURVE: A MEASURE OF LUNG FUNCTION IN PRESCHOOL CHILDREN

Caroline Pesant MD* Miriam Santachi MD Mario Geoffroy RRT Theophile Niyonsega PhD Mario E. Dumas MS Jean Paul Praud PhD Helen Vlachos MD Centre Hospitalier Universitaire de Sherbrooke, Fleurimont, PQ, Canada

PURPOSE: Preschool children have recently been shown to perform reliable forced spirometry. Due to their different physiology and shorter expiratory times, several measurements have been proposed for the evaluation of lower airway obstruction. As Area under the maximum expiratory flow-volume curve (Aex) appears to be a sensitive, and convenient parameter in detecting bronchoconstriction and bronchodilation, our aim was to establish normative data for an extensive number of parameters including Aex in healthy 3 to 5 year old children in our population.

METHODS: The study population consisted of healthy Caucasian children aged between 3 and 5 years in 11 different daycare centers in the Eastern Townships of Quebec . Measurements were obtained as recommended by ATS guidelines using the Ms Pneumo spirometer (Jaeger) . As children have been shown to exhale in less than one second, expiratory manoeuvres lasting less than one second were included. Aex was calculated from the curve showing the highest sum of FEVx (where x can be one second or less) + FVC and analysed in relation to sex, age, height and weight.

RESULTS: One hundred forty three children were tested of which 69 were males (48%). Twenty-three were 3 years old, 56 were 4 years old and 64 were 5 years old. One hundred and twenty-eight (90%)were able to perform at least two technically acceptable expiratory manoeuvres. Log Aex = -16.989 + 3.749 Log height (r=0.574, p less than 0.001) and Log Aex = -16.019 + 3.528 Log height (r=0.651, p less than 0.001) were the best equations for boys and girls respectively.

CONCLUSION: Aex can be easily and successfully performed in 3 to 5 year old children and can be predicted from height using power equations in both the males and females of our population.

CLINICAL IMPLICATIONS: Aex is a promising measure of lung function which can potentially be used in the the diagnosis and follow up of obstructive airways disease in very young children.

DISCLOSURE: Caroline Pesant, Grant monies (from sources other than industry) Quebec Foundation for Research; Grant monies (from industry related sources) Merck Frosst Canada.

THE RELATIONSHIP OF FORCED EXPIRATORY VOLUME IN ONE SECOND AND MAXIMUM MID-EXPIRATORY FLOW RATE IN THE DIAGNOSIS OF EXERCISE INDUCED ASTHMA

Agnes Angela S. Sanchez MD* Arnel Gerald Q. Jiao MD Christine Q. Sua MD Rigmor Dygico RRT Ma. Gina Enano RRT Philippine Children's Medical Center, Quezon City, Philippines

PURPOSE: The relationship of Forced Expiratory Volume in one second (FEV1) and Maximum Mid-expiratory Flow Rate (MMEF) in the diagnosis of exercise-induced asthma (EIA) was analyzed in this study. Specifically, the percent decrease in MMEF and FEV1 was correlated and the sensitivity of MMEF in the diagnosis of EIA was determined.

METHODS: This is a cross-sectional study of 91 asthmatic patients, 7-18 years old, classified as either intermittent or newly diagnosed mild persistent. They underwent exercise challenge test (ECT) using the treadmill protocol and the FEV1 and MMEF responses were recorded as the greatest fall expressed as a percentage of the baseline. Other statistical tools used were the pearson correlation and the linear regression analysis.

RESULTS: Based on a ≥ 15% fall in FEV1, there were 60 patients in the positive exercise induced bronchoconstriction (EIB) group and 31 patients in the negative EIB group. The prevalence of exercise-induced asthma was 65.9%. Baseline spirometry was within normal limits for both groups. There was a significant correlation between the percent decrease in FEV1 and MMEF after an ECT. A fall of ≥ 25% in MMEF approximated a ≥ 15% fall in FEV1 with a sensitivity of 90%. The percent decrease in MMEF that could approximate the percent decrease in FEV1 of 10% or 13% was also computed using the equation derived from the linear regression analysis as follows: (Estimated) MMEF % fall = 10.017 + 1.031 x (FEV1 %fall).

CONCLUSION: This study demonstrated that a ≥ 25% fall in MMEF showed good correlation with a ≥ 15% fall in FEV1, with a sensitivity of 90%.

CLINICAL IMPLICATIONS: The significant correlation between the percent decrease in FEV1 and MMEF confirms that changes occur in both large and small airways. MMEF may serve as an additional parameter or may be a useful alternative in the diagnosis of EIA, especially in patients with a < 15% fall in FEV1 or those with a submaximal effort during a forced expiratory maneuver.

DISCLOSURE: Agnes Angela Sanchez, None.

THE ASSOCIATION OF SPIROMETRY WITH IMPULSE OSCILLOMETRY IN PEDIATRIC PATIENTS WITH ASTHMA

Khalila Lewis-Brown MD* Glenn Hildreth RRT Kevin D. Maupin MD University of Florida Department of Pediatrics/Sacred Heart Children's Hospital, Pensacola, FL

PURPOSE: The purpose of this study is to evaluate the association of spirometry, Forced Expiratory Volume in 1 second(FEV1) and Forced Vital Capacity(FVC), with airway resistance via Impulse Oscillometry at 5 Hz(RAW) in assessing asthmatic pediatric patients.

METHODS: We retrospectively reviewed 84 patient charts with a diagnosis of asthma. The patients were coached to breath passively. Artifacts caused by cough or swallowing show increased resistance. We reviewed the charts for the following parameters: age, sex, percent predicted of FEV1, (value <80% predicted is abnormal), percent predicted of FVC, (value<80& is abnormal), percent predicted of RAW, (value >150% is abnormal), maintenance inhaled steroids, and diagnosis.

RESULTS: The age ranged from 5 years old to 18 years old. 43(51.2%) of the patients were female and 41(48.8%) were male. 76(90.5%) of the patients had an RAW<150%. Of the patients with a normal RAW, 20(26.3%) had a FEV1<80% only, 2(2.6%) had a FVC <80% only, and 5(6.6%) had both an FEV1 and FVC<80%. Of the 8(9.5%) patients with an RAW>150%, 2(25%) had an FEV1<80% only, 3(37.5%) had both an FEV1 and FVC<80%, and 3(37.5%) of the patients had both an FEV1 and FVC>80%. All of the patients wih an RAW >150% were on maintenance inhaled steroids and had a diagnosis of moderate persistent asthma. Overall, 70(83.3%) patients had a diagnosis of moderate persistent asthma and 14(16.7%) patients had a diagnosis of mild persistent asthma. None of the patients were ill when testing.

CONCLUSION: In this study, a patient's FEV1 and FVC were not associated with RAW. RAW could not be predicted by FEV1 and FVC. An increased RAW was not associated with a decreased FEV1 and FVC.

CLINICAL IMPLICATIONS: Spirometry and Impulse Oscillometry should be used together along with clinical history in evaluating patients for asthma. Impulse oscillometry alone should not be used in assessing asthma until further studies have been performed. Further studies are needed to evaluate the role of Impulse Oscillometry in relation to Spirometry when assessing asthmatic pediatric patients.

DISCLOSURE: Khalila Lewis-Brown, None.

DOES INFLUENZA VACCINATION IMPROVE PEDIATRIC ASTHMA OUTCOMES?

Bruce Ong MD* Jordan Pinsker MD Joseph Forester DO Andre Fallot MD San Antonio Military Pediatric Center, San Antonio, TX

PURPOSE: Controversy exists regarding the effectiveness of influenza vaccination in preventing influenza-related asthma exacerbations in the pediatric population. While yearly influenza immunization is widely recommended for asthmatic children, there is currently little evidence to support this practice. Several studies have demonstrated no measurable benefit in asthma outcomes. This study sought to determine if influenza vaccination status is associated with indicators of asthma morbidity within the military pediatric population.

METHODS: A survey of patients aged 3-18 years with a diagnosis of asthma enrolled to the pediatric clinics of Brooke Army Medical Center, Fort Sam Houston, Texas and Wilford Hall Medical Center, Lackland Air Force Base, Texas was conducted. Management practices and outcomes for 80 children were evaluated. Univariate analyses were performed to identify associations between influenza vaccination and selected demographic variables and asthma exacerbation defined by oral steroid prescription, hospital visits and unscheduled clinic or emergency department visits for asthma symptoms. Logistic regression analyses were conducted to detect possible confounding variables.

Table 1—*Univariate Analysis, Distribution of Influenza Vaccination Status Pilot Data, N = 80*

Independent variable	Received vaccination (n = 49) Number (%)	No vaccination (n = 31) Number (%)	Chi Square p Value
Race			
White	26 (53)	9 (29)	0.97
Non-White	13 (26)	22 (70)	
Gender			
Male	24 (49)	20 (65)	0.62
Female	25 (51)	11 (35)	
Has asthma action plan	33 (67)	13 (42)	.025
Received formal asthma education	32 (65)	16 (68)	.0.22
On post housing	13 (27)	5 (16)	0.99
Prescribed oral steroid	32 (65)	15 (48)	0.03
Hospitalized in last 12 months	7 (14)	5 (16)	0.68
Unscheduled ED or clinic visit last 12 months	31 (63)	15 (48)	0.59
Prescribed ICS	42 (86)	27 (87)	0.25
Active duty family member	34 (69)	20 (65)	0.35

RESULTS: In the univariate analyses, current influenza vaccination status was associated with a significant reduction of oral steroid use in the 12 months prior to the survey (Table 1). This relationship was appreciated to a lesser extent with ED or unscheduled clinic visits in last 12 months.

Pediatric Asthma, continued

No significant differences were found regarding the distribution of influenza vaccination status across selected variables. In the multivariate analyses, current influenza vaccination status was independently associated with significantly decreased odds of using oral steroids in the previous 12 months (Table 2). There was no evidence of confounding or effect modification.

CONCLUSION: This study suggests influenza vaccination is associated with fewer asthma exacerbations. After controlling for several potential confounding variables, administration of influenza vaccine was associated with a protective effect against indicators of asthma exacerbations. Our results indicate that pediatric asthmatics in the military beneficiary population may benefit from annual influenza vaccination.

CLINICAL IMPLICATIONS: These measurable differences in asthma outcomes help confirm current recommendations for clinical practice and set the stage for further prospective trials.

Table 2—*Logistic Regression of Asthma Outcomes by Influenza Vaccination Status and Covariates, Pilot Data, N = 80*

Independent variable	Odds of prescribed oral steroid OR (95% CI)	Odds of being hospitalized in last 12 months OR (95% CI)	Odds of ED or unscheduled clinic visit in last 12 months OR (95% CI)
Race			
AA	1.16 (0.37-3.60)	3.73(0.66-21.08)	1.07(0.34-3.37)
MA	1.99 (0.60-6.63)	2.01(0.32-12.70)	0.72(0.23-2.25)
Gender, male	1.70 (0.60-4.84)	0.48(0.12-1.94)	2.41(0.86-6.78)
Received influenza vaccine in last 12 months	0.290(0.10-0.84)	1.39(0.34-5.67)	0.54(0.20-1.49)
On post housing	1.56 (0.49-5.02)	0.59(0.11-3.10)	1.61(0.52-5.02)
Prescribed ICS	2.15(0.48-9.61)	1.48(0.15-15.10)	2.55(0.58-11.30)

DISCLOSURE: Bruce Ong, None.

PROSPECTIVE STUDY COMPARING THE EFFICACY OF ORAL PROCATEROL + LOW DOSE INHALED BUDESONIDE VS HIGH DOSE INHALED BUDESONIDE ALONE IN PREVENTING EXACERBATIONS AMONG MODERATE PERSISTENT ASTHMATICS AGED 7 - 18 YEARS

Ronald Allan F. Austria MD* Arnel Gerald Q. Jiao MD Ma. Cecillia C. Nierva MD Beatriz Praxedes Apo I. Mandanas MD Celia T. Tardaguila RRT Philippine Children's Medical Center, Quezon, Philippines

PURPOSE: The aim of this study was to determine if addition of oral procaterol to low dose budesonide was comparable to high dose budesonide in preventing exacerbations among moderate persistent asthmatics.

METHODS: A 16 week prospective study was conducted in 20 patients aged 7 - 18 years moderate persistent asthmatics.After a 2 week run-in period, patients were randomized to treatment with either oral procaterol 25ug/dose BID + low dose budesonide (400ug/day) or high dose budesonide (800ug/day) alone.Lung function was measured serially and patients kept a diary of symptoms and bronchodilator use.

RESULTS: Forced expiratory volume in 1 second (FEV1) at 6th week was significantly increased in both treatment groups (p-0.03), likewise in symptoms,nocturnal cough(p-0.02) and daytime cough(p-0.01).There was no significant difference between the treatment groups in all the parameters measured.

CONCLUSION: This study demonstrated improvement in pulmonary function and symptom control in both treatment groups.However, clinical efficacy between the two treatment groups showed no significant difference in preventing exacerbations among moderate persistent asthmatics,probably because of the relatively small sample size involved.Thus, the author recommends to increase sample size to achieve significant outcome.

CLINICAL IMPLICATIONS: This study wants to determine that adding oral procaterol to low dose budesonide was comparable to high dose budesonide in preventing exacerbations among moderate persistent asthmatics thereby, may be used as an alternative treatment regimen among moderate persistent asthmatics.

DISCLOSURE: Ronald Allan Austria, Grant monies (from sources other than industry) The Philippine Children's Medical Center research fund shouldered the payment of spirometry fee of all patients in this study.; Grant monies (from industry related sources) otsuka provided the procaterol used by patients in this study while Astra provided the budesonide used by patients in this study.

Topics in Thoracic Surgery
12:30 PM - 2:00 PM

THE PREVENT EFFECT OF STATIN ON PULMONARY ISCHEMIA-REPERFUSION INJURY IN RATS

Birong Dong PhD* Du J. Zhong MD Departmentof Geriatrics, West China Hospital of Sichuan University, Chengdu, Peoples Rep of China

PURPOSE: To evaluate the protective effect of atorvastatin(Lipitor) on the lung ischemia-reperfusion injure(LIRI) and its possible mechanism.

METHODS: Single lung in site ischemia-reperfusion animal model was used. Thirty Wistar rats were randomly divided into three groups(n=10/group): a)sham operate group(SO), b)Pulmonary models of ischemia-reperfusion injury(IR) and c)atorvastatin treated group(AT). The blood flow in two latter groups were blocked up for 60 minutes, then followed by reperfusion for 120 minutes. In the AT group, the rats were fed atorvastatin (10mg/Kg) for seven days before ischemia-reperfusion. The wet-to-dry (W/D) lung weight ratio, lung permeability index(LPI), malondialdehyde contents(MDA)surperoxide dismutase(SOD) activity, myeloperoxidase(MPO) activity in the lung tissue were measured respectively. Lung tissue was observed by light microscope. Immunohistochemical technique was used to detect the inducible nitrioxide synthase(iNOS), endothelial NOS (eNOS) and surfactant protein A(SP-A) expression in lung tissues.

RESULTS: The levels of LPI,MDA contents, MPO activity and W/D were significantly decreased in AT group(0.0230+0.00273; 17.685±1.537; 0.0527±0.002026 and 4.65+0.11434) than in IR group(0.0301+0.00421; 37.364±3.166; 0.0797±0.003902 and 769+0.1063), but the activity of SOD was significantly increased in AT group than in IR group (34.726±0.943 vs 19.728±0.817,$p<0.01$).The expression of SP-A and eNOS were upregulated in AT group compare with IR group (1996.584±260.081 vs 1119.609±348.256,$p<0.05$; 181.933±65.715 vs 69.228±16.759,$p<0.05$), but the expression of iNOS was significantly downregulated in AT group other than in IR group (82.294±41.150 vs 303.739±95.383,$p<0.01$).

CONCLUSION: The data showed that atorvastatin can significantly protect lung ischemia-reperfusion injury by upregulating the eNOS and SP-A expression and downregulating iNOS expression, and maintaining pulmonary surfactant and activity of Enos, decreasing free radicle and anti-inflammatory effect.

CLINICAL IMPLICATIONS: It is worth to further study atorvastatin protecting lung ischemia-reperfusion injury in pulmonary embolism, lung transplantation and cardio-pulmonary surgery.

DISCLOSURE: Birong Dong, None.

SURGERY IN TRACHEAL OBSTRUCTION-MANAGEMENT AND RESULTS

Rajan Santosham MBBS* Santosham Chest Hospital, Chennai, India

PURPOSE: Our objective was to analyse the charecteristics and results of tracheal resection and reconstruction.

METHODS: A total of 287 patients underwent tracheal resection and reconstruction from 1990 to 2004. Postintubation tracheal stenosis was present in 251 patients of which 149 patients had cuff lesions and 97 had stomal lesions. Tracheal resection and reconstruction wee performed for 41 patients who had tracheal tumors. Laryngeal obstructions were seen in 8 patients of which 3 had obstructions in more than one level. The approach was cervical in 232 patients, cervico-mediastinal in 34 patients and through a right thoracotomy in 8 patients. The length of resection of trachea was 1 to 5.5 cm. Preoperatively all the patients were routinely submitted for pulmonary function test, computed tomography of neck and chest with 3 dimension reconstruction and virtual bronchoscopy and flexible fibreoptic bronchoscopy.

Topics in Thoracic Surgery, continued

RESULTS: The results of surgery were good in 94%, satisfactory in 3% and non-satisfactory in 3% of the patients. Eight patients required Montgomery T tube and tracheostomy in the postoperative period. Nine patients died(3%). Suture line granulations were the most common complications and were seen in 28 patients(9.5%). wound infection was present in 12 patients(4%) and glottic dysfunction in 8 patients(2.7%). Two patients who developed tracheo-innominate artery fistula in the postoperative period underwent emergency exploration and repair. One patient developed quadriplegia following acute neck flexion in the post-operative period.

CONCLUSION: Tracheal resection and reconstruction remains the best option for patients with tracheal obstruction and yields good results.

CLINICAL IMPLICATIONS: Tracheal obstructions due to postintubation tracheal stenosis and tumors in the trachea, the defintive curative treatment is tracheal resection and reconstruction.

DISCLOSURE: Rajan Santosham, None.

THORACIC APPROACH IN HEPATO-BILIARY SURGERY

Alexandru M. Botianu MD* Petre A. Botianu RN University of Medicine and Pharmacy from Targu-Mures, Romania, Targu-Mures, Romania

PURPOSE: Thoracic approach in hepato-biliary surgery is a debated problem since it has the advantage of a very good access but the disadvantage of a supplementary morbidity and the need of some specific postoperative care. The aim of our study is to evaluate the results of this approach.

METHODS: In a period of 15 years in our unit, thoracic approach has been used in 15 patients: 8 bilio-thoracic fistulae, 2 hydatid hepatic cysts associated with right pulmonary hydatid cysts (one of which bilateral), 2 hydatid hepatic cysts associated with left pulmonary hydatid cysts solved through left thoracophrenotomy (in one case we also practiced cholecystectomy and transcistic drainage, which seems to be a new approach), 2 hepatic abscesses with subphrenic abscesses, one hepatothorax solved by polipropilene-mesh phrenoplasty associated with intrathoracic cholecystectomy for colesterolosis of the gall-bladder.

RESULTS: In all cases we had a very good access on the hepatic lesion; in some cases we avoided a supplementary laparotomy. The reason why we preferred the thoracic approach was: existence of some severe thoracic lesions, which dominated the clinical course - 8 patients (bilio-thoracic fistulae), association of the hepatic lesions with uncomplicated intrathoracic lesions - 4 patients, difficult abdominal approach due to the location and previous abdominal procedures - 2 patients, one patient with a hepatotorax.

CONCLUSION: In hepato-biliary surgery the thoracic approach is indicated in patients with associated intrathoracic lesions and in those with a much more difficult abdominal approach - re-operations, peculiar locations.

CLINICAL IMPLICATIONS: In the aforementioned situations, co-optation of a thoracic surgeon may be beneficial, since the access is very good and for trained centers this approach poses no special problems.

DISCLOSURE: Alexandru Botianu, None.

THORACOSCOPIC DIAPHRAGMATIC PLICATION FOR PARALYZED DIAPHRAGM

John R. Roberts MD* Maggie C. Oldham The Surgical Clinic, Nashville, TN

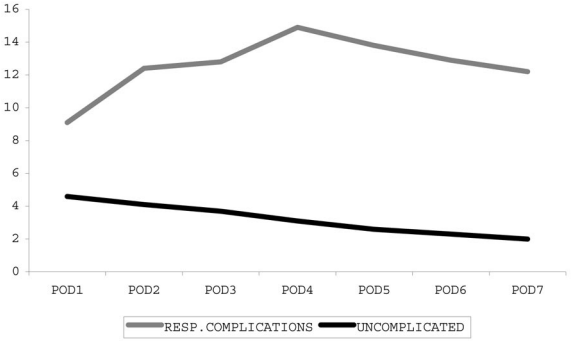
PURPOSE: Diaphragm paralysis may result from surgical, anatomic, or idiopathic causes. Patients with diaphragmatic paralysis present with dyspnea, worsened with lying down, and benefit from plication if the affected diaphragm moves paradoxically with inspiration. Plication is an established intervention for this group of patients, but minimally invasive diaphragm plication has not been well described.

METHODS: All patients with elevated diaphragm on chest radiograph for evaluation of dyspnea were evaluated for surgical intervention. Floroscopy confirmed paradoxical movement of the affected diaphragm, and patients underwent surgical plication. The procedures were begun thoracoscopically, and converted to open procedures if necessary.

RESULTS: Fourteen patients underwent thoracoscopic exploration. Ages ranged from 28-80, with an average of 58. One patient had NSCLC, three had paralysis secondary to thymoma resections, and in nine the cause of the paralysis was not known. Seven were done thoracoscopically, and seven required open plication, due to inability to flatten the diaphragm appropriately. The average length of stay was 4.3 days and the only complications were prolonged air leak in one patient who underwent simultaneous lung resection and supraventricular tachycardia in two patients. There was no operative mortality.The majority of patients dramatically improved both their lung function and their symptoms. The average improvement in FEV1% was 22%, with a range from 10-33%.

CONCLUSION: Thoracoscopic plication of the paralyzed diaphragm is possible, but only in a relatively limited fraction of patients in this series (50%). The procedure was safe and effective, but requires judgment as to proceeding to an open procedure.

CLINICAL IMPLICATIONS: Thoracoscopic approaches can be used for plication of paralyzed diaphragms.



DISCLOSURE: John Roberts, None.

WHO DEVELOPS PULMONARY COMPLICATIONS AFTER THORACOTOMY? POSTOPERATIVE IDENTIFICATION OF HIGH RISK PATIENTS BY THE FLAM SCORE

Francesco Leo MD* Nicolas Venissac MD Daniel Pop MD Marylene Anziani Maria Elena Leon MPH Jèrôme Mouroux MD Thoracic Surgery Dept European Institute of Oncology, Milan, Italy

PURPOSE: A multifactorial score (FLAM score) was developed to standardize postoperative respiratory evaluation and to test the hypothesis that significant respiratory changes are evident at least 24 hours before the onset of pulmonary complications.

METHODS: The FLAM score, created in 2002, is based on 3 main parameters (dyspnea, chest X-ray, delivered oxygen) and 4 minor parameters (auscultation, cough, quality of bronchial secretions, and quantity of bronchial secretions). To validate the FLAM score, we prospectively calculated scores during the first postoperative week in 300 consecutive patients submitted to posterolateral thoracotomy.

RESULTS: Sixty patients (20%) developed pulmonary complications during the postoperative period. In uncomplicated patients (n=240), the highest FLAM score (mean 5.03 $\pm$ 2.16) was recorded on the first postoperative day (POD), with progressive decline to POD7 (mean 2.41 $\pm$ 1.84). By contrast, the FLAM score progressively increased in complicated patients until POD4 (mean 13.5 $\pm$ 11.9). FLAM scores in patients with complications were significantly higher ($p<0.05$) at least 24 hours before the onset of complication, compared to FLAM scores in uncomplicated patients. ROC curve analysis showed that a FLAM score of 7 identified patients likely to develop a pulmonary complication with a good specificity (87.4% and 90% respectively on POD2 and POD3). Based on the highest FLAM scores recorded for each patient during the first postoperative week, 4 risk classes were identified: class I (FLAM 0-7) without respiratory morbidity; class II (FLAM 8-14); 40% risk of respiratory complications but no mortality; class III (FLAM 15-21), 8.3% postoperative mortality; and class IV (FLAM $>$ 21), 22.2% postoperative mortality.

CONCLUSION: Changes in FLAM score were evident at least 24 hours before the onset of pulmonary complications, with the exception of those patients who develop complications on POD1.

CLINICAL IMPLICATIONS: The FLAM score can be used to categorize patients according to risk of respiratory morbidity and mortality and could be a useful tool in the postoperative management of patients undergoing thoracotomy.

Topics in Thoracic Surgery, continued

FLAM Peak Value	n	Respiratory Complications	Respiratory Failure	Death
0 - 7	203	1 (0.5%)	0	0
8 - 14	60	27 (45%)	2 (3.3%)	0
15 - 21	19	18 (94.7%)	7 (36.8%)	3 (15.7%)
> 21	18	18 (100%)	9 (50%)	6 (30%)

DISCLOSURE: Francesco Leo, None.

HYPERHIDROSIS: COMPARATIVE EVALUATION OF THE RESULTS BEFORE AND AFTER SYMPATHECTOMY IN 263 PATIENTS

Evaldo Marchi MD* Vivian M. Amioka MS Tiago S. Santos MS Aline I. Barranco MS Gabriel L. Palma MS Jose R. Campos MD Thoracic Surgery, Medical College of Jundiai, Jundiai, Brazil

PURPOSE: Primary hyperhidrosis is a condition that leads to functional disability with social and psychological effects. Although several therapeutic options are available to treat this condition, thoracoscopic symphatectomy (TS) has been the treatment of choice because of its safety and long-term control of the disease. However, the ablation of the sympathetic chain is irreversible and may lead to compensatory sweating as the main adverse side effect. In this study we report our experience with video-assisted TS in the treatment of hyperhidrosis.

METHODS: Two-hundred and sixty-three adult patients underwent TS to treat primary facial, palmar or axillary predominant hyperhidrosis. Patients were evaluated preoperatively for age, body mass index (BMI) and the intensity and degree of social and functional limitations due to the disease (score 1-4), and at 30 days after the intervention for de degree of compensatory sweating, satisfaction with the results (score 1-4) and the need of re-intervention. Statistics: ANOVA.

RESULTS: Social Limit:*p< 0.001 compared to PalmarFunct Limit:#p< 0.001 compared to Facial and AxillaryComp Sweat:+p< 0.001 compared to Palmar; &p< 0.05 compared to Axillary; ¥p< 0.05 compared to Palmar.

CONCLUSION: Thoracic sympathectomy is an effective method for the treatment of hyperhidrosis, with a high rate of postoperative satisfaction, low morbidity and low rates of re-operation.

CLINICAL IMPLICATIONS: TS is an easy, safety method to control hyperhidrosis.

Results

		Preoperative			Postoperative				
	n	age	BMI	Intensity	Social Limit	Functional Limit	Compens Sweat	Satisfact	Re-operat
Facial	5	38±14	26±3	4.0±0.0	3.8±0.4*	2.0±0.7	2.0±0.0+&	4.0±0.0	0(0%)
Palmar	114	24± 8	23±3	3.8±0.4	2.4±1.2	3.5±0.7#	1.0±0.5	4.0±0.0	1(0.9%)
Axillary	144	25± 8	22±3	3.8±0.4	3.6±0.5*	2.4±1.1	1.2±0.7¥	3.6±0.7	4(2.8%)

DISCLOSURE: Evaldo Marchi, None.

Venous Thromboembolism Prophylaxis and Treatment
12:30 PM - 2:00 PM

META-ANALYSIS: THREE TIMES DAILY SUBCUTANEOUS HEPARIN IS NOT SUPERIOR TO TWICE DAILY THERAPY IN THE PREVENTION OF VENOUS THROMBOEMBOLISM IN MODERATE TO HIGH RISK MEDICAL INPATIENTS

Christopher S. King MD Aaron B. Holley MD* Andrew F. Shorr MD Lisa K. Moores MD Walter Reed Army Medical Center, Washington, DC

PURPOSE: The majority of symptomatic and fatal venous thromboembolic (VTE) events in hospitalized patients occur in the medical population. It has been shown that therapy with both low dose unfractionated heparin (LDUH; defined as 5000 units subcutaneously BID) and low molecular weight heparin (LMWH) reduce this risk by at least 50%, and that LMWH may be more effective in the highest risk subgroups. Despite the lack of any comparative trials, many practitioners have extrapolated this data to suggest that high dose unfractionated heparin (HDUH; defined as 5000 units subcutaneoulsy TID) is superior to LDUH in moderate to high risk medical patients. Our objective was to use meta-analysis to compare the efficacy of LDUH vs. HDUH in this population.

METHODS: We searched MEDLINE, EMBASE, Cochrane Clinical Trials Register, clinical trials.gov, CRISP, ACP Journal Club, CDSR, and DARE databases, as well as bibliographies of retrieved articles. Twelve prospective, randomized controlled trials which evaluated either LDUH or HDUH in acutely ill medical patients were included. Two reviewers independently rated study quality using the Chalmer's and Jadad rating scales. Data were extracted on participants, screening and diagnostic methods, VTE rates, and bleeding rates.

RESULTS: Pooled rates of all major endpoints are shown in table 1. There was no statistical difference between LDUH and HDUH in DVT, PE or combined VTE rates. HDUH was, however, associated with an increased rate of bleeding (major plus minor).

CONCLUSION: Despite its current clinical and research use, there is no evidence that HDUH is superior to LDUH, and this regimen may even be associated with harm. Our meta-analysis is limited by the fact that the two treatments have never been directly compared. However, over 74,000 patients would have to be enrolled in each arm in order to have the power to detect a 20% relative risk reduction in the rates of VTE.

CLINICAL IMPLICATIONS: Until further studies are conducted, HDUH should not be used routinely for VTE prevention in hospitalized medical patients.

	Patients (N)	DVT (95% CI)	PE (95% CI)	VTE (95% CI)	Bleeding (95% CI)
LDUH	6328	0.21% (0.085-0.34)	0.54% (0.34-0.73)	0.82% (0.59-1.04)	0.0024 (0.0011-0.0038)
HDUH	1839	0.31% (0.00-0.62)	0.41% (0.00-0.79)	0.95% (0.00-1.45)	0.017 (0.0073-0.027)*

* P<0.001

DISCLOSURE: Aaron Holley, None.

ANTICOAGULATION THERAPY: A NEW APPROACH

Mark W. Wurster MD* The Ohio State University Medical Center, Columbus, OH

PURPOSE: According to the Centers for Medicare and Medicaid Services and the American College of Chest Physicians, use and implementation of anticoagulation therapy in the United States is sub-optimal. Subspecialty anticoagulation clinics have shown improvements in patient outcomes, but are limited in number by expense and expertise requirements. We evaluated the quality and financial impact of an anticoagulation approach combining computerized decision support (CDS) and point of service (POS) testing in multiple primary care sites.

METHODS: Cohort study, as a collaborative effort between the National Institutes of Health and the OSU Primary Care Research Institute.Participants: Test group (n=306) and control group (n=51) patients undergoing chronic anticoagulation therapy.Intervention: The test group was treated with POS testing and CDS. The control group was treated with a traditional anticoagulation approach (centralized laboratory testing, paper based record keeping, telephone contact).Outcome measures: 1.INR compliance defined by the ratio of therapeutic INR to total INR results; 2.Documentation of treatment indications and goal INR; 3.Clinic revenue generation; 4.Maintenance costs and costs due to treatment complications; 5.Clinic visit volume.

RESULTS: For the control group, INR compliance during baseline evaluation period was 38%. Test group INR compliance was significantly improved at 52%(p<0.01). Documentation of treatment indications and INR goal was 100% for test subjects, compared to 35% and 40% respectively for controls. Revenue production during a 2-year follow up totaled $270,977 from 5,692 encounters. Labor related overhead costs during this period dropped by 83%. Supply costs totaled $22,540. Estimated cost savings from complication avoidance amounted to $1,008,500. For every dollar spent on program implementation and operation, $20.41 was returned from revenue production, cost containment, and complication avoidance.

Venous Thromboembolism Prophylaxis and Treatment, continued

CONCLUSION: Utilizing POS testing and CDS to assist with anticoagulation therapy can improve INR compliance, reduce treatment costs and provide new sources of clinical revenue.

CLINICAL IMPLICATIONS: This anticoagulation approach improves quality of care, and is fiscally efficient enough to allow widespread use in both subspecialty and primary care settings.

DISCLOSURE: Mark Wurster, Grant monies (from sources other than industry) National Institutes of Health

Characteristics of Patients With Community Acquired VTE Versus Those With Hospital Acquired VTE

Demographic	Community Acquired VTE N = 295	Hospital Acquired VTE N = 97	p Value
Mean age, yrs	61	66	P<0.001
Female (%)	55.9	44.3	P=0.05
Race (%)			
White	89.0	89.4	
Black	4.5	2.1	
Hispanic	2.8	6.3	
Other/unknown	3.7	2.2	P=NS
Risk Factors for VTE*			
Other hospitalization last 3 mo.	41.5	40.2	P=NS
Recent Immobility	33.5	65.0	P<0.001
Recent Surgical Proceedures	32.5	42.3	P=NS
Recent Infection	22.7	55.7	P<0.001
Cancer	30.9	28.9	P=NS
Ischemic Heart Disease	17.0	27.8	P=0.02
Recent Central Venous Catheter	9.8	46.4	P=<0.001
Recent ICU Discharge	8.0	45.3	P<0.001
Recent Intubation	10.9	37.1	P<0.001
Recent Fracture	15.9	16.5	P=NS
Congestive Heart Failure	10.5	26.8	P<0.001
Previous DVT	16.1	9.4	P=NS
Cerebrovascular Disease	11.2	19.6	P=0.03
Recent Hormonal Therapy	14.9	7.2	P=0.05
Recent Chemotherapy	10.9	8.2	P=NS
Recent Cardiac Procedures	7.5	17.5	P<0.01
VTE prophylaxis			
During current hospital admission			
Any VTE prophylaxis	N/A	85.6	
Any anticoagulant prophylaxis	N/A	56.7	
After recent surgery	N=95	N=41	
Any VTE prophylaxis	48.3	70.7	P=NS
Any anticoagulant prophylaxis	35.8	53.7	P=NS
During prior hospitalization	N=119	N=39	
Any VTE prophylaxis	65.6	53.8	P=NS
Any anticoagulant prophylaxis	47.1	46.2	P=NS
VTE type			
Deep vein thrombosis	85.4	85.6	P=NS
Pulmonary embolism	25.4	25.7	P=NS
Both	10.8	11.3	P=NS
Hospital Outcomes			
Recurrent VTE	0.3	3.1	P<0.05
Major Bleeding	4.4	13.4	P<0.01
Mortality	3.1	8.3	P<0.05

*Only those with >10% prevalence displayed

RISK PROFILES AND PROPHYLAXIS HISTORY OF PATIENTS DEVELOPING VENOUS THROMBOEMBOLISM IN THE OUTPATIENT SETTING: THE WORCESTER VENOUS THROMBOEMBOLISM STUDY

Frederick A. Spencer MD* Cathy Emery RN Darleen Lessard MPH Frederick A. Anderson PhD Sri Emani MPH Richard C. Becker MD Robert J. Goldberg PhD University of Massachusetts Medical Center, Worcester, MA

PURPOSE: Considerable emphasis has been placed on improving the identification of hospitalized patients at high risk for venous thromboembolism (VTE) so that they receive adequate prophylaxis. However increased availability of outpatient procedures, increased utilization of in-dwelling catheters, and shortened length of hospital stay might be expected to lead to an increasing outpatient population that is also high risk for VTE. The purpose of this study was to compare risk factor profile, previous VTE prophylaxis use, and outcomes of patients who developed VTE in the outpatient setting versus those who developed VTE after admission for another non-VTE related diagnosis.

METHODS: The medical records of all residents from the Worcester,MA area (2000 census=478,000) diagnosed with ICD-9 codes consistent with possible VTE at all 11 Worcester hospitals in 1999 are being reviewed by trained data abstractors. Validation of each case of VTE is performed using prespecified criteria. Information was collected about demographic and clinical characteristics, prior VTE prophylaxis, and hospital outcomes.

RESULTS: A total of 587 cases have been validated as acute VTE events for the year 1999. We present an interim analysis based on data from the first 392 cases enrolled. See Table 1 for characteristics of these patients stratified by setting of VTE development.

CONCLUSION: Patients who develop VTE in the outpatient setting were younger, more often female, and more likely to be on hormonal therapy than those who developed VTE during a hospitalization. They were just as likely to have a history of prior VTE, recent hospitalization or surgery, recent fracture, or recent cancer/chemotherapy. Utilization of prophylaxis (particularly anticoagulant) was suboptimal in patients who developed VTE during a hospitalization. It also was suboptimal after recent surgery or during prior hospitalizations in patients who developed VTE in the outpatient setting.

CLINICAL IMPLICATIONS: These data suggest that patients who develop VTE as outpatients have a high prevalence of risk factors, including recent surgery and/or hospitalization. Further research on the optimal identification of these high-risk patients and targetted outpatient VTE prophylaxis is warranted.

DISCLOSURE: Frederick Spencer, None.

LOW-MOLECULAR WEIGHT HEPARIN FOR DEEP VEIN THROMBOSIS PROPHYLAXIS IN HOSPITALIZED MEDICAL PATIENTS: RESULTS FROM A COST-EFFECTIVENESS ANALYSIS

Andrew F. Shorr MD* William L. Jackson MD Brendan M. Weiss MD Lisa K. Moores MD Washington Hospital Center, Washington, DC

PURPOSE: Options for deep-vein thrombosis (DVT) prevention in medical patients include both unfractionated heparin (UFH) and low-molecular weight heparin (LMWH). Although more expensive than UFH, LMWHs are associated with fewer side-effects. We hypothesized that because of this, LMWH would prove cost-effective for DVT prevention in medical patients.

METHODS: We modeled the cost and efficacy of UFH vs. LMWH for DVT prevention in a hypothetical cohort of 1,000 medically ill subjects. Model estimates were derived from published trials of DVT prophylaxis in this setting and from various meta-analyses describing rates of bleeding and heparin-induced thrombocytopenia (HIT). Costs of clinical events (e.g., DVT, bleeding, HIT) were taken from reports measuring the economic consequences of these outcomes. We used enoxaparin as the representative LMWH and biased the model against LMWH. We reduced literature based estimates of event rates by 20%, did not include fixed, pharmacy administration costs, and assumed that successful DVT prevention altered neither mortality nor quality of life. We performed multiple sensitivity analyses.

RESULTS: In the base-case, enoxaparin had minimal impact on rates of either DVT or bleeding. However, the rate of HIT was reduced by 90% with LMWH. Despite its higher acquisition costs, use of enoxaparin led to net savings. Total costs (e.g., sum of acquisition costs for medications plus costs for treatment of DVT, bleeding, and HIT) were $405 per patient with UFH vs. $316 with LMWH (net savings $89, 95% CI: $7 to $373 by Monte Carlo simulation). Sensitivity analysis revealed the model to be moderately sensitive to the costs of HIT and the frequency of HIT. In a worst-case scenario (all inputs skewed against enoxaparin), routine use of the LMWH still resulted in savings.

CONCLUSION: From a health system perspective, LMWHs are economically attractive for DVT prevention in medical patients. The impact of LMWHs on rates of HIT and bleeding more than balance their acquisition costs.

Venous Thromboembolism Prophylaxis and Treatment, continued

CLINICAL IMPLICATIONS: Physicians should consider side-effect profiles and the costs of potential side-effects when selecting among pharmacologic agents for DVT prevention.

DISCLOSURE: Andrew Shorr, None.

FAILURE OF HEPARIN DOSING GUIDELINES IN OBESE PATIENTS: TIME FOR REEVALUATION

Heena Sheth MD Jennifer Bonner PharmD* Susan Skledar RPh Amy Seybert PharmD Amit Raina MD Christopher N. Faber MD Adele Towers MD University of Pittsburgh, Pittsburgh, PA

PURPOSE: To evaluate the efficacy and safety of weight-based unfractionated heparin (UFH) anticoagulation in obese patients.

METHODS: Retrospective review of electronic medical records for 88 randomly selected obese patients receiveing UFH infusions from June to December 2004 was conducted to report: 1) adherence to existing anticoagulation guidelines; 2) dose-response relationships according to indication for anticoagulation; and 3) anticoagulant complications.

RESULTS: The indications for anticoagulation were venous thromboembolic disease (VTE) in 38 (43%) and acute coronary syndrome (ACS) in 50 (57%) patients. Mean patient age was 55.6 years and mean weight was 124.7 kg. The recommended guidelines for dosing were followed in 11 % (10/88) of patients. Sixty-nine percent (61/88) of patients received an initial bolus (mean dose 53 units/kg). Mean bolus and infusion rates were 48 units/kg/hour and 13 units/kg/hour respectively for VTE and 57 units/kg/hour and 12 units/kg/hour respectively for ACS. Within 24 hours, 17 (19.3%) patients remained sub-therapeutic, 29 (32.9%) therapeutic (aPTT 46-81 seconds) and 42 (47.8%) in supra-therapeutic aPTT range. Forty-five percent of supra-therapeutic patients received higher heparin doses than recommended by the recent guidelines. Weight-adjusted bolus and infusion rates administered to therapeutic and supra-therapeutic patients were comparable (p=0.15.). Sub-therapeutic patients received a lower infusion rate compared to supratherapeutic patients (p=0.03). There were 5 (5.7%) complications: three bleeding episodes (lower gastrointestinal bleed, retroperitoneal hematoma, epistaxis), and two patients developed heparin induced thrombocytopenia. Both major bleeding complications occurred in patients receiving higher than recommended doses (bolus of 7000 and 8000 units for ACS) resulting in supra-therapeutic aPTT.

CONCLUSION: Adherence to established anticoagulation guidelines was poor in obese patients. Despite downward adjustments in bolus doses, supra-therapeutic aPTT still occurred in 47.8% of patients thereby increasing the risk of bleeding complications. This study demonstrated variability in dose-response to heparin in the obese that resulted in excessive anticoagulation in some instances.

CLINICAL IMPLICATIONS: Reevaluation of the dosing guidelines for UFH in obese patients is warranted.

DISCLOSURE: Jennifer Bonner, None.

EFFECTIVENESS OF ANTI-THROMBOTIC PROPHYLAXIS IN CURRENT COMMUNITY PRACTICE

Michelle Dylan PhD* Hsing-Ting Yu MPH Wing Chow PharmD Robert Dubois MD Cerner Health Insights, Beverly Hills, CA

PURPOSE: Clinical trials have demonstrated the efficacy of anti-thrombotic prophylaxis in preventing venous thromboembolic events (VTE). However, its effectiveness outside of the clinical trials setting is less well known. This study explored VTEs occurring during hospital admissions stratified by prophylactic regimen in order to understand the effectiveness of thromboprophylaxis in current community practice.

METHODS: Using a large, geographically diverse, multi-hospital US database, we identified hospitalized patients aged ≥40 years with hospital stays ≥6 days, at risk of VTE medical conditions including respiratory disorders, circulatory disorders, infectious diseases, and neoplasm during calendar years 2001-2003. We examined whether patients received thromboprophylaxis within the first 2 days of admission and compared rates of VTEs identified by ICD-9-CM diagnosis codes during the admission by type of prophylaxis and condition using chi-square. Duration of prophylactic regimen was also determined.

RESULTS: Of 10,142 eligible subjects, 2,588 (25.5%) had respiratory disorders, 3,855 (38%) had circulatory disorders, 969 (9.5%) had infectious diseases and 2,730 (27%) had neoplasms. Mean length of stay was 9.9 days. Overall VTEs rate was 9.4% and was higher among patients with circulatory disorders (15.5%) followed by neoplasms (7%), infectious diseases (5.4%), and respiratory disorders (4.5%). Only 2,447 patients (24%) received thromboprophylaxis with low-molecular-weight heparin (LMWH) or unfractionated heparin with a mean treatment length of 5.8 days. VTEs rates were significantly higher among patients receiving no prophylaxis compared to subjects receiving thromboprophylaxis (9.9% vs 7.9%, respectively, OR=0.8, 95% CI: 0.68-0.93, P=.003) (Table 1). The lowest rate was seen in LMWH group (7.0%, P<.05 compared to "no prophylaxis"). This risk reduction remains significant among patients with infectious diseases (2.4% vs 6.2%, P=.03) or respiratory disorders (2.4% vs 5.1%, P<.01) (Table 2).

CONCLUSION: This study demonstrates the effectiveness of anti-thrombotic prophylaxis in a large, real-world database and shows that VTEs occurred frequently, especially among medical patients receiving no prophylaxis, and that rates varied by condition.

CLINICAL IMPLICATIONS: Using anti-thrombotic prophylaxis in a non-trial community setting has significant impact on reducing VTEs among medical patients at risk for VTE.

Table 1—*Numbers and rates of VTEs occurring during hospital admissions by prophylactic regimen administered and duration of prophylaxis*

Type of anticoagulants	In-hospital events	Duration of prophylactic regimen (days)	N	Frequency	%	Mean	SD
No prophylaxis	7,695	763	9.9	-	-		
UFH	1,919	156	8.1†	5.8	4.8		
LMWH	528	37	7.0†	5.8	4.5		
Total	10,142	956	9.4	-	-		

LMWH = low-molecular-weight heparin; UFH = unfractionated heparin

Table 2—*Numbers and rates of VTEs occurring during hospital admissions by clinical condition and prophylaxis status*

At-risk medical conditions	No Prophylaxis			Received Prophylaxis			*P* value
	N	Frequency	%	N	Frequency	%	
Circulatory disorders	2,878	460	16.0	977	136	13.9	.1233
Neoplasm	2,016	153	7.6	714	39	5.5	.0561
Infectious diseases	761	47	6.2	208	5	2.4	.0324
Respiratory disorders	2,040	103	5.1	548	13	2.4	.0072
Total	7,695	763	9.9	2,447	193	7.9	.003

DISCLOSURE: Michelle Dylan, Grant monies (from industry related sources) Cerner Health Insights received research grants from Sanofi-Aventis. 2:30 PM 4:00 PM.

Intravascular Catheters and Monitoring 2:30 PM - 4:00 PM

PERIPHERALLY INSERTED CENTRAL CATHETER (PICC) ASSOCIATED UPPER EXTREMITY DEEP VENOUS THROMBOSIS (UEDVT) IN CRITICAL CARE SETTING

Srinivas B. Chakravarthy MBBS* Jonathan Rettmann MD Boaz A. Markewitz MD Greg Elliott MD Mark Sarfati MD Robert Nohavec RN University of Utah, Salt Lake City, UT

PURPOSE: The use of PICCs in Intensive Care Units (ICU) is increasing significantly. UEDVT is a known complication associated with placement of catheters. Knowledge about PICC associated UEDVT is primarily limited to retrospective studies and the incidence of PICC

Intravascular Catheters and Monitoring, continued

associated thrombosis varies from 0.3 to 60%. The purpose of this study is to prospectively evaluate the incidence of PICC associated thrombosis in patients admitted to a medical ICU.

METHODS: We are conducting a RCT on prevention of PICC associated UEDVT using prophylactic low-molecular weight heparin (LMWH) versus unfractionated heparin. All ICU patients having a PICC placed were evaluated. Exclusion criteria for enrollment included therapeutic anticoagulation, contraindications to prophylactic anticoagulation, thrombocytopenia and hemodialysis. If the PICC was in superior vena cava, as determined by a radiograph, the patients were enrolled. All patients received prophylactic anticoagulation with unfractionated heparin (5000 units three times a day, subcutaneously) or LMWH (30 to 40 mg per day, subcutaneously). Duplex ultrasonography was performed on the upper extremity prior to removal of the PICC or 10 days after insertion, whichever was earlier.

RESULTS: A total of 31 patients with PICC placed in the ICU completed the study to date. Duplex ultrasonography was positive for a DVT in 20 patients. 8 of them were occlusive and 12, non-occlusive. None of the patients were symptomatic.

CONCLUSION: The incidence of UEDVT associated with PICC in the ICU may be higher than previously reported, despite prophylactic anticoagulation. The majority of patients are asymptomatic.

CLINICAL IMPLICATIONS: Asymptomatic UEDVT associated with PICCs are common. The clinical course is unclear, including the incidence of PE associated with these DVT.

Table: *Results.*

Day # of the Ultrasonography following the PICC placement	Number of patients	Occlusive DVT	Non-occlusive DVT	No DVT
1	None	NA	NA	NA
2	3	1	1	1
3	2	1	0	1
4	3	2	1	0
5	4	0	1	3
6	7	1	4	2
7	3	0	2	1
8	3	0	2	1
9	2	1	1	0
10	4	2	0	2
Total	31	8(26%)	12(39%)	11(35%)
Total DVT: 20 (65%)				

DISCLOSURE: Srinivas Chakravarthy, Grant monies (from sources other than industry) This study was supported by an award from The CHEST Foundation of the American College of Chest Physicians.

GENDER DISPARITY IN FAILURE RATE FOR ARTERIAL CATHETER ATTEMPTS

Taro Minami MD* Lewis Eisen MD Jeffrey Berger MD Mangala Narasimhan DO Paul Mayo MD Beth Israel Medical Center, New York, NY

PURPOSE: To determine risk factors associated with failure of arterial catheter insertion.

METHODS: The study took place in the medical intensive care unit of a large urban teaching hospital. We analyzed 92 consecutive arterial catheter attempts by internal medicine house staff and critical care fellows over a five-month period beginning November 20, 2004. All patients 18 years of age or older requiring arterial catheters were included. We constructed a database that included patient characteristics (gender, body mass index, age, level of consciousness, mean arterial pressure, coagulation parameters, platelet count), procedure characteristics (indication, time of procedure, line site, use of ultrasound, number of skin punctures), post-graduate year of operator and post-graduate year of supervisor. Associations between characteristics and failure were analyzed by means of chi-square. Characteristics significantly associated with failure were entered into a multivariate logistic regression analysis.

RESULTS: There were 92 arterial catheter attempts. Femoral arteries comprised 25/92(27%) of the attempts and radial arteries 67/92(73%). The indications were hypotension 49/92 (53%), frequent blood draws 31/92(34%) and hypertension 12/92(13%). Interns attempted 63/92(68%), residents 24/92(26%) and fellows 5/92(5%) catheters. Ultrasound was used for 6/92(7%) of attempts. Patients were unconscious for 22/92(24%) of attempts. Failure was recorded for 26/92(28%) attempts. Female patients had a significantly higher failure rate than male patients (24/56 (43%) vs. 2/36 (6%), $p<0.001$). Body mass index, age, level of consciousness, mean arterial pressure, coagulation parameters, platelet count, indication for procedure, time of procedure, catheter site, use of ultrasound, number of skin punctures, post-graduate year of operator and post-graduate year of supervisor were not significantly associated with failure. After multivariate regression analysis, the gender of the patient remained statistically significant.

CONCLUSION: Female patients had significantly higher failure rates for arterial line attempts than male patients. Although not investigated in this study, a possible explanation could be smaller arterial size in female patients.

CLINICAL IMPLICATIONS: The increased failure rate for female patients should be considered when arterial catheters are planned.

DISCLOSURE: Taro Minami, None.

CORRELATION OF CONTINUOUS CARDIAC OUTPUT MEASURED BY A PULMONARY ARTERY CATHETER VERSUS IMPEDANCE CARDIOGRAPHY IN VENTILATED PATIENTS

Daniel W. Ziegler MD* Manuel Lois MD David Hess MD Jorge Pinilla MD Geno Tellez MD John Peter Smith Hospital, Fort Worth, TX

PURPOSE: Cardiac output can be measured continuously by an invasive pulmonary artery catheter (PAC) or by noninvasive impedance cardiography. The purpose of this study is to determine how well the two methods correlate in ventilated patients.

METHODS: Patients requiring mechanical ventilation and a PAC were studied in a combined surgical and medical intensive care unit from January 2003 to June 2004. Simultaneous measurements of cardiac output were obtained utilizing a Swan-Ganz CCOmbo V catheter (Edwards Lifesciences, Irvine, CA, USA) and impedance cardiography utilizing a BioZ (Cardiodynamic, San Diego, CA, USA). Measurements were recorded at initial placement and at 12, 24, 36, and 48 hours.

RESULTS: Thirty-seven patients were studied. Twenty-six patients were on volume control ventilation and 11 were on pressure control ventilation. The average PaO2/FiO2 was 213±101. Twenty-six (70%) of the patients required dopamine, norepinephrine and/or dobutamine. There were 172 measurements for each method that were evaluated for correlation. Overall the correlation coefficient was $r=0.42$ and $r^2=0.17$. There was a decrease in the correlation coefficient with time as shown in the table 1. Nine of the patients had cardiac output greater than 9 l/min measured by the PAC. Their correlation coefficient was $r=0.52$ and $r^2=0.27$. In the 29 patients with a cardiac output less than 9 l/min, the correlation coefficient was $r=0.77$ and $r^2=0.59$.

CONCLUSION: The cardiac output measured by impedance cardiography has a better correlation with the PAC in patients with a cardiac output less than 9 l/min. The correlation between the two methods decreases with time.

CLINICAL IMPLICATIONS: Further studies are indicated to determine which method is best suited for ventilated patients.

Table 1

Time	Correlation coefficient, r
Initial placement	.49
12 hour	.43
24 hour	.46
36 hour	.33
48 hour	.36

DISCLOSURE: Daniel Ziegler, None.

Intravascular Catheters and Monitoring, continued

DURABILITY OF ANTISEPTIC CENTRAL VENOUS CATHETERS AS A FUNCTION OF DURATION OF CATHETERIZATION: SILVER/CARBON/PLATINUM VERSUS MINOCYCLINE/RIFAMPIN

Theofilus Matheos MD* Alan Orquiola MD Matthias Walz MD Janice Adams RN Stephen O. Heard MD University of Massachusetts Medical School, Worcester, MA

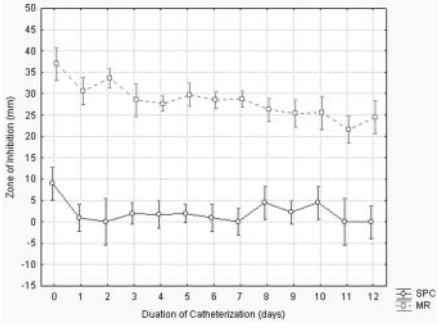
PURPOSE: Three types of antiseptic or antibiotic impregnated central venous catheters (CVCs) are commercially available. Only one study has examined the durability of these catheters (chlorhexidine/silver sulfadiazine vs minocycline/rifampin (MR)). We hypothesized that CVCs coated with MR have a longer antimicrobial activity as a function of duration of catherization compared to silver/carbon/platinum (SPC) CVCs.

METHODS: The UMMS Human Subjects Committee approved this study. Insertion of antiseptic CVCs was rotated on a monthly basis in the surgical intensive care unit. When CVCs were removed, the catheters were flushed and cut in 1 cm segments to be used for modified Kirby-Bauer testing. Bacteria isolates (S. aureus, S. epidermidis, E. coli, enterococcus and P. aeruginosa) were obtained from the hospital microbiology laboratory, grown to 1.5 MacFarland standard and plated onto blood agar plates. The CVC segments were imbedded at right angles into the agar. The plates were incubated at 37°C for 24 hours. The zone of inhibition (ZOI) of bacterial growth was measured with a caliper. Data were analyzed using a general linear model (Statistica, Tulsa, OK). The null hypothesis was rejected for $p<0.05$.

RESULTS: Forty-two SPC and 47 MR catheters were recovered from patients. Baseline activity against the test organisms was significantly higher with the MR CVCs than the SPC CVCs. Inhibition of bacterial growth persisted for a much longer duration of time with the MR CVCs than with the SPC CVCs with the exception of P. aeruginosa (Figure, organism: S. epidermidis).

CONCLUSION: Antimicrobial activity of MR CVCs against the common organisms causing catheter-related bloodstream infections (CRBSI) persisted for a longer period of time as a function of duration of catheterization compared to SPC CVCs.

CLINICAL IMPLICATIONS: These data predict better clinical efficacy of MR CVCs compared to SPC CVCs in the prevention of CRBSI.



DISCLOSURE: Theofilus Matheos, Other Unused catheters were gifts from Cook Critical Care and Edwards Life Sciences.

REAL TIME ULTRASOUND GUIDANCE WITH MICROPUNCTURE TECHNIQUE FOR CANNULATION OF THE INTERNAL JUGULAR VEIN IN THE ICU

Hrushikesh U. Vaidya MD* Peter White MD University Of Arkansas Medical Sciences, Little Rock, AR

PURPOSE: To evaluate the safety and efficacy of micropuncture® technique with a 21G needle in an ICU setting for placement of Internal jugular lines.

METHODS: Retrospective chart analysis was from sept 04 to april 05 on line placement that was done in the medical ICU of 2 tertiary care hospitals. All the lines that were placed under ultrasound guidance and with the use of micropuncture® technique (Cook)® in the internal jugular vein were evaluated . During this time 35 central lines were placed using this technique.All the lines were placed using real time ultrasound i.e the tip of the needle was seen approaching and entering the internal jugular vein.The end points that were measured were failure to place a central line in the first attempt, mechanical complications including but not limited to pneumothorax, carotid artery puncture, brachial plexus injury. Attempt was defined as need for another operator to try the central venous line. All the lines were placed in emergent and semi emergent situations. However none of the lines were placed during the ACLS protocol.

RESULTS: 35 cvl lines were placed during this period using the micropuncture® technique and ultrasound guidance. The success rate was 100%. There were no mechanical complications associated with these line placements.

CONCLUSION: Micropuncture technique with a smaller gauge needle may be associated with high success rate of cannulation and lesser number of mechanical complications for cannulation of the internal jugular in a medical ICU.

CLINICAL IMPLICATIONS: Fine needle may be most suitable for real time ultrasound guided line placement.Ultrasound guidence is shown to be associated with high rate of sucess and less number of complications. Using the micropuncture technique or a finer needle 21G may still reduce the number of mechanical complications in the ICU.However appropriate training and experience is needed for the house staff and the fellows.

DISCLOSURE: Hrushikesh Vaidya, None.

Mechanical Ventilation
2:30 PM - 4:00 PM

BI-LEVEL POSITIVE AIRWAY PRESSURE VENTILATION MAINTAINS ADEQUATE VENTILATION IN POST-POLIO PATIENTS REQUIRING HOME MECHANICAL VENTILATION

Caroline Haegerstrand PhD* Agneta Markström PhD Pia Söderberg MD Hans Barle PhD Dept of Anaesthesiology and Intensive Care, Danderyd, Sweden

PURPOSE: Patients suffering from post-polio syndrome still contribute significantly to the number of patients with chronic respiratory failure requiring home mechanical ventilation (HMV). This group of patients are commonly treated with controlled mechanical ventilation (CMV). We have previously shown that invasive bi-level positive airway pressure ventilation (BiPAP®) decreases the work of breathing (WOB) in tracheostomized post-polio patients as compared to CMV. The aim of this study was to evaluate if adequate ventilation was maintained in post-polio patients when using BiPAP®.

METHODS: Eight post-polio patients on nocturnal CMV were investigated. Five of them are tracheostomized and three of them use a nasal mask. WOB was analyzed by assessing differences in oxygen consumption (VO2) using indirect calorimetry. Bloodgases were obtained regularly to assess pCO2. The minute volume (MV) was measured and compared to the patients normal MV before each assay.

RESULTS: Using BIPAP® ventilation there was a significant decrease in the oxygen cost of breathing as compared to CMV and spontaneous breathing. Furthermore, the pCO2 values measured indicated that the ventilation was maintained.

CONCLUSION: Invasive BIPAP® ventilation maintains an adequate ventilation and reduces the oxygen cost of breathing in post-polio patients on HMV.

CLINICAL IMPLICATIONS: BIPAP® ventilation may be considered an alternative to CMV in post-polio patients requiring HMV.

DISCLOSURE: Caroline Haegerstrand, None.

COUGH STRENGTH AND MENTAL STATUS PREDICT EXTUBATION OUTCOMES

Cong Y. Stonestreet MD* Lin Wang MD Svetlana Gutierrez MD Salam Raslan MD Jorge Gonzalez MD Gaffar Syed MD Nureain Mirza MD Yaw Amoateng-Adjepong MD Constantine A. Manthous MD Mihai Smina MD Bridgeport Hospital & Yale University School of Medicine, Bridgeport, CT

PURPOSE: To determine whether mental status (MS), cough peak flows (CPF) and endotracheal secretions (ES) affect extubation (EXT) outcomes.

METHODS: We prospectively examined MS, CPF and ES of 86 patients recovering from respiratory failure who had passed a SBT.

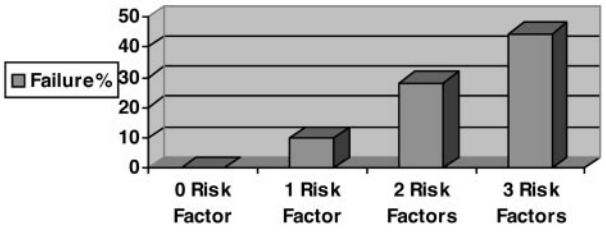
RESULTS: 20 patients failed their initial EXT within 72 h. CPFs of failed patients was lower than successes (38±28 L/min vs. 65±33 L/min, $p=0.002$). Those with CPF<60 L/min were 4-times as likely to fail EXT compared to those

Mechanical Ventilation, continued

with CPF 60 L/min or more (95% CI=1.3–12.9). Patients unable to complete any of 4 simple tasks (follow with eyes, open eyes, stick out tongue, grasp hand) were twice as likely to fail (95%CI=0.9-4.2). Those able to complete all 4 tasks but with CPF<60 L/min were twice as likely to fail (95%CI=1.4-2.7). Those with a required suctioning frequency of <2 h were twice as likely to fail (95%CI=1-5.3). These three "risk factors" (i.e. <4 tasks, <60 L/min, <2 h) were additive in predicting failure (see Figure).

CONCLUSION: CPF, MS and ES contribute to EXT outcomes of patients who have passed a SBT.

CLINICAL IMPLICATIONS: These quantifiable determinants of EXT outcome may be used to stratify pre-EXT risk of failure.



DISCLOSURE: Cong Stonestreet, None.

EVALUATION OF DISCOMFORT CAUSED BY DIFFERENT LEVELS OF SUPPORT PRESSURE DURING MECHANICAL VENTILATION VIA FACE MASK

William D. Marino MD* Mary O'Connell-Szaniszlo MS Our Lady of Mercy Medical Center, Mount Kisco, NY

PURPOSE: Noninvasive ventilation via face mask (MPSV) is widely used for respiratory failure. Although the literature demonstrates that adequate support requires at least 15cmH2O of pressure, many patients are treated with lower pressures for fear that higher pressures would be intolerably uncomfortable. This study was conducted in order to asses this concern's validity.

METHODS: 10 normals and 7 respiratory failure patients were studied. Each was given a series of increasing levels of MPSV and positive end expiratory pressure (PEEP). At each level respiratory rate (RR) and a numerical comfort rating were recorded. Clinical data was obtained from the hospital chart. The patients were followed for 6+/-4 months of daily MPSV. RR and comfort were correlated with support pressures and assessed for patterns. Values were compared using Student's T test for paired data.

RESULTS: In all subjects discomfort rose with increasing MPSV, but not with use of PEEP. In normals RR decreased significantly at MPSV=15cmH2O, but RR did not decrease in patients until 20cmH2O MPSV was provided. Decreases in RR were associated with discomfort, described as the sensation of loss of control of breathing rather than as pain or dyspnea. All patients adapted to MPSV levels of 15-22cmH2O in less than 2 weeks of daily ventilator use with normalization of PCO2 and expressed comfort .

CONCLUSION: There is discomfort with MPSV at levels adequate to support respiration. This is described not as noxious, but as a loss of control of respiration and may represent the neuromuscular "capture" described in the early noninvasive ventilation literature. The fact that RR decreased at 15cmH2O in normals but not until 20cmH2O in patients correlates with the need for greater support in the patients, whose respiratory workload is greater. This need probably helped the patients adapt to MPSV levels which were initially perceived as uncomfortable.

CLINICAL IMPLICATIONS: MPSV should be used with pressures adequate to support ventilation and assurance that any feelings of loss of control of breathing will resolve with continued use of the treatment.

DISCLOSURE: William Marino, None.

UTILIZATION OF A FAILURE MODE EFFECTS ANALYSIS (FMEA) TO EVALUATE THE SAFETY OF VENTILATOR PATIENTS IN A NON-ICU SETTING

Maureen A. Seckel MSN* Billie Speakman RRT Diane Bradtke RN Gerald O'Brien MD Christiana Care Health Services, Newark, DE

PURPOSE: Ventilator alarms and response to those alarms are an integral part of ventilator patient management and safety. The Joint Commission on Accreditation of Healthcare Organizations (JCHAO) published standard LD 5.2 for acute care facilities to implement a FMEA. We examined the risks for ventilator patients outside of the intensive care unit.

METHODS: Using the FMEA process, the team met from 2002 – 2004 and identified 2 primary failure modes; 1) failure to hear alarms and 2) failure to respond to alarms. A hazard score (severity rating multiplied by probability rating) was determined along with a project plan. Several solutions were immediately implemented including, cohorting all non-ICU ventilator patients to one intermediate care unit and mandating a temporary airway pressure monitor (disconnect alarm). KT analysis was done for permanent options for a reliable ventilator alarm system.

RESULTS: The total hazard score decreased from 100 to 36 (range 0-120) demonstrating a 64% reduction in risk along with lack of patient events. Staff satisfaction was measured by survey with an average score of 4.4 (range 1-5). Ventilator patients admitted to the unit included chronic, weaning and home ventilators with admissions ranging from 69 in 2001 to 106 in 2004, a 65% increase in census. Ventilator response time averaged 2.65 minutes prior to implementation of the changes and X minutes post.

CONCLUSION: A significant reduction in patient risk for ventilators outside of an ICU setting was obtained by utilizing the FMEA process and by implementing a ventilator alarm system. Additionally, there was a cost benefit analysis by cohorting patients and focusing caregiver training to a designated unit.

CLINICAL IMPLICATIONS: Patient safety for ventilator patients was enhanced by using a reliable ventilator alarm system that replaced dependence on visual and audio alarms with an additional alarm, including a pager interface to respiratory therapy and nursing. Ventilator care can be provided outside of an ICU setting with staff satisfaction, cost savings, and timeliness of response to ventilator alarms with earlier patient intervention.

DISCLOSURE: Maureen Seckel, None.

SUCCESSFUL WEANING FROM MECHANICAL VENTILATION AFTER FAILING A RESPIRATORY THERAPIST DRIVEN PROTOCOL

Dashant S. Kavathia MD* Alan Betensley MD Henry Ford Hospital, Detroit, MI

PURPOSE: To determine if ICU physicians can identify patients for successful extubation that failed the respiratory therapist driven protocol and, thus, can increase the number of patients successfully weaned from mechanical ventilation.

METHODS: We conducted a retrospective analysis of ICU patients who required mechanical ventilation for more than 24 hours, over a sixty day period. All patients were under the care of one intensivist and were initiated on a respiratory therapist (RT) driven weaning protocol. Medical records were reviewed to determine if patients were extubated the same day that they failed the weaning protocol. Successful extubation was defined as not requiring reintubation for 48 hours. Data was then analyzed in the two groups in terms of initial cause of mechanical ventilation, rates of reintubation and number of days on mechanical ventilation.

RESULTS: Out of a total of 36 mechanically ventilated patients, we identified 7 patients who were extubated despite not fulfilling the respiratory therapist driven protocol. Out of these, one patient with primary cardiorespiratory failure required reintubation whereas six remained successfully extubated. Out of the remaining 6, three patients were intubated for primary neurological process (for airway protection) and three for cardiorespiratory failure. Out of the 29 patients on the RT-driven protocol, 20 were eventually extubated. Nineteen were successful, out of which 4 were intubated for primary neurological process and 15 for cardiorespiratory failure. One patient with cardiorespiratory failure required reintubation. Six patients required tracheostomies and three expired while on mechanical ventilation. The average number of days on mechanical ventilation was lower in the group extubated after failing the RT-driven protocol.

Mechanical Ventilation, continued

CONCLUSION: Weaning protocols may be missing a significant number of patients who could be successfully weaned off the ventilator. It is also possible that protocols may be less reliable in patients on ventilation for neurological indications i.e. airway protection.

CLINICAL IMPLICATIONS: Weaning protocols have been shown to reduce the number of days of mechanical ventilation. In some cases, though, physician judgment can improve the rates of successful weaning.

DISCLOSURE: Dashant Kavathia, None.

REDUCED NEUROMUSCULAR BLOCKADE REQUIREMENTS IN PATIENTS RECEIVING AIRWAY PRESSURE RELEASE VENTILATION

Tristan J. Huie MD* Kenneth Lyn-Kew MD Allen Roberts, II MD Georgetown University Hospital, Washington, DC

PURPOSE: Pressure control ventilation (PCV) is used to limit airway pressures in patients with acute respiratory distress syndrome (ARDS), however it frequently requires neuromuscular blockade (NMB) and heavy sedation for patient comfort. Airway pressure release ventilation (APRV) is an alternative pressure-limited mode of ventilation that allows spontaneous breathing throughout the ventilator cycle and appears to reduce NMB and sedation requirements. We reviewed the use of neuromuscular blockade in patients on APRV and PCV in the medical intensive care unit (ICU).

METHODS: We conducted a chart review of all patients who received invasive mechanical ventilation in the medical ICU of a university hospital from September 2002 until March 2005. APRV was introduced to this hospital in September 2003 and has been used in place of PCV since then. The period of September 2002 to September 2003 was examined to determine frequency of NMB use in patients on PCV. In all patients receiving PCV or APRV we recorded mode of ventilation used, use of neuromuscular blockade, and survival to ICU and hospital discharge.

RESULTS: One of the 52 patients on APRV required NMB in the past 18 months compared to the majority of patients on PCV. We are completing the chart review of PCV patients and expect that more than 60% of these patients received NMB.

CONCLUSION: Use of APRV may significantly reduce NMB requirements compared to PCV. APRV should be the preferred pressure-limited mode of ventilation in patients who have failed volume cycled ventilation.

CLINICAL IMPLICATIONS: APRV appears to offer a pressure-limited mode of ventilation that requires significantly less NMB than PCV. The effects of APRV on sedation requirements and development of critical illness polyneuropathy need to be evaluated.

DISCLOSURE: Tristan Huie, None.

Pulmonary Emboli: Identifying Risk
2:30 PM - 4:00 PM

THE CHANGING LANDSCAPE OF VENOUS THROMBOEMBOLISM: THE WORCESTER VENOUS THROMBOEMBOLISM STUDY

Frederick A. Spencer MD* Frederick A. Anderson PhD Cathy Emery RN Darleen Lessard MS Jayashri Aragam MD Richard C. Becker MD Shauna Malone MS Robert J. Goldberg PhD University of Massachusetts Medical School, Worcester, MA

PURPOSE: There have been marked changes in patient profiles as well as diagnosis and management of venous thromboembolism (VTE) in the last decade. The purpose of this study was to describe the demographic, clinical, and outcome characteristics of a community sample of patients diagnosed with VTE in 1999. Our findings are compared to those reported by the Worcester DVT study of 1988-1989.

METHODS: The medical records of all residents from Worcester, MA (2000 census=478,000) diagnosed with ICD-9 codes consistent with possible VTE at 11 Worcester hospitals in 1999 are being reviewed by trained data abstractors. Validation of each case of VTE is performed using prespecified criteria. The distribution of clinical and treatment characteristics were compared, where possible, in a descriptive fashion to variables previously reported by the Worcester DVT study.

RESULTS: A total of 587 cases have been validated as VTE events for the year 1999. We present an interim analysis based on data from the first 392 cases enrolled. Please see Table 1.

Characteristics of Patients with VTE: The Worcester Venous Thromboembolism Study

Variable	Worcester DVT Study 1988-9 N=1231	Worcester VTE Study 1999 N=392
Mean Age (yr)	65	62
Female (%)	54	53
Risk Factors (%)*		
Recent Surgery	18	35
Recent Prior Hospitalization	55	40
Malignancy	22	30
Recent ICU Discharge	N/A	17
Recent Intubation	N/A	17
Recent Fracture	10	16
Congestive Heart Failure	8	15
Prior VTE	26	19
Setting of VTE Occurrence		
Hospital Acquired	19	24
Community Acquired	81	76
DVT Diagnostic Tests (%)		
US	46	89
Venogram	53	1
IPG	51	0
PE Diagnostic Tests (%)		
VQ	82	59
Pulm Angiogram	10	3
Spiral CT	0	4
Initial Therapy (%)		
IV heparin	91	68
SQ Enoxaparin	0	24
Other	9	8
Length of Stay (mean, d)	15	10
Hospital Outcomes (%)		
Major Bleeding	6	7
Recurrent VTE	2	1
Mortality	8.6	4

*Recent defined as < 6 months in initial Worcester DVT Study, < 3 months in

CONCLUSION: The landscape of VTE has changed significantly over the last decade. Patients are older, have a different profile of risk factors, are more likely to be diagnosed using non-invasive modalities, and are less likely to be treated with IV heparin. VTE remains a disease of the outpatient with the majority of patients presenting to the hospital already with signs and symptoms of VTE. A substantial proportion of these patients had been hospitalized in the past 3 months. Hosptial associated mortality has declined over time but given decreased length of stay, further study of outpatient survival is needed.

CLINICAL IMPLICATIONS: Much of our understanding of the epidemiology of VTE is based on patients enrolled in observational studies more than a decade ago. Data from the ongoing Worcester VTE study will provide insights into changing patient profiles, utilization patterns of diagnostic and treatment modalities, and subsequent outcomes. These insights will, in turn, allow clinicians to optimize the care of these high-risk patients.

DISCLOSURE: Frederick Spencer, None.

Pulmonary Emboli: Identifying Risk, continued

COMPUTED TOMOGRAPHIC PULMONARY ARTERY DIAMETERS IN PREDICTING MODERATE OR SEVERE PULMONARY HYPERTENSION IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

Shirin Sanal MD* Wilbert S. Aronow MD Gautham Ravipati MD George P. Maguire MD Robert N. Belkin MD Stuart G. Lehrman MD New York Medical College, Valhalla, NY

PURPOSE: To determine the accuracy of computer tomographic (CT) measurements of main pulmonary artery diameter (MPAD) and MPAD/ascending aorta diameter (AAD) in predicting moderate or severe pulmonary hypertension (PHT) in acute pulmonary embolism (PE).

METHODS: Ninety-eight women and 92 men, mean age 59±15 years, had acute PE diagnosed by contrast-enhanced CT. A pulmonary artery systolic pressure of ≥50 mm Hg measured by Doppler echocardiography was considered moderate or severe PHT. MPAD of >28.6 mm and MPAD/AAD ratio of ≥1.00 measured by CT were considered abnormal. All measurements of MPAD and of MPAD/AAD were made blindly without knowledge whether PHT was present.

RESULTS: Moderate or severe PHT occurred in 51 of 190 patients (27%). MPAD of >28.6 mm occurred in 38 of 51 patients (75%) with and in 35 of 139 patients (25%) without moderate or severe PHT ($p<0.001$). MPAD/AAD ratio of ≥1.00 occurred in 30 of 51 patients (59%) with and in 25 of 139 patients (18%) without moderate or severe PHT ($p<0.001$). MPAD >28.6 mm had a 75% sensitivity and specificity, a 52% positive predictive value, a 89% negative predictive value, a 3.0 likelihood ratio of a positive test, and a 0.33 likelihood ratio of a negative test. MPAD/AAD ratio of ≥1.00 had a 59% sensitivity, a 82% specificity, a 55% positive predictive value, a 84% negative predictive value, a 3.3 likelihood ratio of a positive test, and a 0.50 likelihood ratio of a negative test.

CONCLUSION: A MPAD of >28.6 mm had a higher sensitivity, a lower specificity, a similar positive predictive value, a higher negative predictive value, a slightly lower likelihood ratio of a positive test, and a higher likelihood ratio of a negative test than a MPAD/AAD ratio of ≥1.00 in predicting moderate or severe PHT in acute PE.

CLINICAL IMPLICATIONS: Doppler echocardiography remains the procedure of choice in diagnosing PHT in patients with acute PE.

DISCLOSURE: Shirin Sanal, None.

ARTERIAL BLOOD GAS ANALYSIS IN COMBINATION WITH D-DIMER IN THE ASSESSMENT OF ACUTE PULMONARY EMBOLISM

Tara Keays MD* Marc A. Rodger MD The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada

PURPOSE: Pulmonary embolism (PE) is a common condition with high untreated mortality rate, however less than 35% of patients suspected of PE have the disease. Arterial blood gas (ABG) analysis has not been shown to safely exclude PE when used alone. The purpose of this study was to evaluate the diagnostic value of ABG in combination with D-dimer in excluding PE.

METHODS: A retrospective analysis was performed using data from a double-blind, randomized controlled trial comparing bedside diagnostic tests to ventilation/perfusion scanning in the exclusion of suspected PE. Validation of the statistically significant findings was attempted using a second database of patients with suspected PE.

RESULTS: Of the 399 participants, 57 were diagnosed with PE after initial investigations. ABG samples were taken in the initial assessment of 69.7% of subjects. In the diagnosis of PE, normal arterial carbon dioxide tension (PaCO2) of >36mm Hg or normal age adjusted alveolar-arterial oxygen gradient (P(A-a)O2) (2.5 + 0.21 X age) alone had sensitivities of only 54% and 90% respectively and negative predictive values (NPV) of 91% and 95% respectively. The sensitivity and NPV increased to 100% when each was combined with a negative D-dimer, however less than 30% of patients could be excluded. When a negative D-dimer was combined with either a normal paCO2 or normal P(A-a)O2, PE was excluded in 38% of patients while maintaining a sensitivity and NPV of 100%. In the validation set of 246 patients, a normal paCO2 or P(A-a)O2 with a negative D-dimer had a sensitivity of 89.2% and NPV of 91.3%.

Table 1—*Diagnostic utility of various combinations of ABG and D-dimer in the exclusion of PE.*

Variable	Sensitivity (95% CI)	Negative Predictive Value (95% CI)	LR^-	True Negative Proportion (95% CI)
$PaCO_2$<36	54.3% (36.7-71.2)	90.6% (85.2-94.5)	0.72	55.4% (49.3-61.3)
Abnormal P(A-a)O_2	89.7% (72.7-97.8)	94.5% (84.9-98.9)	0.39	24.0% (18.4-30.2)
Positive D-dimer	89.3% (78.1-96.0)	96.3% (92.1-98.6)	0.23	40.1% (35.1-45.1)
$PaCO_2$ <36 or positive D-dimer	100% (91.8-100)	100% (96.2-100)	0	28.7% (23.5-34.6)
Abnormal P(A-a)O_2 or positive D-dimer	100% (90.2-100)	100% (92.2-100)	0	17.6% (12.7-23.5)
Positive D-dimer or negative D-dimer with both $paCO_2$<36 and abnormal P(A-a)O_2 -in derivation population in validation population	100% (90.2-100) 89.2% (74.6-97.0)	100% (96.3-100) 91.3% (79.2-97.6)	0 0.26	37.6% (31.1-44.6) 30.0% (22.6-38.3)

Definition of abbreviations: P(A-a)O2 = alveolar-arterial oxygen gradient; PaCO2 = arterial carbon dioxide tension; 95% CI = 95% confidence interval; LR^-= likelihood ratio of a negative test (1-sensitivity/specificity); True negative proportion=number of patients correctly excluded/number of patients tested.

CONCLUSION: In the derivation study, normal PaCO2 or normal P(A-a)O2 in combination with a negative D-dimer appeared useful in objectively excluding PE without diagnostic imaging. However, this clinical prediction rule did not validate in a second set of patients with suspected PE.

CLINICAL IMPLICATIONS: ABG data, alone or in combination, appears not to have a role in excluding PE without diagnostic imaging.

DISCLOSURE: Tara Keays, University grant monies University of Ottawa Medical Associates; Grant monies (from sources other than industry) Heart and Stroke Foundation of Ontario.

PREDICTORS OF ADVERSE OUTCOMES IN HOSPITALIZED PATIENTS WITH HEMODYNAMICALLY STABLE PULMONARY EMBOLISM

Kevin Thompson DO* Gene Colice, MD, FCCP Yin Naing MD Nitin Seam MD Shirin Shafazand, MD, MS, FCCP Washington Hospital Center, Washington, DC

PURPOSE: The specific aim of this study is to determine predictors of adverse outcomes in hospitalized patients who present with hemodynamically stable pulmonary embolism (PE).

METHODS: We retrospectively studied 218 hemodynamically stable patients diagnosed with PE at Washington Hospital Center from 2001 to 2004. Study variables included patient demographics, signs and symptoms, co-morbidities, treatments, and laboratory values. The primary endpoint was a composite of in-hospital mortality, use of mechanical or non-invasive positive pressure ventilation, cardio-pulmonary resuscitation, or hypotension. For all continuous variables we report means ±SD or medians and interquartile ranges. We use frequencies to describe categorical data. As a secondary analysis, we compared patients with and without adverse outcomes using the Chi-square or Mann-Whitney U statistic.

RESULTS: Patient demographics appear in Table 1. 81% of patients were dyspneic and 49% reported chest pain at presentation. Adverse outcomes were observed in 20 of 218 patients (9%) and death in 9 of 218 (4%) (Table 2). History of chronic obstructive pulmonary disease (COPD) ($p=.01$) and pulmonary hypertension ($p=.01$), use of an inferior vena cava (IVC) filter ($p=0.004$), and do not resuscitate code status ($p=0.03$) were associated with adverse outcomes.

CONCLUSION: History of COPD and pulmonary hypertension, use of an IVC filter, and code status are all associated with a higher rate of adverse outcomes in patients with hemodynamically stable PE.

CLINICAL IMPLICATIONS: Few studies have described risk factors for adverse outcomes in hemodynamically stable patients with PE. Despite hemodynamic stability at presentation, 9% of patients with PE experienced adverse outcomes during hospitalization. Early identification of these patients, more intensive monitoring and aggressive treatment may help reduce the incidence of these adverse outcomes. Our study identified several significant predictors. Future investigations involve the development of a clinical prediction model that may be used as a tool to help identify those patients with hemodynamically stable PE who are at risk for adverse outcomes during hospitalization.

Pulmonary Emboli: Identifying Risk, continued

Table 1—*Patient Demographics*

	All Patients N=218	Patients with Adverse Outcomes N=20	Patients without Adverse Outcomes N=198
Age**	58.3 ± 17.9	60.8 ±6.8	58.0 ±18.0
Gender *No.(%)*			
Female	124 (57)	10 (50)	114 (58)
Male	94 (43)	10 (50)	84 (42)
Race *No. (%)*			
African American	176 (81)	20 (100)	156 (79)
Caucasian	34 (16)	0 (0)	34 (17)
Other	8 (4)	0 (0)	8 (4)
Total	218	20 (9)	198 (91)

**Mean ± SD

Table 2—*Adverse Outcomes in Patients with Pulmonary Embolism*

Adverse Outcome	Frequency No. (%) N=218
Death	9(4)
Intubation	11(5)
Non-Invasive Positive Pressure Ventilation (NIPPV)	11(5)
Cardio-Pulmonary Resuscitation (CPR)	6(3)
Hypotension	8(4)
All Adverse Outcomes	20(9)

DISCLOSURE: Kevin Thompson, None.

CLINICAL PROBABILITIES IN PATIENTS WHO SUBSEQUENTLY DIED OF PULMONARY EMBOLISM

Jennifer B. Swisher MD* Heather N. Follett MD Timothy A. Morris MD
University of California, San Diego, San Diego, CA

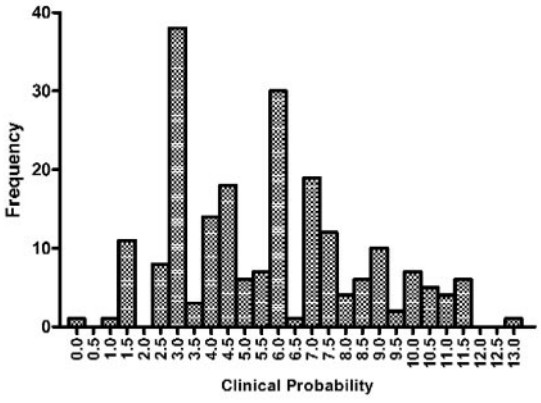
PURPOSE: Fatal pulmonary embolism (PE) is often missed antemortem. A clinical probability score (Wells 2001) is useful, along with the D-dimer test, in identifying which patients need further workup. However, this score was validated in relatively stable outpatients. It is not known whether this score is sensitive for PE in unstable inpatients. We used the records of patients who died from PE to determine whether the clinical probability score upon presentation would have identified them antemortem.

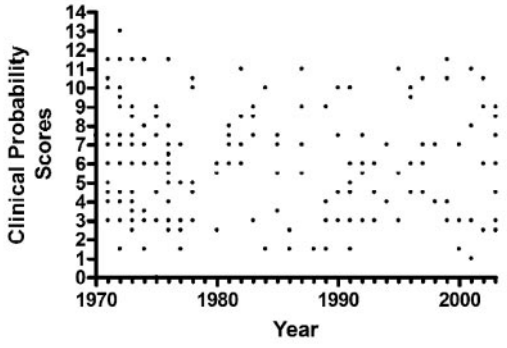
METHODS: We reviewed the reports from all autopsies performed at the University of California, San Diego Medical Center between 1970 and 2004 to find patients who died while in the hospital and in whom PE was deemed to be a contributing cause of death. We calculated a "clinical probability score" for each case by reviewing physician, nursing, and respiratory care notes documented in the records. We calculated the frequency distribution for the scores and performed linear regression to determine whether the distribution had changed over the past three decades.

RESULTS: There were 270 autopsies performed in which the deaths were attributable to PE, of which 214 (79%) were available for review. There was a bimodal frequency distribution of clinical probability scores, with frequency peaks at scores of 3 and 6 (out of 13). Twenty-five percent of patients had scores of 3 or less, which could be attributed to tachycardia and/or immobility in all but 1%. There was no significant change in distribution of the scores over the course of the 35 years ($r = 0.002$).

CONCLUSION: Throughout the study period, fatal PE was found in two distinct populations of patients, those in whom the objective clinical likelihood score was high and those in whom the score was in the low-moderate range. In the later group, most scores reflected non-specific clinical findings.

CLINICAL IMPLICATIONS: Further studies are warranted before using the clinical probability score to distinguish patients at risk of PE-related death from those with other serious cardiopulmonary problems who do not need work-ups for PE.





DISCLOSURE: Jennifer Swisher, None.

COMPUTED TOMOGRAPHY CAN PREDICT ADVERSE OUTCOMES IN PATIENTS PRESENTING WITH PULMONARY EMBOLUS

Peter S. Marshall MD* Mark Siegel MD Kevin Johnson MD Karin Kelley MD Bianca Monteiro MD Yoel Vivas MD Yale School of Medicine, New Haven, CT

PURPOSE: Patients with pulmonary embolism (PE) and right ventricular dysfunction (RVD) are at greater risk for adverse outcomes compared to patients without RVD. Those with non-massive PE (those without evidence of shock) are comprised of a low risk group (small PE) and a higher risk group (sub-massive PE, those with RVD). It is difficult to distinguish the small PE group from the sub-massive group clinically. The CT pulmonary embolism (CT-PE) protocol may detect RVD, thus predict adverse outcomes. We sought to determine if one can predict poor outcomes in PE, specifically normotensive PE patients (those with non-massive PE), using the CT-PE protocol.

METHODS: In a preliminary analysis 44 patients with PE detected by CT-PE protocol were retrospectively examined for an aggregate adverse outcome (intubations, pressors, death, cardiac arrest, ICU admission). Studies were reviewed in the four chambered view for RV/left ventricular (LV) cross sectional area ratio, Aortic (Ao)/ Pulmonary artery (PA) diameter ratio, and presence of septal flattening . Data was analyzed to see

Pulmonary Emboli: Identifying Risk, continued

if a relationship between adverse outcome and the measurements existed in the entire cohort and non-massive group. A multivariate logistic regression was performed to determine if other variables affected the relationship between the CT-PE protocol measures and the adverse outcome.

RESULTS: RV / LV area ratio and PA / Ao diameter ratio did not differ between the adverse outcome and non-adverse outcome group. The RR for septal flattening and adverse outcomes in PE was 2.00 (95% CI 1.15 – 3.48), and significance was maintained after multivariate analysis. In the non-massive PE group the RR was 2.57 (95% CI 1.23 - 5.39).

CONCLUSION: Septal flattening detected by CT-PE protocol identifies PE patients at greater risk for adverse outcomes. It can also identify a higher risk group among those with non-massive PE.

CLINICAL IMPLICATIONS: The CT-PE protocol may provide a rapid means of identifying higher risk PE patients among those with non-massive PE. It may influence further testing, triage and the choice of therapy (i.e. IVC filter, thrombolytics).

Table 2—*CT-PE Measurements for Entire Cohort–comparing Adverse Outcome and Non-adverse Outcome (N = 44)*

CT Measures	Cohort Data	Adverse Outcome	Non-adverse Outcome	p-value
RV area* (mm^2)	2284 (466)	2304 (492)	2263 (451)	0.79
RV/LV ratio*	0.54 (0.14)	0.55 (0.15)	0.53 (0.13)	0.58
PA / Ao ratio*	0.92 (0.12)	0.94 (0.12)	0.91 (0.11)	0.47
LV area* (mm^2)	4362 (950)	4443 (1087)	4284 (818)	0.60
Septal Flattening	>27.3 (12)	27.3 (9)	6.8 (3)	0.03

*Means with t-test as test for significant differences; Measurements and standard deviations are

Table 4—*CT Measurements for Adverse and Non-adverse Outcomes in Non-Massive PE (N = 32)*

CT Measures	Non-Massive PE**	p-values+++	Adverse Outcome (n = 13)	Non-adverse Outcome (n = 19)
RV area*	2313 (461)	2163 (525)	0.42	
RV / LV ratio*	0.56 (0.15)	0.50 (0.13)	0.30	
PA / Ao ratio*	0.91 (0.10)	0.94 (0.13)	0.40	
LV*	4356 (156)	4275 (834)	0.82	
Septal Flattening+	18.75 (6)	6.25 (2)	0.04	

*Means with standard deviations

DISCLOSURE: Peter Marshall, None.

Pulmonary Hypertension: Echocardiography and Other Evaluation
2:30 PM - 4:00 PM

EXPIRATORY AIRFLOW LIMITATION DURING EXERCISE AS A CAUSE OF VENTILATORY IMPAIRMENT IN PULMONARY ARTERIAL HYPERTENSION

Alpana Chandra MD* Robert Garofano Erika B. Rosenzweig MD Allison Widlitz David Prezant MD Robyn J. Barst MD Montefiore Medical Center, Bronx, NY

PURPOSE: The pathophysiology of exercise limitation in patients with pulmonary arterial hypertension (PAH) remains unclear. In addition, whether the peripheral airway obstruction observed at rest contributes to exercise limitations is also unknown. We hypothesized that exercise induced expiratory airflow limitation occurs in PAH patients contributing to their ventilatory constraint and dyspnea with exercise.

METHODS: We examined the degree of airflow limitation in PAH patients (n=12; age=27±13 yrs; PAPm=64±18 mmHg) and healthy volunteers (n=6; age=32±4yrs) by plotting the tidal flow-volume responses to graded exercise in relation to the maximal flow-volume loops (MFVL) obtained at rest. Inspiratory Capacity (IC) maneuvers were performed to follow changes in end-expiratory lung volume (EELV) during exercise; the degree of airflow limitation was assessed as percentage of the tidal volume (VT) that met or exceeded the expiratory boundary of the MFVL; tidal FV loops were measured at rest and at 40%, 60%, and 80% of peak workload during cardiopulmonary exercise testing. EELVs are one of the reserves that contribute to the VT increases during exercise.

RESULTS: EELV progressively decreased in controls as exercise intensity increased. In contrast, in PAH patients, although the EELV initially decreased with light exercise, it increased to ≥ baseline as minute ventilation and expiratory airflow limitation increased with greater workloads. Significant airflow limitation occurred at as low as 40% of the patients' peak workload; at 80% peak workload it was 46±23% of the VT in PAH patients versus 5% of the VT in controls($p<0.05$).

CONCLUSION: We conclude that moderate to severe exercise induced airflow limitation occurs with dynamic hyperinflation during exercise resulting in ventilatory constraint that may contribute to the exercise intolerance in PAH patients.

CLINICAL IMPLICATIONS: Bronchodilators, by decreasing airflow limitation, may improve patients' dyspnea on exertion.

	Rest	40%	60%	80%
Airflow Limitation (%)				
PAH	0	45 ± 17*	52 ±12*	46 ± 23*
Controls	0	0	0	5
EELV (L)				
PAH	2.8 ± 0.3	2.7 ± 0.2	2.8 ± 0.2	2.9 ± 0.2
Controls	3.1 ± 0.2	3.1 ± 0.3	3.0 ± 0.3	2.8 ± 0.2
Inspiratory Flow/Capacity (%)				
PAH	44 ± 7	49 ± 8	57 ± 7	68 ± 7
Controls	39 ± 7	43 ± 7	50 ± 7	65 ± 18

*$p<0.05$ vs controls

DISCLOSURE: Alpana Chandra, None.

N–TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE AS AN INDICATOR OF DISEASE SEVERITY IN PULMONARY ARTERIAL HYPERTENSION

Daniele Bendayan MD* David Shitrit MD Ruth Tor PhD Jaqueline Sulkes PhD Mordechai Kramer MD Rabin Medical Center, Petah Tikva, Israel

PURPOSE: Plasma brain natriuretic peptide (BNP), which serves as a noninvasive marker of left-side heart failure, was recently reported to increase in proportion to right ventricular dysfunction in patients with pulmonary hypertension. Pro BNP is a prohormone cleaved into the inactive N terminal portion (NT pro-BNP) and the active BNP. The aim of this study was to determine whether the NT pro- BNP is a potential indicator of the disease severity for pulmonary hypertension and may be a guide for efficacy of treatment.

METHODS: Forty-three patients with a diagnosis of pulmonary arterial hypertension being followed at our clinic.All patients underwent right heart catheterization and clinical assessment. Treatment consisted of vasodilators. Blood was drawn for the measurement of NT pro-BNP, and findings were correlated with hemodynamic parameters (mean pulmonary arterial pressure, cardiac index), clinical factors (6-min walk, New York Heart Association class) and 6-month outcome.

RESULTS: Two patients died of the disease during the follow-up period. Plasma NT pro-BNP level was found to be a significant predictor of mortality ($r=-0.7$, $p<0.0001$) and correlated with New York Heart Association class ($r= 0.2$, $p= 0.06$). Division of the patients by etiology yielded higher NT pro-BNP levels in those with idiopathic pulmonary hypertension than in the other groups (pulmonary hypertension associated with collagen vascular disease, chronic pulmonary emboli, Eisenmenger syndrome) ($r=-0.3$, $p= 0.02$). No statistical significant correlation was

Pulmonary Hypertension: Echocardiography and Other Evaluation, continued

found between plasma NT pro-BNP level and distance in the 6-min walk(r=-0.2, p=0.11).

CONCLUSION: A high plasma NT pro-BNP level is strongly associated with increased mortality in patients with pulmonary hypertension and suggests the need for aggressive treatment.

CLINICAL IMPLICATIONS: Further studies are warranted to evaluate the role of NT pro-BNP as a biological marker to replace right heart cathetrization. Repeated measurement may be helpful as a guide for selecting therapy.

DISCLOSURE: Daniele Bendayan, None.

CARDIAC ADAPTATION IN PATIENTS WITH RIGHT VENTRICULAR PRESSURE OVERLOAD: IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION COMPARED TO THE EISENMENGER SYNDROME

Tji-Joong Gan MS* Christa Boer PhD Tim Marcus PhD Pieter Postmus PhD Anton Vonk Noordegraaf PhD VU University Medical Center, Amsterdam, Netherlands

PURPOSE: Patients with Eisenmenger syndrome have a better prognosis than patients with idiopathic pulmonary arterial hypertension (iPAH) Preserved biventricular function has been suggested to be the primary reason, which might be attributed to a favorable adaptation of the heart to an increased right ventricular (RV) afterload. Therefore this study compared cardiac morphology in iPAH and Eisenmenger syndrome patients with increased RV afterload.

METHODS: 10 iPAH, 6 Eisenmenger patients and 7 healthy controls were studied. Right heart catheterization was performed in all patients to assess mean pulmonary artery pressure. Cardiac magnetic resonance imaging was performed in all individual and measured right and left ventricular ejection fractions, free wall and septal myocardial mass.

RESULTS: In iPAH mean pulmonary artery pressure was not different (63 ± 19 mmHg vs. 69 ± 12 mmHg) compared to Eisenmenger patients, and RV (21 ± 6 % vs. 35 ± 11%, $p < 0.01$) and LV (48 ± 10 % vs. 70 ± 11 %, $p < 0.01$) ejection fractions were depressed. Compared to controls all patients showed RV and septal hypertrophy. However, RV mass increase in iPAH was less than in Eisenmenger (54 ± 15 g/m2 vs. 75 ± 13 g/m2, $p < 0.05$), while septal mass was equally distributed (36 ± 7 g/m2 vs. 32 ± 4 g/m2) in both patient groups. LV mass was decreased in iPAH patients compared to controls (33 ±7 g/m2 vs. 42 ± 8 g/m2) and Eisenmenger (33 ±7 g/m2 vs. 44 ± 10 g/m2, $p < 0.05$).

CONCLUSION: These data show that to a similar increase in RV afterload iPAH patients had depressed RV and LV function compared to Eisenmenger. This might be due to a less favorable adaptation of the right and left ventricle in iPAH.

CLINICAL IMPLICATIONS: In patients with RV pressure overload RV adaptation and function remains the main focus. However, in iPAH LV remodeling, i.e. myocardial hypotrophy, and impaired function might have an additional value in the clinical management and prognosis.

DISCLOSURE: Tji-Joong Gan, None.

DIFFERENCES IN RIGHT VENTRICULAR FUNCTION AND MORPHOLOGY BETWEEN IDIOPATHIC AND SCLERODERMA RELATED PULMONARY ARTERIAL HYPERTENSION

Micah R. Fisher MD* Paul R. Forfia MD Ela Chamera Reda E. Girgis MB, BCh Mary Corretti MD Paul M. Hassoun MD Johns Hopkins University, Baltimore, MD

PURPOSE: Idiopathic pulmonary arterial hypertension (IPAH) and pulmonary arterial hypertension related to scleroderma (PAH-SSc) are characterized by progressive increases in pulmonary vascular resistance with resultant right ventricular dysfunction, failure, and eventual death. Despite similar hemodynamics, patients with PAH-SSc have poorer response to therapy and worse outcomes. Differences in echocardiographic measures of right ventricular function and morphology may have important prognostic significance in this patient population.

METHODS: Comprehensive evaluations were performed in consecutive patients with IPAH or PAH-SSc including right heart catheterization and transthoracic echocardiograms. The echocardiograms were interpreted with special attention to right sided chamber function and morphology including right atrial and ventricular areas, eccentricity index, and tricuspid annular plane systolic excursion (TAPSE). The echocardiograms were interpreted without knowledge of the right heart catheterization results or the patient's diagnosis. The patients were then prospectively followed to determine long-term survival.

RESULTS: Thirty-three patients (15 IPAH and 18 PAH-SSc) were included in the study. Patients with PAH-SSc were older (60.5 ± 12.7 vs. 44.5 ± 12.4, P-value < 0.001). There was no difference between right atrial pressure and cardiac index between groups; however, patients with PAH-SSc had lower mean pulmonary artery pressures (45.2 ± 9.9 vs. 54.5 ± 14.5, P-value 0.036). There was a trend towards increased right atrial size and right ventricular area, and a decreased eccentricity index for the PAH-SSc group. Pericardial effusions were more likely in the PAH-SSc patients then the patients with IPAH (50% vs. 7%, Chi-squared=0.007). Right ventricular function as measured by TAPSE was significantly reduced in the PAH-SSc group (1.7 ± 0.5 vs 2.1 ± 0.7, P-value 0.042). One-year outcomes are pending.

CONCLUSION: Patients with PAH-SSc have reduced right ventricular function and are more likely to have a pericardial effusion present despite having milder pulmonary hypertension. These results suggest that the right ventricle in patients with PAH-SSc is less adaptable to elevation in pulmonary artery pressure.

CLINICAL IMPLICATIONS: Echocardiographic measurements of right ventricular function may have prognostic significance for long-term survival.

DISCLOSURE: Micah Fisher, None.

CORRELATION OF NT-PROBNP WITH OTHER NONINVASIVE PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

Charles W. Hargett MD* Alicia K. Gerke MD Terry A. Fortin MD Victor F. Tapson MD Duke University Medical Center, Durham, NC

PURPOSE: The manifestations of pulmonary arterial hypertension (PAH) are nonspecific and the course variable, creating a need for reliable parameters to guide clinical decision making. Traditionally, right heart catheterization, transthoracic echocardiogram (TTE), 6-minute walk (6MW), and WHO functional classification have been employed to characterize disease. However, there is increasing evidence that B-type natriuretic peptide (BNP) may be a useful marker for dysfunction of the right ventricle and, as such, may help inform clinical decision making in patients with PAH. To help clarify the role of BNP in PAH, we evaluated the correlation of NT-proBNP with other noninvasive parameters.

METHODS: We measured 490 plasma NT-proBNP levels from 166 patients with PAH or pulmonary hypertension due to thromboembolic disease and who also had a recent TTE and/or 6MW. Patients with left-sided heart disease or renal insufficiency (serum creatinine > 1.5 mg/dL) were excluded. Descriptive statistics were used to compare NT-proBNP, 6MW, and TTE parameters (including right ventricular systolic pressure (RVSP), right ventricular (RV) size, and right atrial (RA) size).

RESULTS: NT-proBNP levels positively correlated with TTE parameters, including RV size ($r = 0.52$, $p < 0.0001$), RA size ($r = 0.56$, $p < 0.0001$), and RVSP ($r = 0.46$, $p < 0.0001$). NT-proBNP negatively correlated with 6MW distance ($r = -0.41$, $p < 0.0001$). In the TTE subgroup analysis, the highest correlation occurred with NT-proBNP and RV size in patients with PAH associated with connective tissue disease ($r = 0.65$, $p < 0.0001$). Patients with idiopathic PAH showed the highest correlation between NT-proBNP and 6MW ($r = -0.50$, $p < 0.0001$). Over 90% of patients with NT-proBNP > 1000pg/mL had moderate or severe RV enlargement by TTE.

CONCLUSION: NT-proBNP levels correlate with noninvasive parameters of right heart dysfunction and functional capacity in patients with PAH. Highly elevated levels of NT-proBNP are particularly specific for significant RV enlargement.

CLINICAL IMPLICATIONS: Our study supports the expanding evidence that NT-proBNP may serve as a surrogate marker in the clinical evaluation and management of PAH.

DISCLOSURE: Charles Hargett, None.

Pulmonary Hypertension: Echocardiography and Other Evaluation, continued

BASELINE VENOUS ENDOTHELIN-1 (ET1) PLASMA LEVELS DOES NOT PREDICT CLINICAL RESPONSE TO BOSENTAN IN PULMONARY ARTERIAL HYPERTENSION

Carmine D. Vizza MD* Claudio Letizia MD Roberto Badagliacca MD Susanna Sciomer MD Roberto Poscia MD Roberto Ciuffa MD Mariella Montano MD Michele D'Alto MD Luigi Petramala MD Dario Cotesta MD Francesco Fedele MD Dept Cardio Resp Sciences Univ Rome La Sapienza, Rome, Italy

PURPOSE: ET-1 is a key mediator in the pathogenesis of pulmonary hypertension, and ET-1 venous plasma levels are a strong prognostic factor in patients with pulmonary arterial hypertension (PAH). Bosentan, a dual ETA and ETB receptor antagonist, is an effective therapy for idiopathic PAH and PAH related to connective tissue disease (CTD). The purpose of this study was to evaluate the clinical efficacy of Bosentan in relationship to baseline ET1 plasma levels in patients with PAH.

METHODS: Twenty-four patients with PAH (idiopathic n=16, CTD n=8) in WHO functional class II-III were included in this study. All patients had a baseline venous ET1 plasma levels and were treated with oral bosentan (62.5 mg b.i.d for the first month and then 125 mg b.i.d.). Patient clinical status (WHO class), 6-minutes walking test (6MWT) and 2D-echo Doppler estimation of pulmonary artery pressure (PAPs) were assessed at baseline and at 6- month. On the basis of the median value of ET-1 plasma levels the population was divided in two groups (Gr1 <19.4 pg/ml, Gr2 >19.4 pg/ml).

RESULTS: We did not find significant differences between the two groups' baseline characteristics regarding gender, WHO functional class (Gr1: 2.5+0.5 , Gr2: 2.8+0.5), effort capacity (6MWT distance Gr1: 427+77 meters, Gr2: 372+99 meters) and PAPs (Gr1: 85+22 mmHg, Gr2: 90+22 mmHg). After 6 months treatment both groups showed a significant improvement (ANOVA for repeated measures) in 6MWT (Gr1: +34+19 meters, Gr2: +30+21 meters) without differences between groups. WHO class had a trend towards lower class (Gr1: -0.5+0.2, Gr2: -0.4+0.2) while PAPs did not show significant changes (Gr1: -4+8 mHg, Gr2: -2+9 mmHg).

CONCLUSION: These preliminary data suggest that the clinical efficacy of bosentan is independent to baseline venous ET1 plasma levels.

CLINICAL IMPLICATIONS: Circulating ET1 is probably the expression of systemic neuro-hormonal activation and does not reflect the paracrine activation at pulmonary circulation. ET1 pulmonary uptake/production should be investigated further in order to clarify if there is a relationship with the clinical efficacy of bosentan.

DISCLOSURE: Carmine Vizza, None.

Sarcoidosis and Other ILD
2:30 PM - 4:00 PM

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF INFLIXIMAB IN PATIENTS WITH CHRONIC PULMONARY SARCOIDOSIS

R. P. Baughman MD* M. A. Judson MD U. Costabel MD R. M. duBois MD M. Drent MD M. Kavuru MD K. H. Lo PhD C. Andresen MD R. Schlenker-Herceg MD E. S. Barnathan MD University of Cincinnati Medical Center, Cincinnati, OH

PURPOSE: To evaluate the safety and efficacy of infliximab, a TNFα inhibitor, in improving lung function, symptoms, and functional capacity in patients with chronic sarcoidosis with pulmonary involvement who are symptomatic despite treatment.

METHODS: Patients (n=138) were randomized (1:1:1) to infliximab [3 or 5mg/kg] or placebo at 34 centers in US and EU. Patients were infused at week 0, 2, 6, 12, 18, 24 and followed through week 52. Eligibility criteria included a diagnosis of sarcoidosis for ≥1 year, an American Thoracic Society dyspnea score of ≥1 despite treatment with ≥3 months of prednisone (≥10mg) or immunomodulator therapy or both, evidence of parenchymal disease (Stage II or III) on chest radiograph and a forced vital capacity (FVC) of ≥50-≤85% predicted. The 1° endpoint was defined as the change from baseline in the % of predicted FVC at week 24. Major secondary endpoints included the St. George's Respiratory Questionnaire, 6-minute walk distance, and Borg's CR10 dyspnea score.

RESULTS: Baseline characteristics were well balanced, with 42% of patients receiving immunomodulators and corticosteroids. There was a significant improvement in the 1° endpoint in the combined infliximab group (delta 2.5%, p = 0.038). Results did not differ substantially between the infliximab doses. Subgroup analysis demonstrated greater benefit in patients with more extensive sarcoidosis disease burden, duration, activity or severity. There were no significant differences in major secondary endpoints. Ten percent of patients had infusion reactions and ~5% discontinued treatment due to adverse events (no difference between placebo and infliximab). There were no instances of delayed hypersensitivity reactions or anaphylaxis. One patient (receiving placebo) died of respiratory failure due to pulmonary hypertension secondary to sarcoidosis.

CONCLUSION: Infliximab appears to be effective in improving pulmonary function in symptomatic patients with chronic pulmonary sarcoidosis with a reasonable safety profile.

CLINICAL IMPLICATIONS: Addition of infliximab to corticosteroid therapy with or without immunomodulators is a promising new treatment strategy. These results should be confirmed in a larger, more severely affected chronic pulmonary sarcoidosis population.

DISCLOSURE: R Baughman, Grant monies (from industry related sources) Research grants; Consultant fee, speaker bureau, advisory committee, etc.; Employee.

ASSESSMENT OF INFLIXIMAB EFFICACY IN EXTRAPULMONARY SARCOIDOSIS USING A NOVEL ASSESSMENT TOOL: RESULTS FROM A RANDOMIZED TRIAL

M. A. Judson MD* U. Costabel MD M. Drent MD M. Kavuru MD R. M. duBois MD K. H. Lo PhD R. Schlenker-Herceg MD E. S. Barnathan MD R. P. Baughman MD Medical University of South Carolina, Charleston, SC

PURPOSE: Anecdotal evidence has suggested improvement in extrapulmonary sarcoidosis with infliximab therapy, but this has not been prospectively studied. The purpose of this study was to evaluate the efficacy of infliximab on extrapulmonary sarcoidosis in patients with chronic pulmonary sarcoidosis who are symptomatic despite treatment.

METHODS: One hundred thirty-eight patients were randomized (1:1:1) to placebo, 3 or 5mg/kg infliximab at 34 centers. Patients were infused at week 0, 2, 6, 12, 18, 24 and then followed through week 52. Patients were included with a diagnosis of sarcoidosis for ≥1 year and therapy for ≥3 months with prednisone (≥10 mg/day) and/or immunomodulators. Physicians assessed each of 17 extrapulmonary organs and the lungs for involvement at each visit on a 0-6 scale (0=not affected; 6=very severe). The total of extrapulmonary scores were compared across the groups. Serum angiotensin converting enzyme (ACE) levels were measured as an indication of total granuloma burden.

RESULTS: The mean (±SD) extrapulmonary total scores and ACE levels were similar at baseline across the groups. Mean scores fell steadily throughout the 24 week period in both treated groups. At week 24, there was a significant reduction in combined infliximab group (p=0.002). Mean ACE levels rose in the placebo group at 12 and 24 weeks whereas they fell significantly in both treatment groups at both times.

CONCLUSION: Infliximab appears to be effective in reducing extrapulmonary sarcoidosis involvement as assessed by physicians using a novel 7 point assessment tool. ACE levels are also reduced by infliximab, prior to the detection of any clinical improvement in the extrapulmonary total score.

CLINICAL IMPLICATIONS: Addition of infliximab to corticosteroid therapy with or without immunomodulators is a promising new treatment strategy for patients with extrapulmonary involvement. Further validation of the clinical meaningfulness of changes in the total score needs to occur. Additional follow up off treatment will be important to assess the duration of the improvements noted.

Sarcoidosis and Other ILD, continued

	Extrapulmonary Total Score					ACE Level (IU/L)				
	Placebo	3mg/kg		5mg/kg		Placebo	3mg/kg		5mg/kg	
Baseline	4.0±5.4	3.6±3.9		3.5±4.5		44±28	51±47		48±30	
Week 12*	-0.8	-1.0	p=0.437	-0.8	p=0.552	+6.9	-13.2	p<0.001	-9.8	p=0.009
Week 24*	-0.4	-1.5	p=0.006	-1.4	p=0.008	+7.9	-13.9	p=0.004	-9.8	p=0.015

*Change from baseline

DISCLOSURE: M Judson, Grant monies (from industry related sources) Research grants; Employee; Consultant fee, speaker bureau, advisory committee, etc.

CHEST X-RAY ASSESSMENT USING A DETAILED SCORING METHOD IN A RANDOMIZED TRIAL OF INFLIXIMAB IN SUBJECTS WITH CHRONIC PULMONARY SARCOIDOSIS

M. Kavuru MD* R. M. duBois MD U. Costabel MD M. A. Judson MD M. Drent MD K. H. Lo PhD C. Andresen MD R. Schlenker-Herceg MD E. S. Barnathan MD R. P. Baughman MD R. T. Shipley MD Cleveland Clinic Foudation, Cleveland, OH

PURPOSE: A radiographic scoring method (Muers et al Sarcoidosis Vasc Diffuse Lung Dis 1997;14:46) was devised to enable rigorous evaluation of chest radiographs (CXR) in subjects with pulmonary sarcoidosis. The purpose of this study was to evaluate the effect of infliximab on the radiographic appearance of pulmonary sarcoidosis using this scoring system.

METHODS: One hundred thirty-eight subjects were randomized to placebo, 3 or 5mg/kg infliximab at 34 centers. Subjects were infused at week 0, 2, 6, 12, 18, 24 and followed through week 52. Inclusion criteria included a diagnosis of sarcoidosis for ≥1 year; a forced vital capacity (FVC) of ≥50-≤85% predicted and stage II or III on CXR. Two experienced radiologists, blinded to treatment and time of exam, scored the baseline, 6 and 24 week CXR for extent (0-4) and profusion (0-4) for each of four types of shadows: reticulonodular (R), mass (M), confluent (C), and fibrosis (F). Over 90% of CXR at each time point were available for review.

RESULTS: Scores in each domain were reasonably balanced at baseline. There were no significant differences in the M, C or F scores over time in any group. However, there were significant reductions in the R score at both time points in both treatment groups compared to baseline, with no change in the placebo group. Subgroup analyses showed that improvement in the primary endpoint (change in % predicted FVC at week 24) appeared to be restricted to subjects (n=78) with an R score >0 at baseline (5.2% improvement, p<0.001).

CONCLUSION: Infliximab appears to be effective in improving reticulonodular infiltrates on CXR without affecting the other type of shadows in subjects with chronic pulmonary sarcoidosis.

CLINICAL IMPLICATIONS: The treatment effect of infliximab in improving FVC appears restricted to patients with baseline CXR evidence of reticulonodular infiltrates.

Time Point	R Score					
	Placebo		3 mg/kg		5 mg/kg	
Baseline	N=43	3.9 ± 4.1	N=42	3.1 ± 3.8	N=44	4.1 ± 4.3
6 Week (change)	N=43	+0.2 ± 1.6	N=40	-0.8 ± 1.6 p=0.002	N=43	-0.9 ± 2.9 p=0.008
24 Week (change)	N=42	+0.3 ± 2.2	N=41	-1.0 ± 2.0 p=0.001	N=43	-0.9 ± 3.6 p=0.016

Mean ± SD

DISCLOSURE: M Kavuru, Grant monies (from industry related sources) Research grants; Employee; Consultant fee, speaker bureau, advisory committee, etc.

CLINICAL SIGNIFICANCE OF ANTI-GM-CSF ANTIBODIES IN IDIOPATHIC PULMONARY ALVEOLAR PROTEINOSIS

Fang Chi Lin MD* Geen-Dong Chang PhD Yi-Chu Chen MD Shi-Chuan Chang PhD Department of Medicine, Yuan-Shan Veteran Hospital, I-Lan, Taiwan ROC

PURPOSE: To evaluate the clinical relevance of anti-GM-CSF antibodies in idiopathic pulmonary proteinosis.

METHODS: Twelve idiopathic pulmonary alveolar proteinosis patients were examined on 19 occasions. To serve as controls, 2 patients with secondary pulmonary alveolar proteinosis, 54 patients with other pulmonary disorders, and 11 subjects without lung lesions were studied.

RESULTS: Anti-GM-CSF antibodies were detected using immunoblotting analysis and the titers determined semiquantitatively by serial dilution. Clinical parameters used to indicate severity of idiopathic pulmonary alveolar proteinosis were measured. Anti-GM-CSF antibodies were detected in 18 of 19 (95%) blood and 12 of 19 (63%) bronchoalveolar lavage fluid samples in 12 idiopathic pulmonary alveolar proteinosis patients on 19 occasions, but were absent in blood and bronchoalveolar lavage fluid samples obtained from all other studied subjects. Blood levels of anti-GM-CSF antibodies showed no significant correlation with the clinical variables indicative of severity of idiopathic pulmonary alveolar proteinosis. In contrast, the levels of bronchoalveolar lavage fluid anti-GM-CSF antibodies correlated significantly with those of serum lactate dehydrogenase, arterial oxygen tension, alveolar-arterial PO2 difference, ventilatory parameters, and all lung lesion scores measured on chest radiographs and thoracic computed tomography scans.

CONCLUSION: Our results confirmed that the presence of anti-GM-CSF antibodies in blood or bronchoalveolar lavage could serve as a diagnostic marker for idiopathic pulmonary alveolar proteinosis. Additionally, bronchoalveolar lavage fluid levels of anti-GM-CSF antibodies correlated well with the severity of idiopathic pulmonary alveolar proteinosis.

CLINICAL IMPLICATIONS: The titers of anti-GM-CSF antibodies in bronchoalveolar lavage fluid may reflect the severity of idiopathic pulmonary alveolar proteinosis.

DISCLOSURE: Fang Chi Lin, None.

INTERMEDIATE-TERM OUTCOMES FOLLOWING TRANSPLANT FOR SARCOIDOSIS RELATIVE TO SURVIVAL AFTER TRANSPLANT FOR IDIOPATHIC PULMONARY FIBROSIS

Andrew F. Shorr MD* Darcy Davies MS Donald L. Helman MD Christopher J. Lettieri MD Steven D. Nathan MD Washington Hospital Center, Washington, DC

PURPOSE: Understanding outcomes from lung transplant (LT) is central to both more efficient organ allocation and to efforts targeted at improving recipient survival. Unlike idiopathic pulmonary fibrosis (IPF), sarcoidosis (SAR) generally affects younger patients who therefore have the potential to live for longer durations after LT. However, little is known about survival following LT for SAR.

METHODS: We reviewed the records of all patients with either SAR or IPF who underwent LT in the US from Jan 1994 to Dec 2002. Mortality at 2 years following LT served as the primary endpoint. To examine potential confounders which might affect survival we also recorded patient demographics, lung function, pulmonary hemodynamics, functional status, and corticosteroid use.

RESULTS: The final study cohort included 197 patients with SAR and 1155 subjects with IPF. Those with SAR were younger than persons with IPF (mean age: 46.7 vs. 53.9 yrs, p <0.01). Nonetheless, individuals with SAR had worse lung function at time of LT (FVC 43.5 ± 15.6 vs. 48.2 ± 16.8 % predicted, p<0.01). Pulmonary hypertension was also more common in SAR (mean PA pressure 33.2 ± 12.3 vs. 25.3 ± 10.5 mm Hg, p<0.01). Prior to LT there was no difference in the proportion of patients with either disease hospitalized, requiring substantial assistance with their activities of daily living, or classified as corticosteroid dependent by the LT center. Two-year actuarial survival was similar between the two populations (61% for SAR vs. 62% for IPF, p=0.45). In each cohort, the greatest decline in survival occurred during the first year following LT.

CONCLUSION: Patients with SAR appear to be more severely ill when listed for LT compared to persons with IPF. However, intermediate-term outcomes for LT for SAR are similar to those seen in LT for IPF.

CLINICAL IMPLICATIONS: Those with SAR seem to do well with LT. Concern about the effect of LT on survival in SAR should not

Sarcoidosis and Other ILD, continued

preclude physicians from referring patients with advanced SAR for LT evaluation.

DISCLOSURE: Andrew Shorr, None.

INTERFERON GAMMA-1B INHIBITS INTERLEUKIN-4, ENDOTHELIN-1, AND TRANSFORMING GROWTH FACTOR-BETA--INDUCED UP-REGULATION OF TYPE I COLLAGEN IN CELLULAR MODELS OF LUNG FIBROSIS

Osman N. Ozes PhD * Lawrence M. Blatt PhD Scott Seiwert PhD InterMune, Inc., Brisbane, CA

PURPOSE: Idiopathic pulmonary fibrosis (IPF) is a progressive, fatal disease characterized by hyperproliferation of type II epithelial cells in the interstitial space. IPF is thought to result from epithelial cell injury followed by aberrant wound healing and excessive accumulation of collagen, which lead to the development of fibroblastic foci or lesions. Interleukin (IL)-4, endothelin (ET)-1, and transforming growth factor beta (TGF-β) all induce transcriptional up-regulation of type I collagen, suggesting that all could enhance the accumulation of extracellular matrix (ECM) during the development of IPF. Interferon gamma-1b (IFN-γ 1b) has demonstrated anti-infective properties and is currently indicated for use in chronic granulomatous disease and malignant osteopetrosis. It is also under clinical study for the treatment of IPF, for which it may offer a survival benefit (Raghu G, Brown KK, Bradford WZ, et al. N Engl J Med. 2004;350(2):125-133).

METHODS: To evaluate the effect of IFN-γ 1b on type I collagen synthesis, we studied its effect on IL-4, ET-1, and TGF-β–induced type I collagen synthesis in human lung fibroblasts. Secreted collagen levels were determined by the ratio of total and collagenase-stable ^{3}H-labeled protein in cell culture supernatants.

RESULTS: Relative to untreated cells, 5 ng/mL IL-4, ET-1, or TGF-β induced the expression of type I collagen by 42%, 58%, and 78%, respectively ($p < 0.05$). The collagen-inducing activities of IL-4, ET-1, and TGF-β were additive; collagen secretion increased 2.2-fold when cells were stimulated with all three ($p < 0.05$). A 5 ng/mL IFN-γ 1b dose reduced ET-1 and IL-4–stimulated collagen production to a level at or below that observed without stimulation; TGF-β–induced collagen secretion was decreased by 17% ($p < 0.05$). IFN-γ 1b was also effective in reducing collagen production from cells treated with any combination of IL-4, ET-1, and TGF-β. In cells treated with all three, IFN-γ 1b reduced collagen secretion by 18% ($p < 0.05$).

CONCLUSION: These results indicate that IFN-γ 1b may modulate fibrotic microenvironments that are associated with pathogenesis in IPF.

CLINICAL IMPLICATIONS: Our results support ongoing clinical research.

DISCLOSURE: Osman Ozes, Shareholder ; Employee All authors are employees of InterMune, Inc.; Product/procedure/technique that is considered research and is not yet approved for any purpose.

Smoking Cessation
2:30 PM - 4:00 PM

RANDOMIZED TRIAL OF A SMOKING CESSATION INTERVENTION IN PATIENTS HOSPITALIZED IN A CARDIO-RESPIRATORY INSTITUTE

Yves Lacasse MD* Rejean Lamontagne MA Sylvie Martin MS Marie Arsenault MD Hopital Laval, Ste-Foy, PQ, Canada

PURPOSE: To determine whether a smoking cessation intervention of moderate intensity consisting of education and psychological support, with or without pharmacological therapy, associated with follow-up phone calls would increase the smoking cessation rate at 1-year follow-up in hospitalized smokers aged ≤ 70.

METHODS: This randomized trial comparing a smoking cessation intervention to usual care took place at Laval Hospital, the Quebec Heart and Lung Institute. The intervention included: (1) a strong quit smoking message from the treating physician; (2) self-help motivational quitting or relapse prevention materials; (3) brief cessation counseling; (4) the use of nicotine replacement therapy when indicated; and (5) follow-up support. Patients in the usual care group were not given any specific instructions on how to stop smoking. Self-reported abstinence from smoking was recorded and validated by urinary cotinine measurement. The primary outcome was cessation rate at 1-year follow-up.

RESULTS: 468 patients were screened; 196 were randomized. We found no difference in smoking cessation rates at 12-month follow-up (intervention: 30%; control: 28%; number needed to treat: 41; lower bound of the 95% confidence interval: 13). Similar results were obtained from patients whose smoking status was validated at 12-month follow-up by urinary cotinine measurement (intervention: 33%; control: 35%). In logistic regression analyses, length of stay and dependence to nicotine were the only significant predictors of smoking cessation at 12-month follow-up.

CONCLUSION: A smoking cessation intervention of moderate intensity delivered in a tertiary cardio-pulmonary centre did not increase the smoking cessation rate at 1-year follow-up.

CLINICAL IMPLICATIONS: The effect of a smoking cessation intervention of higher intensity should be investigated. Recent studies suggest that enhanced follow-up after hospital discharge is a key element of a successful smoking cessation program.

DISCLOSURE: Yves Lacasse, None.

A STUDY OF GENDER DISCREPANCIES AMONGST SMOKERS REGARDING PERCEPTIONS OF CIGARETTE USE

Virginia C. Reichert* Pat Folan RN Colleen DeGaetano RN Dan Jacobsen RN Lorana Miceli RN Nina Kohn MBA Christine Metz PhD Arunabh Talwar MD North Shore-LIJ Health System, Great Neck, NY

PURPOSE: Reported variability in successful quitting between genders, prompted us to study the perceptions of smokers. Many factors influence the decision of a smoker to make a quit attempt. We studied the factors smokers, who were motivated to quit, experienced at the start of a tobacco dependence treatment program and evaluated discrepancies between the genders.

METHODS: Six sessions emphasized behavior modification and pharmacological interventions. Demographics, co-morbidity and smoking information was obtained from questionnaires on day 1. Quit status verified at 1 month with exhaled carbon monoxide levels.

RESULTS: 1139 smoking patients total (482 males [median age 45.2 years]; 657 females [median age 48.6]); of these, median 'pack years' for males was 33 vs. 27.5 for females. No difference in Fagerstrom scores-scale of nicotine addiction (6.0 out of possible 10 for both men and women), or the number of previous quit attempts (2). More females 71.9% vs. males 63.1% reported smoking "light" cigarettes; believing them to be less harmful than regular cigarettes ($p<0.01$) and more females 71.8% vs. 59.4% males believed that nicotine causes cancer ($p<0.01$). 75.0% females vs. 64.5% males report worrying that their smoking may give them cancer ($p<0.01$). Females also reported 'feeling guilty about their smoking' more often than males 77.2% vs. 61.7% ($p<0.01$). In regard to obstacles to this quit attempt, more females than males reported: a 'fear of failure' 17.5 vs. 10.7% ($p<0.01$), and a 'fear of weight gain' 41.1% vs. 14.6% ($p<0.01$). More females also reported 'being worried about managing their stress without cigarettes' 63.1% vs. 55.0% ($p<0.01$). We found no difference in the quit rates of males and females at 30 days (59.1% vs. 54.9%).

CONCLUSION: Both genders quit similarly, howver, both demonstrated significant knowledge deficit about tobacco and its health hazards. Female concerns about tobacco use far outweighed concerns of males.

CLINICAL IMPLICATIONS: Comprehensive cessation programs need to include not only pharmacotherapy, and behavior modification but also need to emphasize intensive education for both genders to maximize success rates.

DISCLOSURE: Virginia Reichert, None.

IMPACT OF AN INPATIENT SMOKING CESSATION PROGRAM PRELIMINARY OUTCOMES

Kathy Garrett-Szymanski RRT* Peter R. Smith MD Jeanne McCabe RN Rosemarie Samuels RN Latoya Fyffe Ute Rosa MD Long Island College Hospital, Brooklyn, NY

PURPOSE: Hospitalization affords a unique opportunity to assist smokers with a cessation attempt. Abstinence is automatic, motivation high, and the cessation message can be delivered multiple times. Inpatient smoking cessation programs (ISCPs) are more successful than ambulatory

Smoking Cessation, continued

programs with 1 year abstinence rates as high as 70%. We report our preliminary experience with an ISCP at our 450 bed community hospital.

METHODS: Since 7/04, smokers have been identified by the hospital's case managers during their AM rounds. A daily roster is faxed to the Smoking Cessation Center (SCC) and patients are seen that day by the counselors. Those who accept counseling are given written materials and receive a 5 -10 minute message based on the DHHS guidelines (1996). Physicians caring for smokers are encouraged to prescribe nicotine patches (NRT) and/or bupropion. We attempt monthly contact with patients agreeing to follow-up. Demographic, clinical and follow-up data are entered into an electronic database. A stepwise logistic regression model was used to analyze the data presented below.

RESULTS: In the first 6 months since inception, 421 patients were seen by the ISCP and 129 (30.6%) were contacted 1-6 months after hospitalization. Sixty-eight of 129 (46.5%) remained abstinent at 1-6 months. NRT and/or bupropion were used by 13 patients (13.1%) during 1 or more months after discharge. In univariate analyses, Caucasian patients and those admitted with cardiovascular diseases had a greater likelihood of remaining abstinent (OR=2.70, 95% CI 1.132-6.455, p=.025 and OR=2.308, 95% CI 1.009-5.276, p=.047 respectively). Multivariate analysis confirmed these as independent predictors of abstinence. Age, gender, pack-years of smoking, and lung disease were not predictive.

CONCLUSION: Our data, although preliminary, suggest that ISCPs are highly effective in assisting patients in cessation attempts. As previously reported, smokers with cardiovascular diseases are most likely to benefit from this intervention.

CLINICAL IMPLICATIONS: ISCPs offer smokers the prospect of a successful quit attempt. This opportunity to provide repetitive, expert cessation guidance should not be missed.

DISCLOSURE: Kathy Garrett-Szymanski, None.

SMOKING INCIDENCE AND THE EFFECT OF SMOKEFREE EDUCATION PROGRAMS IN JUVENILES IN ISHINOMAKI DISTRICT (NORTHEAST COASTAL REGION OF JAPAN)

Masaru Yanai MD* Masaaki Abe BA Hiroshi Chiba MD Seiichi Kobayashi MD Ishinomaki Red Cross Hospital, Ishinomaki, Japan

PURPOSE: To investigate the appropriate ages when juveniles receive smokefree education, we examined their intention of smoking, incidence of smoking, and family smoking history.

METHODS: We used questionnaires to assess smoking history among juveniles (elementary school 5th and 6th grade pupils (11-12yo, n=175), junior high school 8th grade students (14yo, n=122), and high school students (16-18yo, n=579)) after giving them smokefree education. The questionnaire includes asking about the student's and family smoking history, and the student's intentions regarding future smoking. The latter was compared between before and after smokefree education.

RESULTS: 1) Among high school students, 44% of boys have tried smoking and 34% are current smokers; 24% of girls have tried smoking and 16% are current smokers. 20% of them started smoking in elementary school, 60% began in junior high school, and only 20% began in high school. 2) High school students were significantly more likely to try smoking if family members are current smokers, compared with students without smokers in the family. Among both high school and junior high school students, significantly more students intended to smoke if they had smokers in their family. 3) Less than 15% of those who have tried smoking are habitual smokers in elementary school and junior high school; however, more than half are habitual smokers in high school. 4) Smoke free education had a substantial effect on quitting smoking or giving up smoking intention in elementary school pupils, but only a moderate effect in junior high school students, and little effect in high school students.

CONCLUSION: In Ishinomaki, smokefree education is much more effective if it is started at the earlier ages of at most 11-12yo.

CLINICAL IMPLICATIONS: It is important to start smokefree education programs before juveniles start to smoke.

DISCLOSURE: Masaru Yanai, None.

SMOKING CESSATION AND THE USE OF SUSTAINED-RELEASE BUPROPION AS AN AID TO SMOKING CESSATION AMONG FILIPINOS

Manuel Hector Silos MD Lenora C. Fernandez MD* Lirio Covey PhD University of the Philippines-Manila, Manila, Philippines

PURPOSE: Smoking is very prevalent in the Philippines with 45% among Filipinos being ever-smokers and the number of current smokers increased from 32.7% in 1999 to 34.8% in 2003. This study aims to assess the rate of successful smoking cessation among Filipino smokers with the use sustained-release bupropion hydrochloride as the pharmacologic aid in achieving abstinence. Safety in the use of bupropion hydrochloride and factors that may promote smoking abstinence among Filipinos were also determined.

METHODS: This was a non-randomized, non-comparative and prospective study where willing smokers underwent individualized smoking cessation sessions at the Philippine General Hospital and took Sustained-Release Buproprion hydrochloride at 300 mg/day for 8 weeks . They returned weekly during the first four weeks and then at 6 and 8 weeks for follow-up. Self-report of smoking abstinence at the end of 8 weeks was confirmed by urine cotininine determination. Psychological well-being and adverse effects were also monitored during the study.

RESULTS: A total of 84 Filipino smokers were included and all of the subjects completed 8 weeks of sustained release bupropion hydrochloride treatment at 150 to 300 mg/day. Urine cotinine-confirmed abstinence rate was 57% after 8 weeks in the study. Predictors of smoking abstinence were higher educational attainment (odds ratio 3.17, 95% confidence interval 1.1-9.2), older age when the subject started smoking (p value <0.05), absence of another smoker at home ($p<0.05$), and lower baseline carbon monoxide level ($p<0.05$). There was no difference between abstainers and non-abstainers regarding safety and psychological well-being. There were no serious adverse events in the study.

CONCLUSION: Urine cotinine-confirmed smoking abstinence was 57% after 8 weeks of individualized smoking cessation intervention and sustained-release bupropion hydrochloride administration among Filipinos. Minimal adverse effects were encountered with the use of bupropion hydrochloride.

CLINICAL IMPLICATIONS: Smoking cessation intervention with the concomitant use of sustained-release bupropion hydrochloride was quite effective among Filipinos and was at par in effectivity with other Asian and developed countries. Side effects to pharmacologic treatment for smoking cessation were minimal.

DISCLOSURE: Lenora Fernandez, Grant monies (from sources other than industry) US National Institutes of Health National Institute on Drug Abuse (US NIDA) under the program NIDA RO1 #13490 through the Research Foundation for Mental Hygiene, Columbia University, New York, USA.

NICOTINE DEPENDANCE AND PATIENTS' FUNCTIONAL STATUS

Branislav S. Gvozdenovic MD* Ika Pesic PhD Vesna Bjegovic PhD Vozdovac, Belgrade, Serbia

PURPOSE: The aim of our study was to evaluate the relationship between the nicotine dependance and functional status of patients on smoking cessation program.

METHODS: In the cross-sectional study, 72 patients (48 females; mean age was 44.1 $\pm$ 12.2 years) have filled standardised questionnaire DAL (List of Daily Activities), that consists of 11 questions about physical daily activities. Its score depend of the number of positive answers (from 0 to 11). The lower the score, the better the physical performance and the patients' functional status. Nicotine dependance was determined by means of standardised Fagestrom test, which scores range from 0 to 10, with a higher score indicating a greater dependance. According to the level of nicotine dependance, we assigned patients in 3 groups: group I (3 patients) - low dependance: scores 0-3; group II (23 patients) - moderate dependance: scores 4-6; group III (46 patients) - high dependance: scores 7-10. Mean smoking duration was 24.8 $\pm$ 11.6 years, and mean index pack-years was 34.6 $\pm$ 19.3.

RESULTS: Mean DAL scores were 0.67 in group I, 1.04 in group II and 2.93 in group III. Statistically highly significant difference between the average DAL scores with regard to the patient groups was established by means of ANOVA ($F = 5.39$, $p = 0.007$). Pearson's coefficient of linear correlation also showed a statistically highly significant correlation be-

Smoking Cessation, continued

tween the values of DAL scores and the Fagestrom test scores (r = 0.371, p = 0.001).

CONCLUSION: The functional status in smokers, that could be well determined by the DAL questionnaire, strongly reflects their nicotine dependance as assessed by means of the Fagestrom test.

CLINICAL IMPLICATIONS: The functional status of smokers could be successfully used in clinical research and practice as an outcome in smoking cessation programs.

DISCLOSURE: Branislav Gvozdenovic, None.

Treatment of Advanced Thoracic Malignancies
2:30 PM - 4:00 PM

TEMPORAL TRENDS IN LUNG RESECTION SURGERY, UNITED STATES, 1988 TO 2002

Stavros G. Memtsoudis MD* Melanie C. Besculides PhD Namrata Patil MD Selwyn O. Rogers MD Brigham and Women's Hospital, Harvard Medical School, Boston, MA

PURPOSE: We hypothesized that patient characteristics and procedure choice for lung resections is evolving over time. The purpose of this study was to characterize temporal changes in lung resection surgery (pneumonectomies (PE), lobectomies (LE) and segmentectomies (SE)) from 1988 to 2002.

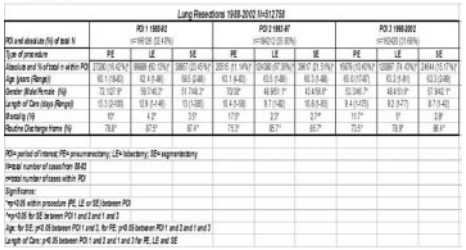
METHODS: Raw data collected in the National Hospital Discharge Survey (NHDS) from 1988 to 2002 were accessed, read into a statistical software package, and concatenated. Lung resection procedures (PE, LE, SE) were identified using ICD-9 procedure codes (32.5, 32.4 and 32.3, respectively). Five year periods of interest (POI) were created for temporal analysis (1988-1992= POI 1, 1993-1997=POI 2, and 1998-2002= POI 3) and changes in the prevalence of procedures were examined by POI. Changes in mortality, length of care (LOC), disposition of discharge to home, age, and gender were evaluated for each procedure across POI. Significance of changes over time within procedure was assessed using Z scores and general linear models for categorical and continuous variables, respectively.

RESULTS: There were 512,758 lung resection procedures performed during the study period; of those 32.4 % were performed in POI 1, 35.9% in POI 2, and 31.7% in POI 3 (Table 1). The proportion of LE increased over time while that of SE and PE decreased. The average patient age increased for SE and PE procedures between POI 1 and POI 3, while the LOC decreased for all procedures over time. Except for SE, the proportion of females undergoing lung surgery increased from POI 1 to 3. A decline in the proportion of patients with a disposition of discharge to home was found for PE and LE. There were no consistent trends in mortality.

CONCLUSION: We were able to identify temporal trends in lung resection procedures over a 15 year period. Further analysis is needed to evaluate our findings in more detail.

CLINICAL IMPLICATIONS: Our results are based on nationally representative data. By identifying trends associated with lung resection surgery, these results may aid in hospital policy planning, such as resource allocation/management.

Table 1



DISCLOSURE: Stavros Memtsoudis, None.

PROSPECTIVE PHASE II PROTOCOL OF STEREOTACTIC BODY RADIOTHERAPY FOR MEDICALLY UNRESECTABLE PATIENTS WITH STAGE 1 NON-SMALL CELL LUNG CANCER

Mark D. Williams MD* David Miller MD Ron McGary MD Robert Timmerman MD Indiana University, Franklin, IN

PURPOSE: To determine the risk/benefit profile of stereotactic body radiotherapy in patients with medically unresectable stage 1 non-small cell lung cancer (NSCLC).

METHODS: We recently completed a phase II study of stereotactic body radiotherapy, which enrolled patients with medically unresectable stage 1 non-small lung cancer. Patients with T1N0 and T2N0 biopsy-proven tumors received 2000 cGy/fraction times 3 fractions and 2200 cGy/fraction times 3 fractions, respectively. Baseline pulmonary function tests (FEV1, FVC, DLCO) and p02 were performed at baseline, 3 and 6 months. Kaplan Meier estimates for overall and disease-free survival were calculated. Treatment toxicity was assessed using standard National Cancer Institute guidelines. In addition an independent safety board determined whether any death was possibly related to the radiotherapy.

RESULTS: A total of 34 T1N0 and 36 T2N0 patients were enrolled from 11/2002 to 08/2004. 30/70 (43%) were on oxygen at baseline. Kaplan Meier estimates indicate a median survival of 32.6 months and actuarial 1-yr overall and disease-free survival of 81.1% and 79%, respectively. As of 5/01/2005, 25 patients have died with 5 deaths felt to be possibly related to the radiotherapy. After a median follow-up of 23 months, 2 local, 4 regional and 2 distant recurrences occurred. 14 patients developed a decrease in pulmonary function and 3 patients suffered radiation fibrosis. Baseline pulmonary function values were: FEV1 1.12 liters, FVC 2.31 liters, DLCO 11.17 and pO2 72.6. At 3 months values were: FEV1 1.19, FVC 2.54, DLCO 10.67 and pO2 67.7. At 6 months post radiotherapy values were: FEV1 1.14, FVC 2.54, DLCO 10.67 and pO2 67.6.

CONCLUSION: In this fragile population, high dose stereotactic body radiotherapy for medically unresectable stage 1 NSCLC appears to have a favorable benefit/risk profile. Specifically, there was no significant decrease in pulmonary function for the overall population at 3 and 6 months.

CLINICAL IMPLICATIONS: Frail patients with medically unresectable stage 1 NSCLC appear to tolerate high doses of targeted radiotherapy. This novel therapy should be further studied in a large multicenter trial.

DISCLOSURE: Mark Williams, None.

SINGLE INSTITUTION EXPERIENCE OF INDUCTION THERAPY FOLLOWED BY SURGERY FOR LOCALLY ADVANCED NSCLC IN 102 CONSECUTIVE PATIENTS

Yukihito Saito MD* Tomohiro Maniwa MD Hiroyuki Kaneda MD Ken-ichiro Minami MD Hiroji Imamura MD Kansai Medical University, Osaka, Japan

PURPOSE: Neoadjuvant treatment for locally advanced non-small-cell lung cancer stage IIIA and IIIB promises higher resection rates because of a reduction of the primary tumor and sterilisation of mediastinal nodes. In this study we analyse the perioperative course and the long-term survival of patients with induction therapy.

METHODS: Between Jan. 1990 and Dec. 2004, 102 patients with NSCLC underwent resection after induction treatment. Included were 82 males and 20 females, median age 63 year-old (39–74), of whom 81 were stage IIIA patients, 21 were stage IIIB patients. Induction therapy included four different regimens, intravenous mitomycin C+vindesine+and cisplatin (MVP), bronchial arterial infusion of CDDP and mitomycin C followed by intravenous vindesin (BAI-MVP), concurrent chemoradiothreapy with 30Gy irradiation+ CBDCA and CBDCA+PTX. 30 patients received MVP, 10 patients received BAI-MVP and 60 patients received CBDCA with concurrent irradiation, 2 patients received CBDCA+PTX followed by surgery. In patients with N3 disease and malignant pleural effusion were excluded.

RESULTS: Resections included 20 pneumonectomies (19.6%), 5 sleeve lobectomies (4.9%), 67 lobectomies (65.7%), and 10 explorative thoracotomies (9.8%). In-hospital mortality rates amounted to 4.9% (5 patients). Bronchopleural fistulas occurred in 2 patients (1.9%). The protection of the bronchial stump or anastomosis with viable tissue, like pedicled pericardial flap or intercostals muscle flap, proves to be a significant factor for the reduction of septic complications. For NSCLC, the 5-year survival rates were 40.2%. Induction therapy significantly increases the survival rate of stage IIIA and IIIB NSCLC compared with

Treatment of Advanced Thoracic Malignancies, continued

historical controls. There was a significant difference in the survival between patients with a major pathologic response to induction therapy as opposed to those who had a minor response.

CONCLUSION: This intensive treatment proves to be feasible. Treatment-related toxicities are overall moderate and acceptable. Accurate cardiopulmonary evaluation before surgery and reinforcement of bronchial stump or anastomosis can contribute to reducing complications. Long-term survival rates for selected groups look very promising when compared to historical controls.

CLINICAL IMPLICATIONS: Pathological response is good prognostic indicator for the patient who underwent induction therapy.

DISCLOSURE: Yukihito Saito, None.

ANALYSIS OF QUALITY OF LIFE AFTER CHEST WALL RESECTION

David Heuker MD Christian Ngongang MD Benoit Lengele MD Véronique Delecluse Birgit Weynand Philippe Noirhomme MD Alain Poncelet MD* Cliniques Universitaries Saint-Luc Département de Chirurgie Cardio-Vasculaire et, Brussels, Belgium

PURPOSE: To study the quality of life and the functional assessment after major chest wall resection.

METHODS: Retrospective analysis of 50 patients operated on between 1983 tand 2001. The etiologies were bronchogenic carcinoma (pT3), primary parietal tumor and chest wall metastasis from sarscoma in 12, 17 and 18 patients respectively. Median rib resection was 3. We performed a complex reconstruction with prosthetic and/or autologuous material in 28 patients.Beside survival analysis, quality of life of long-term survivors (> 36 months) was assessed both by the Borg dyspnea scale (0-10) and the OMS performance status score (0-3).The functionnal assessment was calculated using the Mahler index (0-12) as well as the pulmonary function tests (PFT's) pre and post-operatively.

RESULTS: There was no perioperative mortality. The resection was complete in 42 patients (80%). Overall 3 and 5 years survival were 60 and 57 % , respectively. Among the 26 deaths (52%) registered during follow up, 20 were cancer-related. All the 24 long-term survivors participated in the questionnaire survey. Out of those, 21/24 patients had a score on the Borg scale of 0 to 2 and OMS performance status 0 to 1. Fifteen survivors had a Mahler index between 9 and 12. From the PFT's studies, we found that the mean reduction of the FEV1 and the VC was respectively 18% and 15%.

CONCLUSION: Despite extensive chest wall resection , our study shows that with appropriate technique, long term survival and excellent quality of life can be achieved in the most majority of those patients.

CLINICAL IMPLICATIONS: Reabilitation program.

DISCLOSURE: Alain Poncelet, None.

PREVALENCE AND MORTALITY OF ACUTE LUNG INJURY AND ACUTE RESPIRATORY DISTRESS SYNDROME AFTER LUNG RESECTION

Alina Dulu MD* Stephen M. Pastores MD Bernard Park MD Neil A. Halpern MD Valerie Rusch MD Memorial Sloan-Kettering Cancer Center, New York, NY

PURPOSE: To describe the frequency, predictors of mortality and outcome of acute lung injury (ALI) and/or acute respiratory distress syndrome (ARDS) after lung resection.

METHODS: We retrospectively reviewed the case records of all patients who underwent lung resection and developed ALI/ARDS requiring mechanical ventilation and admission to the Intensive Care Unit (ICU) between January 1, 2002 to December 31, 2004. ALI/ARDS were defined according to the American-European Consensus Conference. Perioperative and in-hospital information including ICU-specific data were collected. All patients received supportive treatment for ALI/ARDS including low tidal volume ventilation. Data are presented as mean +/- SD, absolute numbers or percentages. Statistical analyses used were Student's t-test and chi-square tests. P-values < 0.05 were considered significant.

RESULTS: During the study period, 1801 patients underwent lung resection (Table 1). Of these, 50 (2.8%) developed ALI and/or ARDS. The majority of patients (92%) underwent resection for cancer. There were 28 men (56%) and 22 women (44%) with a mean age of 69±10 years. Eight (16%) received neoadjuvant chemotherapy and 5 (10%) had radiotherapy. The mean postoperative day (POD) to ICU admission was 5±4 days. The mean ICU LOS was 14.4±10.6 days and mean hospital LOS was 30.5±20.2 days. 20 patients (40%) died, 16 in the ICU and 4 after ICU discharge. The mortality rate was highest after pneumonectomy followed by lobectomy and sublobar resections. Older age was associated with higher mortality but not gender, preoperative lung function, use of neoadjuvant therapy, mean POD to ICU admission, glucose and lactate level on ICU admission and paO2/FiO2 ratio (Table 2).

CONCLUSION: The prevalence rate of ALI/ARDS after lung resection requiring MV and ICU admission was 2.8% with an overall mortality rate of 40%. Mortality was highest after pneumonectomy. Older age correlated with poor outcome.

CLINICAL IMPLICATIONS: Implementation of risk-reduction strategies and advances in ICU support are necessary to reduce the mortality rate associated with ALI/ARDS after lung resection.

		ALI/ARDS	ALI/ARDS Mortality
Total lung resections	N=1801	N=50 (2.8%)	N=20 (40%)
Pneumonectomy	118	10	5
Lobectomy/Bilobectomy	1091	31	13
Sublobar resections	592	9	2

	ALIVE (N=34)	DEAD (N=16)	
Variable	Mean± SD	Mean± SD	p Value
Age	67 ± 10	73 ± 9	0.035*
POD to ICU admission	4 ± 3	6 ± 5	0.1 (NS)
ICU LOS	13 ± 10	18 ± 11	0.97 (NS)
Hospital LOS	32 ± 21	28 ± 19	0.534 (NS)
Glucose	151.24 ± 42.59	133 ± 26.83	0.13 (NS)
Lactate	1.72 ± 1.14	1.66 ± 0.97	0.861 (NS)
pO2/FiO2	154 ± 63.65	141 ± 60.76	0.5 (NS)
FEV1 %	78.65 ± 21.91	87.69 ± 15.45	0.145 (NS)
DLCO %	68.55 ± 19.92	70.73 ± 14.82	0.711 (NS)

DISCLOSURE: Alina Dulu, None.

Imaging in Critical Care
10:30 AM - 12:00 PM

LIMITED BEDSIDE ECHOCARDIOGRAPHY PERFORMED BY INTENSIVISTS IN THE MEDICAL INTENSIVE CARE UNIT (MICU)

Roman Melamed MD* Steven Hanovich MD Robert Shapiro MD Mark Sprenkle MD Valerie Ulstad MD James Leatherman MD Hennepin County Medical Center, Minneapolis, MN

PURPOSE: To evaluate the ability of the intensivists with limited echocardiography (ECHO) training to assess left ventricular (LV) performance with the portable ECHO machine.

METHODS: 4 intensivists had 2 hours of didactics and 4 hours of hands-on training in obtaining and interpreting echocardiographic images. 41 consecutive patients who had a standard ECHO during their MICU stay underwent a bedside examination by an intensivist. The bedside exam was performed and recorded with the SonoSite 180 machine on the same day as the standard ECHO. The LV performance was visually estimated as category 1 (ejection fraction (EF) > 50%), category 2 (EF 30 - 50%) or category 3 (EF < 30%). The recorded exams were independently graded by a staff cardiologist. All participants were blinded to the results of the standard ECHO. Comparisons between the interpretation of the bedside exam by the intensivist and the cardiologist were made. Discrepancies between the bedside exam and the standard ECHO were evaluated.

RESULTS: The review of the bedside exams by the cardiologist revealed category 1 LV performance in 18 patients (45%), category 2 in 14

Imaging in Critical Care, continued

(35%) and category 3 in 8 patients (20%). One recording was technically inadequate. The intensivists estimated LV function correctly in 72% of patients, overestimated in 23% and underestimated in 5% (kappa statistic = 0.55). The majority of discrepancies (10/11) were within 1 category range. The sensitivity of the bedside ECHO performed by an intensivist to detect any LV dysfunction was 77% and the specificity was 94%. The positive predictive value was 94%. The negative predictive value was 77%. When compared to the standard ECHO, suboptimal bedside images resulted in the discrepancy in 4 cases.

CONCLUSION: Medical intensivists were able to make a correct estimate of the LV EF in the majority of patients.Additional training in image acquisition and interpretation may improve the performance of the intensivists in the bedside echocardiography.

CLINICAL IMPLICATIONS: Bedside ECHO may become a valuable tool in rapid assessment of LV function in patients admitted to the MICU.

DISCLOSURE: Roman Melamed, None.

THE VALUE OF ROUTINE CHEST X-RAY (CXR) IN MECHANICALLY VENTILATED INTENSIVE CARE UNIT (ICU) PATIENTS

Marleen E. Graat Esther K. Wolthuis MD Goda Choi MD Johanna C. Korevaar PhD Marcus J. Schultz PhD* Avademic Medical Center, Amsterdam, Netherlands

PURPOSE: It is uncertain whether daily routine chest radiographs (routine CXR) truly affect daily management of critically ill patients. In the present study we determined the clinical efficacy of routine CXRs, by comparing two periods with different CXR-strategies: for 6 months (period I) routine CXRs were made in all ICU-patients until discharge/death; in addition CXRs were made on indication (i.e. admission to ICU, clinical deterioration, introduction of any invasive devices). In a second period of 6 month (period II) only on demand CXRs were made.

METHODS: Questionnaires were completed for all CXRs, addressing indication and expected findings. The presence of pulmonary abnormalities (atelectasis, major infiltrates, any pneumothorax, pulmonary congestion or significant pleural fluid), and abnormal position of any invasive device (tube, central venous lines) was scored by the radiologist. Furthermore, it was determined whether the abnormalities truly initiated a change in therapy (i.e., order for cultures/start of antimicrobial therapy, ultrasound/pleurocenthesis, and change (in position) of malpositioned devices). Mortality and length of stay in the 2 periods were compared. Statistics: non-parametric testing.

RESULTS: During the period I, 5118 CXR were made in 885 patients (3396 routine and 1722 on demand CXR). Of all routine CXR, only 221 revealed an unexpected abnormality (6.5%) compared to 188 of the on demand CXRs (10.9%) ($P < 0.0001$); these findings included (on the routine CXR:) 1.2% malposition of tube – 1.1% central venous lines – 1.2% atelectasis. In only 74 (2.2%) of all routine CXRs these abnormalities resulted in a change in therapy/replacement of devices. In period II, the number of on demand CXR was slightly higher compared to period I: 1701 CXR were made in 687 patients. Of all on demand CXRs, 239 (14.1%) revaled unexpected abnormalities. Mortality and length of stay was similar in the two study periods.

CONCLUSION: Routine CXRs have minimal value in guiding management decisions.

CLINICAL IMPLICATIONS: We propose to abandon routine CXRs in ICU-patients.

DISCLOSURE: Marcus Schultz, None.

CORRELATION OF THORACIC COMPUTED TOMOGRAPHY AND PORTABLE CHEST RADIOGRAPHS IN INTENSIVE CARE UNIT PATIENTS

Pervaiz Iqbal MD Arshad Ali MD* Francis M. Schmidt MD J. Quist MD Gerald Posner MD Pranjal Agrawal MD M. Zahir MD S. Natarajan MD Interfaith Medical Center, Brooklyn, NY

PURPOSE: To assess the diagnostic value of thoracic computer tomography scans in comparison with portable chest radiographs in intensive care unit patients.

METHODS: Images obtained in 109 consecutive thoracic computer tomography (CT) examinations, the associated bedside chest radiographs and medical records in the intensive care unit (ICU) of an institution (Interfaith Medical Center, Brooklyn) were retrospectively reviewed. CT findings were compared with concurrent bedside chest radiographic findings.

RESULTS: Of the 109 thoracic CT-scans of the patients, 63.6% were females, 36.4% were males, the patient's age ranges from 18-94 years with 46.7% were more than 65 years old, 58% were blacks and 55.2% of patients admitted to the ICU had dyspnea. In 70 patients (64.2%), thoracic CT revealed additional findings, in comparison with the corresponding bedside radiographs. In 25 (23%) of the 109 CT examinations had at least one new clinically important finding. These important new findings most often were (a) mediastinal Lymphadenopathy (b) malignancies that were detected, staged, or evaluated; (c) pericardial effusions; (d) unsuspected pneumonia; or (e) aneurysm. In 36 cases (33%), pleural effusions could only be visualized by CT. In 8 out of 109 (7.3%) and 7 out of 109 (6.4%) masses and mediastinal Lymphadenopathy, respectively, were detected by CT-scans only. In 10 out of 109 (10.2%) normal portable chest radiographs CT scan revealed infiltrates and effusions and these CT findings resulted in changes in clinical management of these patients. There were no significant complications during transport or (CT) examination.

CONCLUSION: Thoracic (CT) may provide significant information in addition to plain chest radiographs, particularly in cases of unsuspected pneumonia, malignancies and effusions causing change in the management of ICU-patients. (CT) of the chest offers improved resolution and sensitivity for evaluating chest pathologic conditions compared with other imaging techniques and has a strong impact on patient management in critical-care medicine.

CLINICAL IMPLICATIONS: This study highlighted the importance of thoracic(CT) in the management of critically ill patients compared with the portable chest radiographs.

DISCLOSURE: Arshad Ali, None.

YIELD OF SPIRAL CT: A FREQUENT ALTERNATIVE DIAGNOSES IN PATIENTS UNDERGOING CT-PA FOR SUSPECTED PULMONARY EMBOLISM

Seema G. Naik MD* Alexandra Ionescu MD Stephen Yang MD Sotir Polena MD Rick Conetta MD Brookdale University Medical Center, Fresh Meadows, NY

PURPOSE: Pulmonary embolism (PE) remains one of the most underrecognized medical diagnoses. Clinical presentation, D-dimer and imaging studies combined, remain the cornerstone of the PE diagnosis. Currently used imaging studies (CT-PA and VP scan) are similar in sensitivity and specificity of. The availability and the relative rapidity of the CTPA make it the first diagnostic tool in the inpatient settings. There is a large number of disorders incidentally discovered during the CTPA especially in elderly population with multiple morbidities. The aim of our study is to quantify the frequency of such findings in this group of population.

METHODS: We retrospectively analyzed 47 charts of elderly patients (more than 65 years of age) who underwent CTPA for diagnosis of pulmonary embolism. All the patients had a moderate to high pretest probability for PE. CT findings, clinical presentation and the past medical history were analyzed in detail.

RESULTS: Out of 47 elderly patients (mean age 74,5) included in the study, 10 of them were found to have PE, 3 bilateral central and 7 cases with segmental/subsegmental filling defects. Interestingly, alternative findings were seen in more than 50% of CTPA results: bilateral atelectasis (4), consolidations (8), unilateral/bilateral effusions (11), pericardial effusion (1), SVC thrombus (1), IVC thrombus (1), brachiocephalic vein thrombus (1), aortic aneurysm with mural thrombus (1), aspergilloma (1), loculatedpneumothorax (1), thymic/mediastinal mass (3), large substernalgoitre (1), lung mass (2). All the alternative findings were not part of the clinical presentation or the past medical history of the patients.

CONCLUSION: CTPA allows assessment of not only pulmonary thromboembolism, but also the evaluation of the bronchi, lung parenchyma, mediastinum and heart. Unknown disorders can be incidentally identified during the CTPA especially in the elderly population with multiple comorbidities.

CLINICAL IMPLICATIONS: CTPA is increasingly used for the detection of pulmonary embolism. The availability and the relative rapidity of the CTPA and the possibility to identify other pathologies makes it the preferred procedure compared to other modalities, especially in elderly population.

DISCLOSURE: Seema Naik, None.

Imaging in Critical Care, continued

BEDSIDE CANNULATION OF THE AXILLARY VEIN UNDER ULTRASOUND GUIDANCE

Vipin Malik MD Harish Bhaskar MD* William Pascal MD Kabu Chawla MD Yizhak Kupfer MD Sidney Tessler MD Maimonides Medical Center, Brooklyn, NY

PURPOSE: The axillary vein offers theoretical advantages for use in line cannulation. It is less likely to cause a pneumothorax and is more readily compressible than subclavian approaches. It has not been frequently used due to the lack of easily obtainable percutaneous landmarks to direct cannulation. We report the use of ultrasonographic guidance to direct axillary venous cannulation of triple lumen central venous catheters.

METHODS: Bedside ultrasonographic guidance to locate and direct axillary venous cannulation was performed. The operator was highly experienced in the placement of central venous catheters. The size and depth of the vein was studied, number of attempts and complications were evaluated. All patients were hemodynamically stable and required central venous lines due to poor peripheral venous access.

RESULTS: Axillary vein cannulation was attempted in 12 patients and was successful in 8 (66%). In 2 patients the needle successfully entered the vein, but the guide wire could not be passed, while in 2 patients venous entry was not successful despite multiple attempts. In 3 of 4 patients that axillary cannulation failed, subclavian cannulation on the ipsiletaral side was successful. The average depth from the skin of the axillary vein was 2.73 cm and did not correlate with ability to cannulate. The average caliber of the axillary vein was 0.99 cm and did not correlate with successful cannulation. The procedure time decreased from 90 minutes to 25 minutes over the first 10 patients. There were 2 arterial punctures and no pneumothoraces for a total complication rate of 16.7%.

CONCLUSION: Axillary vein cannulation of central lines under sonographic guidance requires a significant operator learning curve. It is more time consuming than the subclavian approach and is associated with a high rate of arterial punctures and failure to achieve cannulation of the vein.

CLINICAL IMPLICATIONS: Axillary vein cannulation is technically difficult to perform, difficult to learn, and is associated with a relatively high rate of complications.

DISCLOSURE: Harish Bhaskar, None.

Interventional Bronchoscopy in Lung Cancer
10:30 AM - 12:00 PM

RELIEF OF MALIGNANT AIRWAY OBSTRUCTION: A PROSPECTIVE AND RANDOMISED COMPARISON OF FIVE DIFFERENT ENDOSCOPIC TECHNIQUES

Felix J. Herth MD* Ralf Eberhardt MD Heinrich D. Becker MD Armin Ernst MD Department of Pneumology and Critical Care Medicine, Heidelberg, Germany

PURPOSE: Central airway obstruction (CAO) is a common indication for therapeutic bronchoscopy. Different techniques are available; but they have never been compared directly in their efficacy and outcome.

METHODS: Consecutive patients with malignant CAO due to endoluminal tumor growth were enrolled. If a patent airway distal to the obstruction could be verified, the patient was randomised to the following techniques: mechanical debridement (M), laser resection (L), Argon-Plasma Coagulation(APC), combined mechanical and laser resection (L-M) or mechanical and APC recanalization (APC-M). The results were controlled bronchoscopically after 6 weeks.

RESULTS: 323 patients (109 females, 214 males, mean age 62,3 y) were examined until 250 patients (87 females, 163 males, mean age 65,3 y) could be included; 50 in every arm. The success rates without changing the technique were: M 76%, L 56%, APC 54 %, L-M 76 %, APC-M 96%. The mean procedure times were M 7,6 min., L 23,2 min., APC 13,5 min., L-M 13,5 min., APC-M 10,5 min. APC-M provided superior results (P 0,003); M was the fastest (p=0,02). The number of patients, which received a stent was not different (M 76%, L 84%, APC 74%, L-M 62 %, APC-M 52%). The 6 week survival rates were: M 96%, L 94%, APC 98 %, L-M 92 %, APC-M 96% p=0,2), none of the deaths were procedure related. Airway patency after 6 weeks in the patients without stenting was: M 0 %, L 60%, APC 72 %, L-M 72 %, APC-M 70%.

CONCLUSION: The combination of APC and mechanical debridement seems the superior technique for airway recanalization in patients with malignant CAO.

CLINICAL IMPLICATIONS: APC and mechanical debridement seems the best technique in recanalisation of Malignant Airway Obstruction.

DISCLOSURE: Felix Herth, None.

FURTHER EXPERIENCE WITH MICRODEBRIDER BRONCHOSCOPY: A NEW TOOL FOR TREATING CENTRAL AIRWAY OBSTRUCTION

William Lunn MD* Matthias Loebe MD Rabih Bechara MD Simon Ashiku MD Malcom DeCamp MD David Feller-Kopman MD Armin Ernst MD Baylor College of Medicine, Houston, TX

PURPOSE: After initial encouraging results, we report our further experience with the microdebrider, a new airway tool, in treating both benign and malignant obstruction of the central airways.

METHODS: From April 2002 to May 2005, 44 patients undergoing treatment of central airway obstruction were managed with the microdebrider. All procedures were done under general anesthesia with either a rigid bronchoscope (40 patients) or a suspension laryngoscope (4 patients). The microdebrider was employed in an oscillating mode with rotation speeds of 1000-3000rpm to resect obstructing tissue. Patients were followed for a range of 1-36 months.

RESULTS: Twenty-four patients had tracheal granulation tissue from prior intubation or tracheostomy, 4 had idiopathic subglottic stenosis, 4 had stent related granulation tissue, 1 had granulation tissue after surgical airway repair, 1 had papillomas, and 10 had malignant disease (8-non small cell, 1-small cell, 1-thyroid carcinoma). Obstructing lesions were rapidly removed in all patients with dissections lasting between 2 and 20 minutes. There were no episodes of significant airway bleeding and no other procedure related complications.

CONCLUSION: Microdebrider bronchoscopy is a new technique that is useful for both benign and malignant airway obstruction. The tool allows for precise, rapid, and safe removal of obstructing lesions, even those that are friable and considered at risk for bleeding.

CLINICAL IMPLICATIONS: The microdebrider provides physicians with an alternative to thermal modalities. Airway fires, tracheoesophageal fistulas, and other complications of thermal modalities may thus be avoided.

DISCLOSURE: William Lunn, Grant monies (from industry related sources) I have received grants from Karl Storz Endoscopy and Richard Wolf Endoscopy to support CME courses that I am directing at Baylor College of Medicine.

INTERVENTIONAL BRONCHOSCOPY PERMITS PARENCHYMA SPARING SURGERY IN PATIENTS WITH LUNG CANCER

Prashant N. Chhajed MD* Ralf Eberhardt MD Hendrik Dieneman MD Heinrich D. Becker MD Andrea Azzola MD Martin H. Brutsche MD Michael Tamm MD Felix J. Herth MD Pulmonary Medicine, University Hospital Basel, Basel, Switzerland

PURPOSE: To assess the utility of therapeutic bronchoscopy in the combined endoscopic and surgical management of malignant airway lesions to allow curative parenchyma sparing surgery.

Interventional Bronchoscopy in Lung Cancer, continued

METHODS: All 74 consecutive patients (Switzerland and Germany) with non-small cell lung carcinoma undergoing an interventional bronchoscopic procedure (laser, argon plasma coagulation, electrocautery, stent insertion, mechanical debridement) followed by surgery with a curative intent were included. Indications for interventional bronchoscopy were endobronchial staging of lung cancer and symptomatic relief of central airway obstruction due to dyspnea and/or post obstructive pneumonia.

RESULTS: A single interventional bronchoscopic method was used in 27 (36%) patients and a combination of methods in 47 (64%) patients. There was a mean increase of 19% in the FVC after interventional bronchoscopy. Pneumonectomy was performed in 28 (38%) patients, sleeve upper lobectomy in 22 (30%) patients, upper bilobectomy in 16 (22%) patients, pneumonectomy with sleeve resection in two (3%) patients and lower bilobectomy in two (3%) patients. Following surgeries were performed in one patient each: sleeve middle lobectomy, sleeve lower lobectomy, carina resection and complex reconstruction and exploratory thoracotomy. Overall, parenchymal sparing surgery was performed in 45 (61%) patients. Furthermore, parenchyma sparing surgery was performed in 30 patients (41%) with lesions in the main bronchi. There was no mortality in the first 30 days following surgery.

CONCLUSION: Parenchyma sparing surgery could be performed in 61% patients with non-small cell carcinoma after therapeutic interventional bronchoscopy for malignant endobronchial obstruction.

CLINICAL IMPLICATIONS: The role of interventional bronchoscopy is well established and commonly associated with the palliative treatment of malignant central airway obstruction. The findings of our study show that interventional bronchoscopy has an important role in patients with malignant airway obstruction with potentially resectable lung cancer. Furthermore, therapeutic interventional bronchoscopy permits parenchyma sparing surgery in patients with lung cancer undergoing surgery with a curative intent.

DISCLOSURE: Prashant Chhajed, None.

IMPACT OF INTERVENTIONAL BRONCHOSCOPY ON QUALITY OF LIFE OF PATIENTS WITH ADVANCED SYMPTOMATIC MALIGNANT AIRWAY OBSTRUCTION: A PROSPECTIVE PILOT STUDY

Kayvan Amjadi MD* Yves Cruysberghs MD Roel Lemmens MD Marc Noppen MD Queen's University, Kingston, ON, Canada

PURPOSE: Using the validated European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 version 3.0 (EORTC QLQ-C30 (v3)), we evaluated the impact of interventional bronchoscopic procedures aimed at re-establishing airway patency, on quality of life (QoL) of individuals who were considered inoperable and unsuitable for chemotherapy and/or radiation therapy.

METHODS: Over a six months period, we prospectively enrolled all patients who fulfilled the above criteria and performed laser ablation, cryotherapy, and/or airway stenting in order to re-establish airway patency. Quality of life was evaluated by EORTC QLQ-C30 (v3)) at baseline (T1; 1 day prior to procedure), 7 days after (T2), and 1 month after procedure (T3).

RESULTS: Final analysis could be performed on 88% (21/24) of the participants (Male/Female 15/6, mean age 61.9/66.7 years, range 37 – 78/53 – 75). Although dyspnea scores had improved in 87% of participants (T3 vs. T1, P = 0.02), only 13/21 (62%) reported an improvement or stabilization of their overall global health status (T3 vs. T1, P=0.002). These individuals also noted improvements in their symptoms of fatigue, appetite loss, and insomnia which did not achieve statistical significance. During the study period 8/21 (38%, T3 vs. T1) reported a decline in global health status (P = 0.02) and emotional functioning (P = 0.05). Also, patients reported increased difficulty with pain, nausea and vomiting, fatigue, appetite loss, and finances, with changes in pain scores achieving statistical significance (P = 0.03). The reduction of dyspnea scores in this group was not statistically significant (P = 0.23).

CONCLUSION: Endoscopic procedures can effectively palliate symptoms associated with malignant central airway obstruction (CAO), but this may not translate into improvements of individual's overall QoL, given the progressive nature of malignant disease and the multi-factorial constitution of QoL.

CLINICAL IMPLICATIONS: Administration of QoL questionnaires is feasible, may help identify domains contributing to patient's decline, and thereby improve patient care. The results of this study emphasize the need for a multi-disciplinary approach for the care of patients with malignant CAO.

DISCLOSURE: Kayvan Amjadi, None.

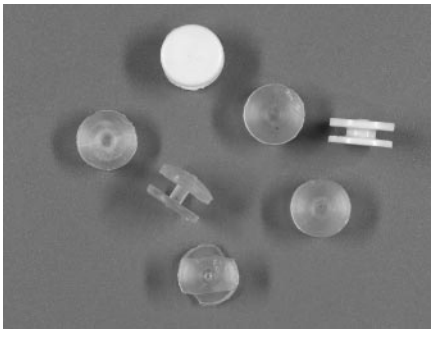
NEW CUFFLINK-SHAPED SILICON PROSTHESIS FOR THE PALLIATION OF MALIGNANT TRACHEOBRONCHIAL-ESOPHAGEAL FISTULA (MTEF)

Pablo Diaz-Jimenez MD* Bellvitge University Hospital, Bellvitge, Spain

PURPOSE: Malignant tracheoesophageal fistula (MTEF) is a serious complication of cancer arising in the esophagus, lung or tracheobronquial tree. Approximately 77% of MTEF are related to esophageal cancer while around 16% are originated from a primary lung neoplasm. Treatment is usually palliative and involves restoration of the swallowing mechanism and prevention of aspiration. Prosthesis placement is considered to be appropriate for most patients with MTEF, a variety of them are available.

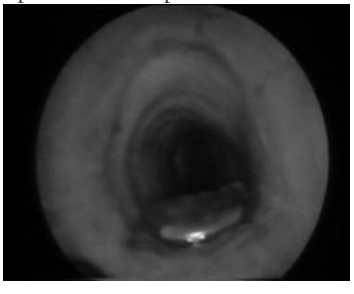
METHODS: We have designed a new cufflink-shaped soft silicon prosthesis, directed to occlude the aero digestive connection. (Picture 1) The DJ® silicon prosthesis, (Barcelona, Spain) can be safely placed under direct vision using a rigid bronchoscope and a biopsy forceps. The new stent is available in different sizes, in order to be able to select the appropriate one according to the patient we are treating. Some patients may require costume-made prosthesis.

RESULTS: Under general anesthesia and after tracheal intubation with the rigid bronchoscope, the place and size of the lesion is assessed and the stent selected. The device is then folded with a biopsy forceps, flattening both wings. Under direct vision, the flattened stent is introduced through the fistula orifice with a soft rotation and pushing motion, until one of the wings is thought to be into the esophageal lumen. Then the stent is allowed to deploy, obtaining complete and immediate occlusion of the fistula. (Picture 2).



CONCLUSION: We are presenting this preliminary report because we believe the new prosthesis design offers advantages over the stents generally used for palliation of MTEF. It is a soft, easy to place silicon prosthesis that is sized exactly to the fistula diameter, offering a very small contact area, which can avoid potential complications such as increase fistula size, wall erosion, perforation and bleeding.

CLINICAL IMPLICATIONS: More experience is needed in order to recommend its generalized use, but the DJ® prosthesis appears as a good supportive care option in selected patients with MTEF.



DISCLOSURE: Pablo Diaz-Jimenez, Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Dr

Interventional Bronchoscopy in Lung Cancer, continued

Diaz-Jimenez has designed the DJ (R) Prosthesis, which is not in the market at the moment

EBUS GUIDED BIOPSY FOR THE DIAGNOSIS OF MEDIASTINAL LYMPH NODES IN A RADIOLOGICALLY NORMAL MEDIASTINUM

Felix J. Herth MD* Ralf Eberhardt MD Peter Vilmann MD Armin Ernst MD Mark Krasnik MD Department of Pneumology and Critical Care Medicine, Heidelberg, Germany

PURPOSE: EBUS-TBNA is highly accurate in staging patients with non-smaIl ceIl lung cancer (NSCLC) who have enlarged mediastinal lymph nodes on CT scan. In this study we report the accuracy and yield of EBUS-TBNA in staging patients without enlarged mediastinal lymph nodes by CT.

METHODS: Patients with NSCLC and CT scan showing no enlarged mediastinal lymph nodes (> 1 cm for aIl nodes) in the mediastinum underwent bronchoscopy with EBUS. TBNA was performed on identifiable lymph nodes in the locations 2r, 2l, 3, 4r, 4l, 7, 10r, 10l, 11r and 11l. All patients underwent subsequent surgical staging and the results were compared to operative findings.

RESULTS: 100 patients (68 male, 32 female, mean age 58.9 y.) were evaluated, 119 lymphnodes punctured. EBUS-TBNA detected malignant mediastinal lymph nodes in 22 of 100 patients, all surgical confirmed. The mean diameter of the punctured lymph nodes was 8.1 mm (SD±0,7). The sensitivity of EBUS-TBNA for mediastinal disease was 92.3 %, the specificity was 100 % and the negative predictive value 96.3 %.No complications were seen.

CONCLUSION: EBUS TBNA can detect advanced mediastinal disease and avoid unnecessary surgical exploration in 1 of 5 patients who have no evidence of mediastinal disease on CT scan. This data suggests that all potentiIly operable patients with clinically nonmetastatic NSCLC may benefit from presurgical EBUS-TBNA staging.

CLINICAL IMPLICATIONS: This data suggests that all potentiIly operable patients with clinically nonmetastatic NSCLC may benefit from presurgical EBUS-TBNA staging.

DISCLOSURE: Felix Herth, None.

Lung Transplantation
10:30 AM - 12:00 PM

THE INDUCTION OF ROBUST TOLERANCE IN AN MHC-MISMATCHED PORCINE PULMONARY ALLOGRAFT MODEL PREVENTS OBLITERATIVE BRONCHIOLITIS

Hisashi Sahara MD Tsuyoshi Shoji MD Ashok Muniappan MD Dax A. Guenther MD John C. Wain MD Stuart L. Houser MD Akshat Pujara BA Marjory A. Bravard BA David H. Sachs MD Joren C. Madsen MD James S. Allan MD* Massachusetts General Hospital, Boston, MA

PURPOSE: Obliterative bronchiolitis (OB) remains the principal cause of graft loss and death following lung transplantation. Here, we utilize a tolerogenic immunosuppressive regimen to determine whether the induction of a robust state of tolerance leads to the abrogation of OB in a partially-inbred miniature swine model.

METHODS: Group 1 (control) consisted of recipients of class I-disparate lung allografts treated with a 12-day course of cyclosporine (~10-13 mg/kg/d) (n = 6). Group 2 was comprised of similarly transplanted recipients treated with a 12-day course of high-dose tacrolimus (0.15 mg/kg/d) (n = 3). Group 3 consisted of recipients immunized with peptides derived from the donors' class I MHC 21 days prior to transplantation, and then treated similarly with tacrolimus. All recipients were monitored for the development of OB by serial open lung biopsy, and long-term acceptors (>350 days) were challenged with skin grafting prior to sacrifice.

RESULTS: In Group 1, 4/6 developed OB within 8 months. In Group 2, all swine maintained their grafts for > 497, > 451, and > 432 days. In Group 3, grafts survived for >417, >402, >374 days. Some lung grafts in Groups 2 and 3 had transient mononuclear cellular infiltrates; but none developed OB on multiple biopsies. All recipients exhibited donor-specific hyporesponsiveness in cell-mediated lymphocytotoxity.

CONCLUSION: This study demonstrates that robust tolerance can be achieved using a clinically practical induction regimen. Furthermore, this state of tolerance can be induced in recipients previously sensitized to donor antigen, and is not broken by repeat exposure to donor antigen following transplantation. Most importantly, these data demonstrate that transplantation tolerance abrogates the development of OB.

CLINICAL IMPLICATIONS: We are currently extending these findings to fully mismatched allografts, and anticipate that the induction of tolerance will be an important therapeutic strategy in the prevention of OB without the requirement of chronic immunosuppression.

DISCLOSURE: James Allan, None.

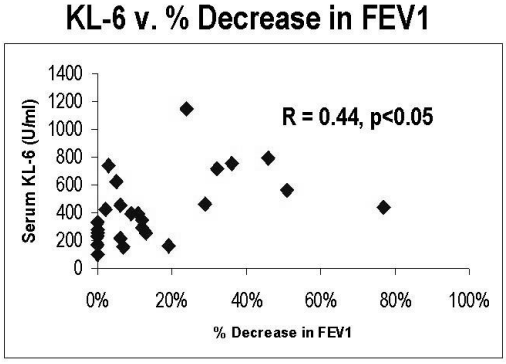
SERUM KL-6 AS A MARKER FOR BRONCHIOLITIS OBLITERANS AFTER LUNG TRANSPLANTATION

Joseph N. Walter MD* Minh Doan MD Haibin Zhang MD George B. Mallory MD Remzi Bag MD Leland L. Fan MD Okan Elidemir MD Baylor College of Medicine, Houston, TX

PURPOSE: Bronchiolitis obliterans (BO) is a major problem that decreases the long-term survival of lung transplant recipients. The early diagnosis of BO is very difficult and requires invasive diagnostic tests such as a lung biopsy. The term Bronchiolitis Obliterans Syndrome (BOS) was adopted due to the poor sensitivity of biopsy for diagnosing early BO. Patients are diagnosed with BOS when they have a sustained drop in FEV1 of at least 20% from their post-transplant baseline. By the time the diagnosis is made, most patients have significant and irreversible loss of lung function. There is a need for a simple and accurate diagnostic test for BO in lung transplant recipients. KL-6 is a protein expressed on the surface of pulmonary epithelial cells and has been reported to be elevated in the sera of patients with interstitial lung diseases. We hypothesized that serum levels of KL-6 would be elevated in patients who develop BOS after lung transplantation.

METHODS: We collected single serum samples from 26 lung transplant recipients and 20 healthy controls. The BOS status of the lung transplant recipients was determined based upon routinely collected lung function testing. Of the 26 lung transplant recipients, 8 met the criteria for BOS and 18 did not. The serum KL-6 levels were determined using a sandwich ELISA technique.

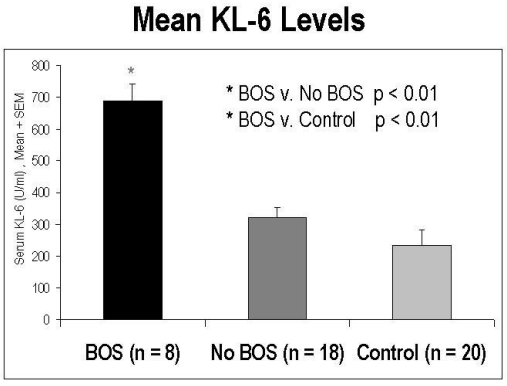
RESULTS: Mean serum KL-6 concentration ± standard deviation in lung transplant recipients with BOS, without BOS and controls were 688.7 ± 225.8, 321.3 ± 163.9 and 235.2 ± 141.5 U/ml, respectively ($p<0.01$, for patients with BOS vs. patients without BOS and patients with BOS vs. controls). There was a significant correlation between the decrease in FEV1 from the post-transplant baseline and the serum KL-6 levels ($R=0.44$, $p<0.05$).



CONCLUSION: Serum KL-6 levels were significantly elevated in lung transplant recipients with BOS when compared with lung transplant recipients without BOS.

CLINICAL IMPLICATIONS: Our results indicate that serum KL-6 measurement has the potential to serve as a non-invasive diagnostic test for the detection of BO in lung transplant recipients.

Lung Transplantation, continued



DISCLOSURE: Joseph Walter, None.

T-CELL PROFILES IN CONSTRICTIVE BRONCHIOLITIS OBLITERANS MODELS: A SEARCH FOR A DIAGNOSTIC MARKER

Jennifer A. Svetlecic MD* YaYan Chen MD Agostino Molteni MD Betty Herndon PhD University of Missouri-Kansas City, Kansas City, MO

PURPOSE: Constrictive bronchiolitis obliterans (CBO) restricts long-term survival following lung transplantation. CBO may also develop following exposure to inhaled or systemic toxicants. A marker to detect early development of CBO via BAL or lung biopsy has not been elucidated. Our laboratory has created both transplant and toxicant CBO models in the rat with pathology replicating human disease. Early T-lymphocyte activation (Eta-1), a cytokine secreted by activated T-lymphocytes that recruits and activates pulmonary macrophages, was highly elevated early in our toxicant model but at nonsignificant levels in the mature transplant CBO model. We hypothesized that a T-cell subpopulation (gamma delta) would precede Eta-1 expression, thus would be an early marker of CBO.

METHODS: Sequential sections of 4-6 wk samples of lung tissue from both models (n=12) were immunostained for Eta-1, total T cells (CD3), and gamma-delta T-cells. Lung areas of staining were quantified by morphometric means, intensity of staining, and cell counts in 20 high-power fields. Statistical analysis of the data groups was performed.

RESULTS: Eta-1 was elevated and widely present in the transplant model although the 4-week toxicant model showed limited staining. Transplant vs. toxicant CBO Eta-1 staining was significantly different, p=0.004. Gamma-delta T-cells were sparse in the largest perivascular lymph nodes, appearing throughout the lungs of both models. Their presence did not correlate with lung tissue osteopontin in sequential lung sections, however. Total T cell (CD3) counts showed an equal amount of perivascular inflammation in both models.

CONCLUSION: Differences in cytokine and T-cell staining suggest different pathophysiologic pathways in the development of toxicant vs. transplant-induced CBO. These data propose that T-cell subpopulation differences do not account for the significant difference in Eta-1 between the two models.

CLINICAL IMPLICATIONS: A marker of bronchial injury identifying progression could be of vast importance in the diagnosis of CBO. Further studies continue to uncover early immunologic markers of CBO.

DISCLOSURE: Jennifer Svetlecic, None.

PULMONARY FIBROSIS: IS LUNG TRANSPLANTATION A VALID AND VIABLE ALTERNATIVE TO MEDICAL THERAPY?

Carlo Banfi MD* Andrea M. D'Armini MD Mauro Rinaldi MD Carlo Pellegrini MD Mario Viganò MD Division of Cardiac Surgery IRCCS Policlinico S Matteo, Pavia, Italy

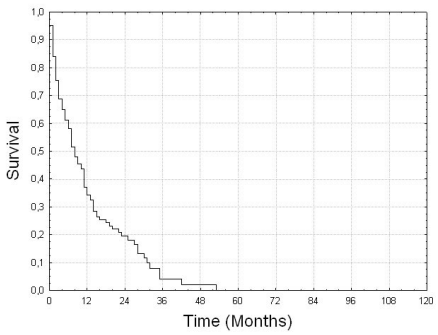
PURPOSE: Interstitial lung disease is a heterogeneous group of subacute or chronic illnesses, which may lead to respiratory failure and death in a large number of patients. Idiopathic pulmonary fibrosis is the most common form of such a diseases.

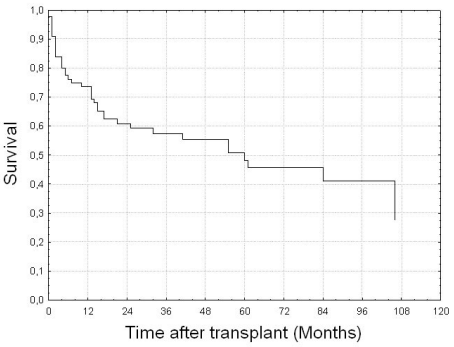
METHODS: From January 1991 to April 2005, 243 patients affected by pulmonary fibrosis were referred to lung transplantation waiting list: 110 (45%) died, 90 (37%) underwent lung transplantation, 22 (9%) are still enrolled and 21 (9%) were suspended from the list. Actuarial survival of patients on waiting list (medical therapy) is summarized on table 1.

RESULTS: 90 patients affected by pulmonary fibrosis underwent 94 transplantations, with 4 patients undergoing retransplantation. There were 80 (89%) single lung transplants with 45 twinning procedures, 9 (10%) double lung transplants and 1 (1%) heart-lung transplant. Cardiopulmonary by-pass was used in 11% of patients (mean time 163±84 min), total ischemic time was 242±86 minutes. Median of mechanical ventilation was 2 days; median ICU and hospital stay was 5 and 17 days, respectively. Postoperative mean FEV1 increased from a preoperative level of 46% of the predicted value to 69% at 1 month and 74% at 12 months. Actuarial survival after lung transplant is summarized on table 2. The incidence of postoperative complications was 1,02 patient. Airway complications occurred in 20 patients (23%). Comparison of survival rates between transplanted patients and patients on waiting list are highly significant (p<0,000001).

CONCLUSION: Lung transplantation is an excellent but, by now, the only one therapeutic option for patients affected by end-stage pulmonary fibrosis. Currently medical treatment of pulmonary fibrosis with single or combined immunosuppressive therapy has not been found to improve survival of these patients. Lung transplantation is also effective in improving respiratory function and returning many patients to active life.

CLINICAL IMPLICATIONS: The high mortality of patients affected by pulmonary fibrosis on waiting list and the lack of donors for lung transplant impose the search for new therapeutic modalities in pulmonary fibrosis.





DISCLOSURE: Carlo Banfi, None.

Lung Transplantation, continued

SHORT TERM OUTCOME AFTER LUNG TRANSPLANTATION IN ELDERLY PATIENTS

Francisco G. Alvarez MD* Cesar A. Keller MD Javier Aduen MD Octavio E. Pajaro MD Jefreey A. Shalev BS Lawrence R. McBride MD Mayo Clinic, Jacksonville, FL

PURPOSE: To analyze the short term outcome after lung transplantation performed in patients above the recommended age of 65 for single lung transplant (SLTx); 60 for double lung transplant (DLTx); and 55 for heart lung transplant (HLTx).

METHODS: Retrospective analysis of 75 patients who underwent 77 transplantations distributed as follows: SLTx (n=46), DLTx (n=26) or HLTx (n=5). Of these, 21 patients were above the recommended age for the procedure (Average age = 65.3 ± 2.6); and 54 were within the recommended age for the specific type of transplant (Average age = 49.9 ± 11). All patients in the elderly group underwent single or double LTx except one patient who underwent a HLTx at age 61.

RESULTS: There were no significant differences between the groups in terms of hospitalization days; time spent in the intensive care unit or on mechanical ventilation; incidence of acute reperfusion injury; incidence of episodes of acute rejection and 3 and 6 months survival. Infection by cytomegalovirus was significantly more frequent in the elderly group.

CONCLUSION: Short term outcome of Lung, and possibly heart lung, transplantation in well selected patients above the recommended age is similar to the outcome in patients under the recommended age limits.

CLINICAL IMPLICATIONS: Established age limits for lung or heart-lung transplantation should be revised to include patients without significant co-morbidities that exceed the recommended age. Follow-up for longer period of time is needed to determine long term outcome in this group of patients.

DISCLOSURE: Francisco Alvarez, None.

OUTCOMES OF LUNG TRANSPLANT RECIPIENTS (LTR) PREVIOUSLY INFECTED WITH HEPATITIS C VIRUS

Hina Sahi MD* Marie Budev DO Holli Blazey Other Atul Mehta MBBS Cleveland Clinic Foundation, Cleveland, OH

PURPOSE: Outcomes of Lung Transplant in Hepatitis C virus (HCV) positive Recipients is not known. We describe our experience with 5 such patients.

METHODS: Charts of LTR known to be HCV positive prior to transplantation were reviewed for demographics, HCV etiology, HCV RNA viral load pre and post transplantation, liver biopsy results, transaminase levels during various points post transplantation, the development of acute hepatitis and survival.

RESULTS: 454 lung transplants were performed during a 14 year period, only five patients (1%) [age (yrs± SD): 48 ± 9.7, 3 females], were anti-HCV seropositive. Etiology of HCV infection included IVDA (n=1), unknown causes (n=4), and two patients had concomitant liver disease due to alpha-1-antitrypsin deficiency and cystic fibrosis. All patients were diagnosed with HCV prior to transplantation and confirmed with HCV qualitative RNA testing. All recipients had disease severity documented by liver biopsy (minimal peri portal fibrosis n=3, no cirrhosis n=5). The median duration from HCV diagnosis to transplantation was 2 years [inter quartile range, 1 to 8.2 yrs). Pre transplantation median quantitative HCV RNA levels were 50,300 IU/ml [inter quartile range, 16,897 to 200,780,000 IU/ml]. Post transplantation median quantitative HCV RNA level were noted to markedly increase [level (IU/ml): 2,470,000 IU/ml (inter quartile range, 646,825 to 2,897,500 IU/ml)]. There was no statistically significant increase in transaminase levels pre and post LTX despite increase in HCV RNA levels. The longest surviving patient in this cohort is 5 yrs post transplantation, the shortest survival being 8 months. The patient died of respiratory complications with no evidence of hepatic failure at the time of death [mean survival (months ± SD): 32.6±23.9].

CONCLUSION: Although viral loads tended to significantly increase post transplantation, there was no significant difference in the episodes of acute hepatitis, hepatic failure or cirrhosis during the duration of follow up. Post transplant monitoring of quantitative RNA HCV levels was not of any prognostic value.

CLINICAL IMPLICATIONS: Further studies are needed to provide guidelines for monitoring of this population post transplantation.

DISCLOSURE: Hina Sahi, None.

Occupational and Environmental Lung Diseases
10:30 AM - 12:00 PM

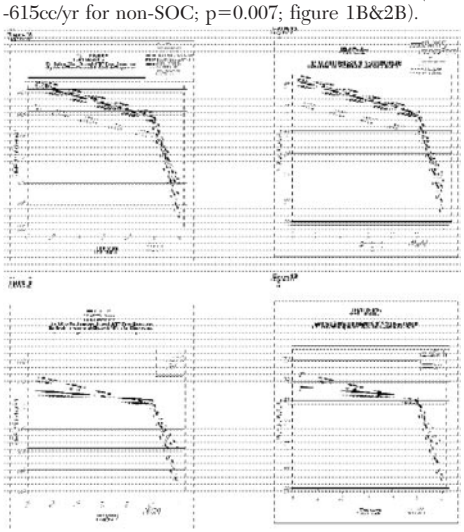
ACCELERATED PULMONARY FUNCTION DECLINE AFTER WORLD TRADE CENTER PARTICULATE EXPOSURE IN THE NEW YORK CITY FIRE DEPARTMENT WORKFORCE

Gisela Banauch MD* Michael Weiden MD Charles Hall PhD Hillel W. Cohen Thomas K. Aldrich MD Nicole Arcentales BS Kerry J. Kelly MD David J. Prezant MD Albert Einstein College of Medicine, New York, NY

PURPOSE: On September 11th 2001, the World Trade Center (WTC) collapse created an enormous urban disaster site with high levels of "WTC-Dust" (respirable particulates and combustion by-products). Rescue workers and residents have since developed respiratory symptoms and pulmonary function abnormalities. We investigated whether WTC-Dust exposure affected spirometric decline rates (forced expiratory volume in one second [FEV1], forced vital capacity [FVC]) in the New York City Fire Department (FDNY) workforce.

METHODS: Longitudinal cohort study of pulmonary function before and after 09/11/2001 in 12,079 FDNY rescue workers employed on/before 09/11/2001. Declines were computed separately for pre- and post-9/11 periods and analyzed for differences according to WTC-Dust exposure intensity. Exposure intensity was assessed with (1) initial arrival time at the WTC site (early arrival before/during WTC collapse, intermediate after collapse during 09/11/2001-09/12/2001, late after 09/12/2001; non-exposed never present) and (2) work assignment (Special Operations Command [SOC] vs. non-SOC).

RESULTS: FEV1 decline after 09/11/2001 correlated linearly (p for trend<0.001) with arrival time-based WTC-Dust exposure intensity and was fastest for those with early, high exposure, reaching more than twice the magnitude for the non-exposed group (-845cc/yr for early vs. -405cc/yr for non-exposed, p<0.001; figure 1A&2A). The intermediate exposure group had a decline between that of early and late groups. The late group had a decline 50% above the non-exposed. In addition, SOC workers experienced 50% faster decline than non-SOC workers (-926cc/yr for SOC vs. -615cc/yr for non-SOC; p=0.007; figure 1B&2B).



CONCLUSION: WTC-Dust exposure produced accelerated declines in spirometric measures of lung function in 12,079 WTC exposed FDNY rescue workers during the first year following 09/11/2001.

CLINICAL IMPLICATIONS: Findings are of potential relevance for less exposed populations. The long-term time course of spirometric decline is not certain. For these reasons, WTC-exposed occupational and community cohorts merit continued close medical monitoring.

DISCLOSURE: Gisela Banauch, None.

Occupational and Environmental Lung Diseases, continued

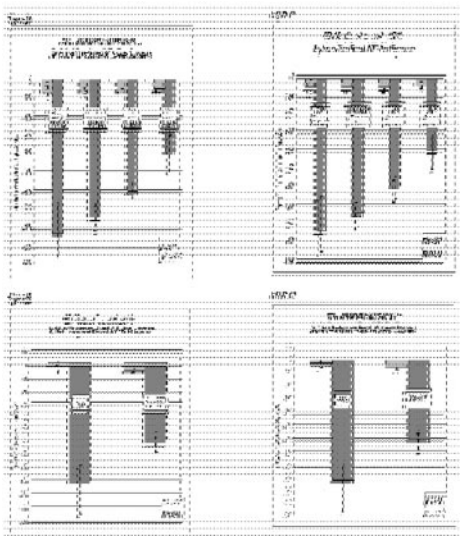
SILICOSIS: EXPLAINING THE INCONSISTENCY BETWEEN DECLINING PUBLIC HEALTH STATISTICS AND THE EPIDEMIC IN LITIGATION

Robert E. Glenn MPH* Paul W. Kalish Fred Krutz, Partner Crowell & Moring, Washington, DC

PURPOSE: During the early part of the last century, silicosis and silicotuberculosis were major causes of mortality among workers exposed to silica dusts. By the end of the century, the National Institute for Occupational Safety and Health (NIOSH) had reported an 84% decrease in silicosis-related mortality during the period 1968 to 1999. However, even though the data demonstrate a decline in mortality over the last century the number of silicosis lawsuits filed in the last few years has skyrocketed. For instance, one large insurer suddenly experienced more than 25, 000 silicosis claims in twenty-eight states and over 17,000 silicosis claims were filed in Mississippi alone.

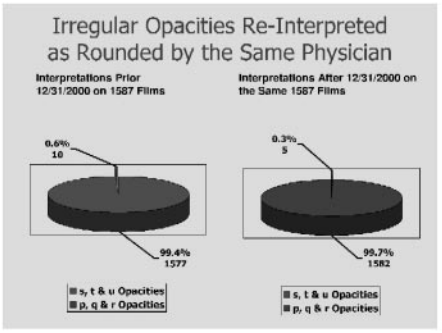
METHODS: The study analyzed 9,875 cases of silicosis from eight states that were removed to U. S. District Court. In addition, medical data from the Manville Trust for a large numbers of thse same claimants were analyzed. Radiographic patterns from multiple interpretations for shape of small opacities were examined.

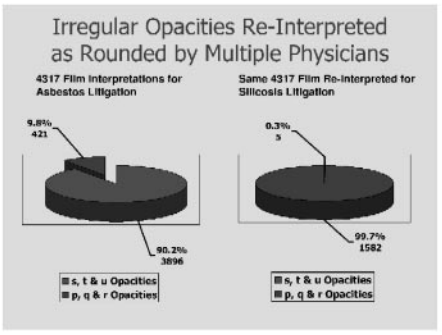
RESULTS: Of 8,629 plaintiffs matched with claimants in the Manville Trust, it was determined that 5,174 (60%) had already filed an asbestos claim. Of 4,317 chest films originally interpreted in asbestos litigation, 3,896 (90.2%) were classified with small opacities of primary shape s, t, u. When the same 4,317 films were interpreted in silicosis litigation, the primary shape of 4,304 (99.7%) were now classified as p, q, r. One physician alone interpreted 99.4% of 1,587 chest films in asbestos litigation with a primary shape of s, t, u, and afterwards re-interpreted the same 1,587 in silicosis litigation as 99.7% having small opacities primarily p, q, r shape. Other anomalies with the diagnoses in the 9,875 claimants will be presented.



CONCLUSION: Pneumoconioses interpretations provided for litigation purposes give the picture of a reader bias for a pattern consistent with asbestosis or silicosis depending on the legal outcome desired.

CLINICAL IMPLICATIONS: Opinions will be presented as to what the medical and legal systems can do to avoid future litigation epidemics for which there is no underlying medical support.





DISCLOSURE: Robert Glenn, This work was supported by the Coalition for Litigation Justice. Mr. Glenn serves as a science consultant to the coalition and Mr. Kalish serves as counsel to the coalition.

LONG-TERM RESPIRATORY DISORDERS IN CLAIMERS WITH EXPOSURE TO CHEMICAL WARFARE AGENTS (CWA): REVIEW OF BRONCHOSOPIC FINDINGS

Abbas Nemati MD* Ali Moghimi MD Mahdi Rahmati MD Farshad Najafipour MD Homayoun Eftekhari MD Artesh University of Medical Sciences, Tehran, Iran

PURPOSE: It is well documented that inhalation of sulfur mustard causes injury of the respiratory system. While all of the reports and surveys thoroughly document long-term pulmonary effects after significant exposure to mustard, there is no direct evidence that addresses the issue of long-term respiratory effects in individuals who were exposed to very low level of mustard and suffered no acute respiratory tract injury. The aim of this study is to evaluate the respiratory histopathological findings in the veteran claiming exposure to CWA during Iran-Iraq war.

METHODS: We studied 395 subjects which were selected among all those who were in chemically contaminated areas with chemical warfare agents (CWA) and had been registered for an annual checkup. Background data were collected. All subjects underwent diagnostic bronchoscopy and biopsy which was performed and interpreted by one pneumatologist and one pathologist.

RESULTS: Subjects were 395 men with the mean age of 41.46 (SD, 5.43) years which exposed to CWA averagely 18.7 (SD, 1.74) years ago. In the bronchoscopic evaluation 363 patients (91.8%) had no lesion and were normal. 16 patients (4.5%) had mucopurulaent secretions. Bronchoscopic findings did not relate to the cigarette consumption ($p=0.62$) and length time after exposure ($p=0.44$) but age ($p=0.03$). Minimal to moderate changes of interstitial fibrosis were the most prevalent abnormal changes (75%) which was not related to cigarette smoking ($p=0.9$), age ($p=0.24$) and the time after exposure ($p=0.21$).

CONCLUSION: This study shows that findings of gross bronchoscopy is not suggestive and characteristic for the patients exposed CWA and near all patients had normal bronchoscopy. Our results also showed that a major proportion of patients showed interstitial fibrosis in their specimens.

Occupational and Environmental Lung Diseases, continued

CLINICAL IMPLICATIONS: There is no characteristic finding in the bronchoscopy of patients exposed to CWA.

DISCLOSURE: Abbas Nemati, None.

SPIROMETRY PARAMETERS AND QUALITY OF LIFE IN MINERS WITH LUNG BURN INJURY AFTER METHANE EXPLOSURE

Andrzej J. Krzywiecki MD* Liwia Starczewska-Dymek Maciej K. Krzywiecki MA Michal Szydlowski MA Dariusz I. Ziora MD Dariusz Jastrzebski MD Jerzy F. Kozielski MD Dept.Of Pneumonology and TB Silesian Univ. School, Zabrze, Poland

PURPOSE: The aim of this studies was to asses health-related quality of life in miners who survived methane explosure and had lung injury and corelate data from questionnaires SF 36 with results of pulmonary function tests.

METHODS: Two groups were analyzed:Group A:17 miners with lung burn injury after methane explosure, Group B consisted of 15 workers of similar age and number of work yrs.Methods were used to obtain necessary data:SF- 36 survey(Short form-36 to assess quality of life and Master Lab Jaeger for spirometry parameters(FVC,FEV1,PEFR,MEF50,FEV1%FVC).

RESULTS: Analysis demonstrated lack of statistic differences between all parameters of spirometry tests for patients and controls (group A and B) presented in predicted values: FVC ((97% vs 100%), FEV1 (94% vs 97%), FEV1 %FVC (99% vs 100%), PEFR (82% vs 92%), MEF50 (95% vs 99%). All results were within ECCS norms.There were statistical differences between all SF 36 data for patients and controls: Physical Function (52vs91), Role Physical (14vs87), Body Pain (32vs78) General Health (29vs69), Vitlity (34vs74), Social Function (51vs 80), Role Emotional (9.8vs91) Menthal Health (36vs79).

CONCLUSION: As a result of performed analysis we have not found any relation between lung function tests and results of quality of life questionnaire(SF-36)Miners after burn and lung injury have significantly lower health related quality of life than miners without burn injury.

CLINICAL IMPLICATIONS: Burn injury affects quality of life for all parameters and results in decreased quality of mental and physical health what can indicates on the existence of post traumatic stress disorder.

DISCLOSURE: Andrzej Krzywiecki, None.

SPIROMETRIC CHANGES AT HIGH ALTITUDE: THE SHISAPANGMA EXPERIENCE

Marc Meysman MD* Bart Keymeulen PhD Erik Eeckhout PhD Marc Noppen PhD Walter Vincken PhD University Hospital Vrije Universiteit Brussel, Brussels, Belgium

PURPOSE: To examine the effect of altitude on expiratory flow rates, we measured maximal expiratory flow volume curves at sea level in Brussels (1x) and at different altitudes during the ascent of mount Shisapangma in the Himalaya : in Chengdu at 600 m, Lhasa at 3683 m (2x), Xegar at 4340 m and Base camp at 5000 m.

METHODS: Our data were collected from then mountaineers (9 men and one women, mean age 32.8 years).A portable Microspiro HI-298 dry spirometer was used. Test results were compared using Repeated Measures Analysis of Variance, and multiple comparison was done with Bonferroni-t-test. Differences between paired measurements were considered significant at $p < 0.05$.

RESULTS: See also table 1. FVC decreased with increasing altitude. The change was significant above 3683 m compared to sea level values. FEV1 did not significantly change with altitude. PEF (above 3683 m), FEF75% (above 4340 m), FEF50% (above 4340 m) increased significantly when mounting to 5000 m compared to sea level values. For FEF50% the increase was less pronounced than for the other parameters. FEF25 % did not change significantly with altitude. After a nine days stay at high altitude, when returning from 5000 m to 3683 m FVC, FEV1, PEF, FEF75 %, FEF50 % and FEF25 % did return to values recorded earlier at that altitude.

CONCLUSION: These data suggest that the drop in FVC, without change in FEV1, during ascent to high altitude, is due to restrictive pulmonary changes. The rise in PEF, FEF75 %, FEF50 % can be explained by the breathing of gas of decreased density at high altitude. The decrease after returning to 3683 m, the less pronounced increase for FEF 50 % and the absence of changes in FEF25 % favour this hypothesis.

CLINICAL IMPLICATIONS: Real life spirometry done during the ascent to high altitude confirm the observations done in simulation chambers.

Table 1

	Sea level	Chengdu	Lhasa	Xegar	Base camp
FVC	101.2±7.0	96.9±8.3	96.0±9.1	93.9±7.5	91.1±8.0
FEV1	96.0±6.8	93.9±7.5	95.8±7.1	95.5±7.9	94.0±8.7
PEF	77.3±10	76.1±17	91.7±15.3	94.2±13.9	96.6±12.8
FEF75	76.9±15.2	75.8±15.7	84.6±15.0	92.6±22.6	93.5±21.9
FEF50	73.3±19.8	74.0±16.7	81.5±22.5	85.0±26	86.7±30
FEF25	72.7±23.6	69.0±24.2	75.6±28.9	82.5±40	79.4±37.8

Values are expressed as mean (of % predicted) ± SD

DISCLOSURE: Marc Meysman, None.

AGRICULTURAL EXPOSURES IN PATIENTS WITH COPD IN HEALTH SYSTEMS SERVING RURAL AREAS

Kristina L. Bailey MD* Jane L. Meza PhD Lynette M. Smith MS Susanna G. Von Essen MD Holly DeSpiegelaere RN Debra J. Romberger MD University of Nebraska Medical Center, Omaha, NE

PURPOSE: Chronic Obstructive Pulmonary Disease (COPD) is a major health concern. The majority of COPD is caused by cigarette smoking. However, occupational exposures can also lead to the development of COPD in approximately 30% of patients. One industry where occupational exposures frequently lead to lung disease is agriculture. The Omaha Veteran's Administration Hospital (OVAH) serves a largely rural area and many patients have worked in agriculture. However, there are no good estimates of the number of COPD patients with a history of agricultural exposure in our area.

METHODS: We identified a cohort of patients with COPD by reviewing all pulmonary function tests done at the OVAH between November 2004 and March 2005. Obstructive lung disease was defined as a FEV1/FVC ratio of ≤ 70% and FEV1 ≤ 80% as per GOLD Criteria. A random sample of this cohort was administered a telephone survey based on NHANES III questionnaire. It detailed demographic data, smoking history, pulmonary symptoms and history of agricultural exposures.

RESULTS: Participants included 150 veterans with a mean age of 68.2 (standard deviation=10.8). A history of agricultural exposure was elicited in 68% (95% confidence interval: 61%-75%) of subjects. Of those that had worked in agriculture, the types of exposures varied, with 21% working in hog confinement barns, 30% on dairy farms, 12% on poultry farms.

CONCLUSION: In health systems that serve rural areas, patients with COPD commonly have a history of agricultural exposures. Exposures such as these can contribute to the development of COPD.

CLINICAL IMPLICATIONS: Health care workers in rural areas should include agricultural exposures as an important part of the social/occupational history in COPD patients.

DISCLOSURE: Kristina Bailey, None.

Pediatric Chest Medicine
10:30 AM - 12:00 PM

IMMUNOCYTOCHEMICAL DETECTION OF PEPSIN IN ALVEOLAR MACROPHAGES AS A MARKER OF REFLUX ASSOCIATED ASPIRATION

Haibin Zhang MD* Kristin N. Van Hook MD Leland L. Fan MD George B. Mallory MD Okan Elidemir MD Baylor College of Medicine, Houston, TX

PURPOSE: Recurrent aspiration of refluxed material is an important cause of chronic respiratory illness, especially in children. Currently available diagnostic tests such as the lipid-laden macrophage index, milk scan and barium esophagogram lack sensitivity and specificity. Therefore, there is a need for a more accurate diagnostic test. We hypothesized that

immunocytochemical detection of pepsin in alveolar macrophages obtained by bronchoalveolar lavage would serve as a useful diagnostic tool for reflux-associated aspiration.

METHODS: To test our hypothesis we exposed anaesthetized BALB/c mice to a single aspiration of 25 μl of human gastric juice and lavaged their lungs with saline 2, 4, 6, 12, 24, and 48 hours following aspiration. Control animals received same amount of saline aspiration in a similar fashion. Cells obtained by lung lavage was used to prepare cytospin slides. These slides were then stained immunochemically by using goat anti-porcine pepsin antibody and were examined under a light microscope. Three negative controls were used: (1)cells obtained after aspiration of saline; (2)cells obtained after aspiration of human gastric juice and stained without the primary antibody; and (3)cells incubated with isotype-matched goat IgG. Hundred consecutive cells were counted under high-power field and number of positively stained cells was recorded for each time point. Results were expressed in terms of mean percent positive cells (±SD).

RESULTS: At 2, 4, 6, 12, 24 and 48 hours after a single aspiration of gastric juice, mean percent positive staining(±SD) was 4.5±3.0, 2.8±1.3, 16.3±5.1, 16.0±1.4, 24.8±9.0, 33.5±9.0, respectively, (n=4,at each time point). There was no staining in any of the controls(n=6). Differences between the controls and values detected at all time points were statistically significant ($p<0.05$).

CONCLUSION: These findings demonstrate that pepsin can be detected in alveolar macrophages by using immunocytochemistry up to, at least, 48 hours after a single aspiration event.

CLINICAL IMPLICATIONS: Immunochemical staining of alveolar macrophages for pepsin has the potential to become a simple, routine test to detect reflux-related aspiration accurately, if it's validity is confirmed in clinical studies.

DISCLOSURE: Haibin Zhang, None.

DETECTION AND QUANTIFICATION OF PEPSIN IN BRONCHOALVEOLAR LAVAGE FLUID AS A MARKER OF REFLUX ASSOCIATED ASPIRATION

Kristin N. Van Hook MD Haibin Zhang MD Leland L. Fan MD George B. Mallory MD Okan Elidemir MD* Baylor College of Medicine, Houston, TX

PURPOSE: Recurrent aspiration of refluxed material is a risk factor for developing serious lung disease. Accurate diagnosis of gastroesophageal reflux-related aspiration is a clinical challenge due to the lack of sensitive and specific tests. We hypothesized that detection of pepsin in bronchoalveolar lavage fluid (BAL) would serve as a surrogate marker for aspiration.

METHODS: Anesthetized BALB/c mice were exposed to a single aspiration of 25 μl of human gastric juice and control animals received the same amount of normal saline. Lung lavage was performed with 3 aliquots of 0.5 ml of saline 2, 4, 6, 24, 48, and 72 hours following aspiration. Lavage fluid was centrifuged and the supernatant was studied for pepsin concentration using an indirect ELISA technique. To evaluate the sensitivity of the ELISA test, a separate group of mice was exposed to a single aspiration of 25 μl of human gastric juice diluted with normal saline (1:5, 1:10, 1:20, 1:40 and 1:80 dilutions) and lavaged 4 hours after the aspiration.

RESULTS: At 2, 4, 6, 24, 48 and 72 hours after a single aspiration of undiluted gastric juice mean pepsin concentration±SD in the lavage fluid was 14.3±6.2, 8.0±2.8, 2.8±1.2, 0.7±0.2, 0.2±0.1 and 0.17±0.02 μg/ml, respectively, (n=4, at each time point). Mean control value was 0.13±0.04 μg/ml (n=6). Differences between the controls and values detected up to 24 hours after aspiration were statistically significant ($p<0.005$). Mean pepsin concentration±SD of the lavage fluid 4 hours after aspiration of undiluted and 1:5, 1:10, 1:20, 1:40 and 1:80 diluted gastric juice was 3.05±1.0, 0.63±0.28, 0.31±0.14, 0.21±0.11, 0.09±0.02, and 0.1±0.02 μg/ml, respectively, (n=4, at each dilution). Mean control value was 0.08±0.02 μg/ml (n=6). Values up to 1:20 dilution were statistically significantly different from control value ($p<0.005$).

CONCLUSION: These findings demonstrate that pepsin can be detected and quantified in the BAL fluid after aspiration of gastric contents.

CLINICAL IMPLICATIONS: If confirmed in clinical studies, this method has the potential to become a simple, routine test to detect accurately reflux-related aspiration in children and adults.

DISCLOSURE: Okan Elidemir, None.

MANAGEMENT OF BRONCHIOLITIS IN QUEBEC: COMPARISON BETWEEN FIRST-TIME AND RECURRENT EPISODES

Isabelle Rochat MD Denis Berubé MD* Hôpital Sainte-Justine, Montréal, PQ, Canada

PURPOSE: Viral bronchiolitis in infants is an acute obstructive disease of small airways. Asthma, defined as recurrent episodes of lower respiratory tract obstruction, is frequently viral induced in young children. Differentiating between bronchiolitis and asthma is thus often difficult for clinicians. While the benefits of bronchodilators and anti-inflammatory agents are proven in asthma, they are controversial in the management of bronchiolitis. Recurrent episodes of lower airway obstruction should raise the suspicion of asthma and should be treated as such.The purpose of this study was to evaluate whether the current therapeutic practice of Quebec paediatricians differed when treating first-time or recurrent episodes of bronchiolitis.

METHODS: Questionnaires were mailed to all members of the Quebec Paediatric Association in the fall of 2003, followed by a reminder 2 months later. Responses were collected through April 2004. Participants were specifically questioned on the type and frequency of treatment they used for the outpatient management of children with first-time and recurrent episodes of bronchiolitis.

RESULTS: A total of 550 questionnaires were sent, of which 330 (60%) were received within the deadline for analysis.

CONCLUSION: Despite the absence of clear indications, the majority of Quebec paediatricians use pharmacological agents such as inhaled β-agonists and corticosteroids to treat a first-time episode of bronchiolitis. On the other hand, there is a statistically significant ($p\leq0.001$) and appropriate increase in their use of inhaled and systemic steroids, β-agonists and anti-leukotrienes when treating recurrent episodes of lower respiratory tract obstruction.

CLINICAL IMPLICATIONS: This study supports the need to develop and disseminate evidence-based recommendations for the treatment of infectious bronchiolitis in young children and underlines the appropriate use of anti-asthma medication for recurrent episodes of lower airway obstruction.

	1st episode				Recurrent episodes			
	always	sometimes	rarely	no answer	always	sometimes	rarely	no answer
	%	%	%	%	%	%	%	%
anti-leukotriene	1	1	91	7	10	25	57	8
ß-agonist	45	25	24	6	75	14	5	6
anticholinergic	1	3	89	7	1	4	86	9
ß-adrenergic	3	5	81	11	2	4	81	13
oral steroids	8	12	76	4	19	36	40	5
inhaled steroids	19	14	63	4	66	15	15	4
nasal drops (saline)	66	15	15	4	61	18	16	5
nasal decongestant	1	6	89	4	2	8	85	5
physiotherapy	7	15	73	5	9	19	65	7

DISCLOSURE: Denis Berubé, None.

EFFECT ON TUBERCULOSIS AWARENESS AMONG HIGH-SCHOOL STUDENTS IN SELECTED SCHOOLS IN METRO MANILA AFTER USING EDUCATIONAL INTERVENTION

Princess Dionisia M. Nazareno MD* Ana Maria A. Reyes MD Maria Nerissa A. De Leon MD Milagros S. Bautista MD Teresita S. De Guia MD Philippine Heart Center, Quezon City, Philippines

PURPOSE: A.General objectives:To determine if educational intervention would affect the level of TB awareness among High School students in selected schools in Metro ManilaB.Specific Objectives: 1.To determine the level of awareness the students have on the following aspects/components of TB before the intervention :a.Nature/causeb.Transmissibilityc.Effects in physical health d.Prevention2.To determine if the educational intervention improve the students' level of awareness on TB.

Pediatric Chest Medicine, continued

METHODS: Study Design: Experimental non- comparativeStudy sample: high school students Study setting and time period: Study was conducted from July 2004 to January 2005. Permission was granted by the school principals who scheduled the lectures in their audio-visual rooms.. Research Instruments: A pre-tested questionnaire was designed to measure the students' level of awareness on TB before and after the lecture..Statistical Analysis: The scores pre and post educational intervention were calculated for each participant. Comparison of changes in scores were made using T-tests. Categorical data were analyzed using Chi-square tests. Mc-nemars test was used to determine change in response in each questionnaire, and change as to the level of awareness was determined using Wilcoxon matched–Pairs Signed Ranks test.

RESULTS: There was significant improvement post-educational intervention in the students' scores on transmissibility ($p=0.004$) and nature/cause aspect of TB ($p=0.000$).As to prevention and its effects on physical health, scores were insignificant, but with improvement in the mean prevention scores.

CONCLUSION: The study demonstrated the effectiveness of an educational intervention in the students' awareness on TB transmissibility and nature and cause,with that data , a school based TB education program is recommended to be included in the curriculum and should be implemented with the help of all the sectors involved.

CLINICAL IMPLICATIONS: The biggest burden of TB cases (40%) is in Southeast Asia. The Western Pacific regions,particularly Philippines, accounts for 29% of the 375,819 smear (+) cases. In 1998, we ranked 2nd next to china. Considering the threat this disease brings the children, medication costs, and length of treatment, prevention is the best strategy, and is achievable only by education and awareness.

DISCLOSURE: Princess Dionisia Nazareno, None.

HYPERGLYCEMIA IN A HETEROGENEOUS POPULATION OF CRITICALLY ILL CHILDREN

Eliotte L. Hirshberg MD* Stacey Knight Gitte Y. Larsen MD University of Utah, Salt Lake City, UT

PURPOSE: Hyperglycemia in critically ill, non-diabetic adults is associated with increased morbidity and mortality. The natural course of hyperglycemia in a heterogeneous population of critically ill children and its association with mortality is unknown. Our study documents the natural history of hyperglycemia in a university-affiliated, multidisciplinary pediatric intensive care unit (PICU) population.

METHODS: We performed a retrospective cohort analysis of all admissions to a 28 bed PICU during the year 2003. Computerized hospital admission records and hospital laboratory database of all patients admitted to a PICU for greater than 24 hours with at least a single blood glucose level were included. The 1250 patients were stratified by diagnostic code groups. We performed bivariate analysis of hyperglycemia, defined by a threshold of 150 mg/dL, mortality, and length of stay.

RESULTS: Hyperglycemia was identified in 494/1250 (39.5%) patients. Glucose values peaked during the first 12 hours of PICU admission. The 2003 mortality rate for this cohort was 39/1250 (3.1%). The risk of hospital mortality for patients with hyperglycemia was 13.4 times higher than those patients with normoglycemia (95% CI: 4.8-37.5). The average of maximum glucose values over the PICU hospital stay was significantly higher among non-survivors (296 mg/dL) than survivors (147 mg/dL) ($p<0.001$). The median hospital length of stay for patients with hyperglycemia was 3.2 days compared to 2.3 days for patients with normoglycemia ($p<0.001$).

CONCLUSION: Hyperglycemia in the critically ill, pediatric population occurs frequently, peaks in the first 24 hours, and is associated with an increased hospital mortality and length of stay.

CLINICAL IMPLICATIONS: Although mortality in the critically ill pediatric population is low, management of hyperglycemia in a subset of critically ill children may be as important as controlling hyperglycemia in critically ill adults. A large prospective trial of standardized glucose control in critically ill children is warranted.

PICU Diagnostic Group[†]	No.(%)of Patients With Hyperglycemia (>150 mg/dl)
Cardiovascular surgery	150/242 (62)
Sepsis	40/66 (61)
Respiratory failure	374/704 (53)
Traumatic brain injury	7/19 (37)

[†]Patients may be in more than one category

DISCLOSURE: Eliotte Hirshberg, None.

INNOVATIVE TREATMENT OF OBSTRUCTIVE SLEEP APNEA IN DOWN SYNDROME

Jennifer Miller DO* David Josey Jr. MD Vatsala Ramprasad MBBS Cooper Hospital University Medical Center, Camden, NJ

PURPOSE: Down Syndrome is a common genetic disorder with an incidence of 1 in 600-800 live births. Children and infants with this syndrome have a high incidence (15-50%) of Obstructive Sleep Apnea Syndrome (OSAS). OSAS in these children is often diagnosed late. Polysomnograms (PSG) are often difficult to perform because of behavioral and developmental problems. Tolerance of BiPAP via mask is very low, especially in infants. Children with Down Syndrome, unlike children with isolated OSAS, are a higher operative risk and also continue to have abnormal PSGs after adenotonsillectomy.

METHODS: We present a 3 y.o. with Down Syndrome. He was admitted with cardio- respiratory problems several times in infancy, both before and after VSD closure, with diagosis of pneumonia, respiratory distress, and asthma. During his last admission he was noticed to be obstructing only while asleep. He was started on BiPAP several times without success because of poor tolerance of the mask. Since he tolerated O2 via nasal cannula he was tried on a high flow device (Vapotherm). He was placed on 8L O2 via Vapotherm with improvement of symptoms. He was subsequently discharged on Vapotherm at nap and sleep times.

RESULTS: He had a 12 channel PSG using a standard PSG system interfaced with the Vapotherm functioning as CPAP. A modified PSG was performed which showed an Apnea index of 1.6 and a RDI 11.1 with low sat of 68.8% during the diagnostic part of the split study. This improved to an apnea index of 0 and an RDI of 0.5% with a low sat of 78.5% on 9L compressed air via Vapotherm with 1.5L O2. There were no desaturations after O2 was added.

CONCLUSION: The Vapotherm offers a viable alternative to nasal or full-face mask for application of positive pressure in infants and young children with OSAS.

CLINICAL IMPLICATIONS: Vapotherm offers an alternative treatment and/or a way to postpone surgical treatment of craniofacial anomalies in children with Down syndrome.

DISCLOSURE: Jennifer Miller, None.

Pulmonary Hypertension in Interstitial Lung Disease
10:30 AM - 12:00 PM

INCIDENCE AND RELATED OUTCOMES OF PULMONARY HYPERTENSION IN IDIOPATHIC PULMONARY FIBROSIS

Christopher J. Lettieri MD* Andrew F. Shorr MD Scott Barnett PhD Shahzad Ahmad MD Steven D. Nathan MD Walter Reed Army Medical Center, Washington DC

PURPOSE: Pulmonary arterial hypertension (PAH) occurs in many interstitial lung diseases and may contribute to mortality. PAH has been reported in idiopathic pulmonary fibrosis (IPF), but the incidence has not been as well defined and its impact on survival is unknown. We hypothesized that PAH is common in patients with IPF and is an independent risk factor for mortality.

METHODS: Review of consecutive IPF patients undergoing right heart catheterization during evaluation for lung transplantation. We

Pulmonary Hypertension in Interstitial Lung Disease, continued

compared demographics, spirometric and cardiac measurements between those with and without PAH [mean pulmonary arterial pressure (mPAP) >25 mmHg]. The primary endpoint was the incidence of PAH. Mortality related to the measured variables. represented the secondary endpoint.

RESULTS: 79 patients were included. PAH was present in 31.6% (mPAP 29.5±3.3 mmHg versus 19.1±3.7 mmHg). Demographic, spirometric and cardiac measurements did not predict PAH. Those with PAH had lower DLCO (37.6±11.3% versus 31.1±10.1%, p=0.04) and more required supplemental oxygen (66.7% versus 17.6%, p <0.0001). Individuals with DLCO <40% predicted who required supplemental oxygen were 10.2 times more likely to have PAH. Of the measured variables, only mPAP differentiated survivors from non-survivors (21.6±4.7 mmHg versus 24.7±6.1 mmHg, p=0.03). PAH was more common in non-survivors (52.4% versus 24.1%, p=0.008), was associated with greater mortality (48.0% versus 18.5%, OR 2.6, p=0.007) and shorter survival (883±577 versus 530±266 days p=0.01). Both distance walked (143.5±65.5 versus 365.9±81.8 meters, p<0.001) and SpO2 nadir (80.1±3.7% versus 88.0±3.5%, p <0.001) during six-minute walk test were significantly lower in those with PAH. As a screening tool for mortality, PAH had 57.1% sensitivity, 79.3% specificity and 73.4% accuracy.

CONCLUSION: The incidence of PAH in IPF is high, portends worse outcomes and was a better prognostic marker than other measured variables. A reduced DLCO, supplemental oxygen requirement or poor performance on six-minute walk should raise suspicion for PAH.

CLINICAL IMPLICATIONS: Identifying PAH may provide a valuable tool in monitoring disease progression, triaging for lung transplantation and deciding on potential therapies.

DISCLOSURE: Christopher Lettieri, None.

LONG-TERM TREATMENT WITH SITAXSENTAN IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONNECTIVE TISSUE DISEASE (PAH-CTD)

Reda E. Girgis MD* Adaani Frost MD Nick Hill MD David Langleben MD Vallerie McLaughlin MD Ron Oudiz MD Terrance Coyne MD Johns Hopkins University, Baltimore, MD

PURPOSE: PAH-CTD is progressive, difficult to manage, and the leading cause of death in CTD. Endothelin levels are increased in PAH-CTD and have vasoconstrictive and proliferative effects primarily mediated by the smooth muscle cell ETA receptor. Sitaxsentan (SITAX) is a pharmacologically distinct, oral, once-daily, highly selective (6500:1) endothelin ETA receptor antagonist. We previously reported that PAH-CTD patients (pts) in STRIDE-1, a 12 wk, MC, DB, placebo (PBO) controlled trial improved 6MW (58m; p=0.0274), NYHA functional class (NYHA FC) and hemodynamics. For the first time, we report on the long-term follow-up of the PAH-CTD subgroup during the STRIDE-1X extension study.

METHODS: STRIDE-1 evaluated SITAX 100mg, 300 mg, and PBO. Due to similar treatment effects in total ITT population, the SITAX 100mg and 300mg groups were pooled. After STRIDE-1, pts could enter the blinded STRIDE-1X and were treated with either SITAX 100mg or 300mg. Pts on PBO were re-randomized to either SITAX 100mg or 300mg. NYHA FC data were collected in STRIDE-1X. A post hoc analysis was performed to evaluate the effect of SITAX in the intent-to-treat PAH-CTD subgroup. At baseline, 42 of 178 pts had PAH-CTD and were NYHA FC II or III. 41 pts entered STRIDE-1X.

RESULTS: Median and mean treatment was 26 weeks, maximum 55 weeks. Overall, 22 (54%) pts improved by more than one NYHA FC with 11 (50%) pts reporting first improvement during the week 0-12 and 11 (50%) during week 12-52. Two (5%) pts deteriorated by one or more NYHA FC, both occuring by week 4. Both doses of sitaxsentan were well tolerated. One pt (5%) in each group reported liver function abnormalities >3xULN during the entire treatment course. 5 pts discontinued during the study.

CONCLUSION: Short-term treatment with SITAX improves NYHA FC. First time improvements in NYHA FC may also occur late in treatment. Long-term treatment with SITAX is well tolerated.

CLINICAL IMPLICATIONS: SITAX has a favorable safety and efficacy profile in pts with PAH-CTD.

DISCLOSURE: Reda Girgis, Grant monies (from industry related sources) Encysive Pharmaceuticals; Consultant fee, speaker bureau, advisory committee, etc. Encysive Pharmaceuticals; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. sitaxsentan.

PULMONARY HYPERTENSION IN IDIOPATHIC PULMONARY FIBROSIS: EPIDEMIOLOGY AND CLINICAL CORRELATES

Andrew F. Shorr MD* Cindy Cors MS Christopher J. Lettieri MD Donald L. Helman MD Steven D. Nathan MD Washington Hospital Center, Washington, DC

PURPOSE: Pulmonary hypertension (PH) can complicate various forms of interstitial lung disease (ILD)& may adversely affect survival. Both the prevalence and predictors of PH in IPF are unknown.

METHODS: We reviewed the records of all patients with IPF listed for lung transplant (LT) in the US between Jan. 1995 and June 2004 to identify those who underwent right heart catheterization (RHC). We defined PH as a mean pulmonary artery (PA) pressure of ≥ 25 mmHg. Patients with PH were compared to those lacking PH with respect to demographics, pulmonary function, functional status, need for supplemental oxygen, and requirement for corticosteroid therapy. We also recorded the cardiac index (CI) and pulmonary artery wedge pressure (PAWP).

RESULTS: During the study period, 3,667 subjects with IPF were listed for LT and 73.4% had undergone RHC. Among those with PH (n=1210), the mean PA measured 34.3 ± 10.1 mm Hg and 19.9% had severe PH (defined as PA > 40 mm Hg) In univariate analysis, persons with PH had slightly worse lung function (FVC: 48.6 ± 16.9% predicted vs. 49.1 ± 15.1 % predicted, p=0.07; FEV1: 50.0 ± 17.6 % predicted vs. 52.7± 17.2 % predicted, p<0.01), required more supplemental oxygen (3.0 ± 2.2 l/min vs. 2.3 ± 1.8 l/min, p<0.01), and had lower cardiac performance (CI 2.87 ± 0.8 l/min/m2 vs. 2.81 ± 0.7 l/min/m2, p=0.02). Independent factors associated with PH in IPF are shown in the table. As a screening test for the presence of PH, clinical criteria had poor sensitivity and specificity.

CONCLUSION: PH is common in patients IPF listed for LT. The degree of the PH, though, is mild. Race is a strong independent predictor of PH. That FVC does not correlate with PH suggests that mechanisms other than progressive parenchymal destruction contribute to the development of PH.

CLINICAL IMPLICATIONS: Physicians should consider evaluating selected IPF patients for PH. PH may be an important correlate of survival and identifying subjects with PH may improve outcomes by allowing earlier referral for LT.

Variable	Odds Ratio	95% CI
African American	1.51	(1.15,1.99)
Supplemental O2 l/min	1.20	(1.15,1.26)
PAWP (mean) mm Hg	1.19	(1.17,1.21)
FEV1 % predicted	0.99	(0.99,1.00)

DISCLOSURE: Andrew Shorr, None.

LONG TERM EXPERIENCE WITH BOSENTAN IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH) ASSOCIATED WITH ADVANCED IDIOPATHIC PULMONARY FIBROSIS (IPF) AND INTERSTITIAL LUNG DISEASE (ILD): A RETROSPECTIVE CASE SERIES

Ganesh Raghu MD* Jennifer Hayes RN Carolyn Spada RN Jeffrey Moniz RN Steve Yang MBBS Division of Pulmonary and Critical Care Medicine, Seattle, WA

PURPOSE: Bosentan is an experimental antifibrotic agent and approved for the management of PAH. Patients with ILD often manifest PAH as pulmonary fibrosis (PF) advances to endstage. To determine the safety, tolerance and clinical status of consecutive patients who were dyspneic with exertion and received bosentan (>3 months) for PAH secondary to advanced PF, available clinical data was retrospectively analyzed.

METHODS: Echocardiogram confirmed the presence of PAH in all patients. Diagnosis of ILD and underlying specific diagnosis was in accordance with accepted clinical criteria. Exclusions: coexisting COPD (FEV1/FVC <0.7 and RV >120%), concurrent treatment indicated for PAH, other than bosentan, and LVEF<35%. Pulmonary function tests (PFTs) and 6MWT were obtained at baseline and at 3-6-month intervals.

RESULTS: During 1/2000-3/2005, 50 adult, consecutive endstage ILD patients (25 IPF, 12 PF associated with collagen vascular disease, 4

Pulmonary Hypertension in Interstitial Lung Disease, continued

idiopathic nonspecific interstitial pneumonia, 5 sarcoid, 4 other ILD) received bosentan. Mean treatment duration and follow up was 11.1±8.0, range 3-30 months. Concomitant medications included prednisone in 45, azathioprine in 18, N-acetylcysteine in 31, interferon-gamma in 3 and 24h O2 therapy in 39 patients. Compared to pretreatment values, hemodynamics and PFTs did not deteriorate during bosentan treatment (baseline→ 6 mo →12 mo): estimated mean PA systolic pressure±SEM: 54±2.7 → 56 ±2.9→ 53± 6.4 mmHg; FVC predicted: 55.0 ±2.6 →56.5 ±2.8 → 58.5 ±4.1%; DLCO predicted: 33.0 ±1.6→ 35.1 ±2.1 →36.1 ±3.0 %; 6MWT (n=25): Δ resting and lowest SpO2: 8.5 ±0.8→ 9.7 ± 1.5→ 7.0 ± 1.0; 6MWT distance: 670± 79→ 828±105→ 525±249 feet. At last follow-up, 38 patients are alive and stable and 2 lost to follow-up. Abnormal liver function tests > 3x ULN occurred in 1, mild anemia in 4, and leg edema in 8 patients.

CONCLUSION: Bosentan was well tolerated in patients with advanced PF in endstage ILD. During the study period, the vast majority of patients stabilized in PFTs and SpO2 during 6MWT.

CLINICAL IMPLICATIONS: Bosentan may have a useful clinical role in advanced stages of PF associated with ILD.

DISCLOSURE: Ganesh Raghu, Grant monies (from industry related sources) GR is a consultant and advisor for research studies for IPF and scleroderma lung for Actelion,and has received research grants from Actelion. The study was sponsored by Actelion Pharmaceuticals, Allschwil, Switzerland.

SITAXSENTAN, A SELECTIVE ENDOTHELIN-A RECEPTOR ANTAGONIST, IMPROVES EXERCISE CAPACITY IN PULMONARY ARTERIAL HYPERTENSION (PAH) ASSOCIATED WITH CONNECTIVE TISSUE DISEASE (CTD)

James Seibold MD* David Badesch MD Nazzareno Galie MD David Langleben MD Robert Naeije MD Gerald Simonneau MD Robyn Barst MD University of Michigan, Ann Arbor, MI

PURPOSE: PAH is a leading cause of death and late disease morbidity in CTD and is generally regarded as less responsive to therapy than other forms of PAH particularly in the setting of systemic sclerosis (SSc). Endothelin levels are increased in SSc-PAH and have vasoconstrictive effects mediated predominantly via the endothelin-A receptor (ETA). Sitaxsentan is a once daily, orally bioavailable, highly selective (6500:1 - A:B) antagonist of the ETA receptor. We investigated its clinical efficacy in PAH-CTD via analysis of all currently completed sitaxsentan placebo-controlled clinical trials in PAH.

METHODS: Three multicenter, randomized, double-blind, placebo controlled trials of PAH including WHO Class II, III and IV have been completed (STRIDE -1, 2 & 4). Studies were of 12-18 weeks duration and six minute walk distance (6MWD) was the primary or secondary outcome in all. Studies included sitaxsentan at 50 mg, 100 mg and 300 mg qd. 110 of 512 patients had PAH-CTD including 63 with SSc, 22 with overlap/MCTD and 25 with SLE. All studies excluded patients with total lung capacity < 80% predicted or baseline 6MWD > 450 m (two of three studies). These trials also included IPAH and PAH associated with congenital heart defects.

RESULTS: See Table.

	Six Minute Walk Distance (m)			
	Placebo (PBO) N=28	Sitax 50mg N=26	Sitax 100mg N=39	Sitax 300mg N=17
△ from Baseline (mean ± se)	−16 ± 15.0	−2 ± 13.4	21 ± 10.4	2 ± 14.1
PBO-subtracted treatment effect		14.7	37.7	18.3
P-value vs PBO		NS	P=0.042	NS
N (%) Abnormal LFT >3x ULN	1 (3.6%)	0 (0%)	0 (0%)	0 (0%)

CONCLUSION: Sitaxsentan 100 mg improves 6MWD in patients with PAH-CTD with a low incidence of abnormal liver function tests.

CLINICAL IMPLICATIONS: Selective ETA receptor antagonism with sitaxsentan appears to be an effective and well tolerated therapy for PAH associated with CTD.

DISCLOSURE: James Seibold, Grant monies (from industry related sources) Encysive Pharmaceuticals, Actelion; Consultant fee, speaker bureau, advisory committee, etc. Encysive Pharmaceuticals, Actelion; Product/procedure/technique that is considered research and is NOT yet approved for any purpose. Sitaxsentan.

BRAIN NATRIURETIC PEPTIDE LEVELS CORRELATE WITH SIX MINUTE WALK DISTANCE AND WORLD HEALTH ORGANIZATION FUNCTIONAL CLASSIFICATION IN PATENTS WITH CONNECTIVE TISSUE DISEASE -ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

Shiromino Hearth MD Edward L. Salerno MD* Naomi Rothfield MD W. D. Hager MD Raymond Foley MD University of Connecticut Health Center, Farmington, CT

PURPOSE: Previous clinical studies have demonstrated that brain natriuretic peptide (BNP) levels correlate with functional capacity via the six minute walk test in patients with idiopathic pulmonary arterial hypertension (PAH). We sought to determine whether BNP levels correlated with six minute walk distance and World Health Organization (WHO) Functional Class in a unique population of patients with connective tissue disease associated- pulmonary arterial hypertension.

METHODS: A retrospective analysis of 14 patients with connective tissue disease-associated PAH (10 with systemic sclerosis and 4 with mixed connective tissue disease) was undertaken. All patients had a right heart catheterization for diagnostic confirmation. BNP levels, six minute walk distances, and WHO functional classification were extracted from the medical record while patients were receiving therapy with an endothelin antagonist, prostanoid, or a combination thereof. Statistical analysis was performed to determine if BNP levels correlated with six minute walk distance and WHO functional class.

RESULTS: There were 30 data points for BNP verses the six minute walk test. Pearson's correlation for these variables was -0.574 with a P value of P<0.001. For BNP versus WHO functional classification there were 34 variables. The Pearson's correlation was 0.586 with a P value of P<0.001 (Table 1).

CONCLUSION: BNP levels correlate with six minute walk distance and WHO functional class in a population of patients with connective tissue disease-associated PAH.

CLINICAL IMPLICATIONS: In patients with pulmonary arterial hypertension secondary to systemic sclerosis or mixed connective tissue disease, BNP may be a useful marker of exercise capacity and functional class. Additional studies with larger sample size are necessary to confirm these findings.

Table 1

Test Type	Number of Data Points	p Value	Pearson Correlation
BNP vs. 6-MWT	30	P<0.001	-0.574
BNP vs. WHO	34	P<0.001	0.586

DISCLOSURE: Edward Salerno, None.

Shock in Critical Care
10:30 AM - 12:00 PM

THE SAFETY OF DOPAMINE VERSUS NOREPINEPHRINE AS VASOPRESSOR THERAPY IN SEPTIC SHOCK

Jaime J. Simon Grahe DO* Gourang P. Patel PharmD Ellen Elpern RN Robert A. Balk MD Rush University Medical Center, Chicago, IL

PURPOSE: We evaluated a strategy of dopamine (DA) vs norepinephrine (NE) as the primary vasopressor support in patients with septic shock. Concern for potential adverse events or a significant improvement in outcome prompted an interim safety analysis after approximately 50% of the target subjects were enrolled.

Shock in Critical Care, continued

METHODS: MICU patients with septic shock were prospectively randomized to receive either DA or NE as the first-line vasopressor. All patients were treated with early-goal directed medical therapy including luid resuscitation, antibiotics, tight glycemic control and management of adrenal insufficiency, as appropriate. A protocol governed the titration of vasopressors to achieve a mean arterial pressure (MAP) of > 60mmHg or systolic blood pressure (SBP) > 90mmHg. After the maximum dose of either DA or NE was reached, patients received vasopressin at a fixed dose of 0.04 units/minute, followed by titration of phenylephrine to maintain the blood pressure goal. An interim analysis was performed to evaluate safety and efficacy of each vasopressor.

RESULTS: Sixty-six patients, 35 DA and 31 NE, have been enrolled in the study. APACHE II scores, gender, and age were all similar at baseline between the two groups. There was no significant difference in mortality comparing the two groups (DA 40%, NE 41.8%). Cardiac dysrhythmias occurred in 31.4% of the DA group compared to 3.2% for NE (p=0.003). All cardiac dysrhythmias required an intervention.

CONCLUSION: There was a significant increase in cardiac dysrhythmias associated with DA treatment in comparison to NE treatment of septic shock.

CLINICAL IMPLICATIONS: While there was no significant difference in mortality between the two vasopressor regimens, the significant increase in dysrhythmias associated with DA administration raises significant safety concerns. Further testing is needed to confirm the safety of dopamine and ensure that it is not detrimental to septic shock patients.

DISCLOSURE: Jaime Simon Grahe, None.

ACCURACY OF GLUCOSE MEASUREMENT IN CRITICALLY ILL PATIENTS IN SHOCK

Srinivas B. Chakravarthy MBBS* Boaz A. Markewitz MD Chris Lehman MD James F. Orme MD University of Utah Health Sciences Center, Salt Lake City, UT

PURPOSE: Strict normalization of blood glucose level improves outcome in critically ill patients. Accurate glucose measurement is an essential aspect of intensive insulin therapy. The various methods of testing (glucometer, blood gas analyzer and conventional laboratory analyzer) have not been studied simultaneously in patients in shock. This study is designed to prospectively evaluate different methods of glucose monitoring in critically ill patients. The specific aim is to evaluate the accuracy of bedside glucometer and blood gas analyzer in comparison with the clinical laboratory colorimetric method (gold standard).

METHODS: ICU patients in shock, defined as a systolic blood pressure of <90 mm Hg despite adequate volume resuscitation or requiring vasopressor therapy, were considered for enrollment. Arterial, venous and capillary blood samples were obtained simultaneously. A total of 243 samples were obtained from 21 patients. Glucose determinations were made with the glucometer (ACCU-CHEK Comfort Curve, Roche) from each of the vascular compartments. Arterial and venous glucose levels were determined using a blood gas analyzer (Radiometer ABL 700). Arterial and venous blood samples were tested in the clinical laboratory using the colorimetric plasma glucose analyzer (VITRIOS).

RESULTS: Mean venous blood glucose level determined on the VITRIOS analyzer (gold standard) was 129.6 mg/dl with a range of 54 to 350 mg/dl. Capillary blood glucose tested on glucometer was higher than the gold standard by a mean of 20.95 mg/dl (16.99%). The difference changed minimally when arterial or venous samples tested on glucometer were compared to the gold standard. Blood gas analyzer on the other hand, was higher by a mean of 3.07 mg/dl (2.68%) when compared to the gold standard.

CONCLUSION: Blood glucose determination with a glucometer is associated with a risk of obtaining falsely elevated blood glucose level. Blood gas analyzer is significantly more accurate.

CLINICAL IMPLICATIONS: Using glucometers to monitor blood glucose levels in patients with shock is associated with the risk of obtaining falsely elevated results and thus placing the patient at risk for hypoglycemia.

DISCLOSURE: Srinivas Chakravarthy, Grant monies (from sources other than industry) This study was supported by an award from The CHEST Foundation of the American College of Chest Physicians and Ortho Biotech Products, LP.; Grant monies (from industry related sources) The glucometer, chemistry strips and the reagents were provided by Roche.

Table—*Comparison of the glucometer and blood gas analyzer to the gold standard (clinical lab).*

Comparison	Mean of difference (mg/dl)	Standard deviation	p Value
Arterial sample on glucometer vs clinical lab	17.6625	12.1435	<0.001
Arterial sample on blood gas analyzer vs clinical lab	2.21	4.5387	<0.001
Venous sample on glucometer vs clinical lab	22.175	17.7184	<0.001
Venous sample on blood gas analyzer vs clinical lab	4.4625	5.5573	<0.001
Capillary sample on glucometer vs venous sample in clinical lab	20.1	12.5290	<0.001

GLUCOSE DETERMINATION FROM DIFFERENT VASCULAR COMPARTMENTS BY POINT-OF-CARE TESTING IN CRITICALLY ILL PATIENTS

Srinivas B. Chakravarthy MBBS* Boaz A. Markewitz MD Chris Lehman MD James F. Orme MD University of Utah, Salt Lake City, UT

PURPOSE: The most common method of glucose measurement in many ICUs is point-of-care testing (glucometers). Considering the recommendations for strict glycemic control, accurate measurement of glucose level is essential. Accuracy of glucometers is influenced by various factors including mean arterial pressure, tissue perfusion and PaO2. The purpose of this study is to compare the blood glucose levels from various vascular compartments (arterial, venous and capillary), as determined by a glucometer, in critically ill patients.

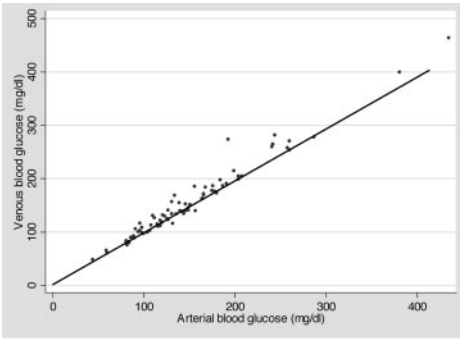
METHODS: All ICU patients in shock, defined as a systolic blood pressure of <90 mm Hg despite adequate volume resuscitation or requiring vasopressor therapy, were considered eligible for enrollment. Arterial, venous and capillary blood samples were obtained simultaneously. A total of 243 samples were obtained from 21 patients. Glucose determinations were made with a glucometer (ACCU-CHEK Comfort Curve, Roche) from each of the vascular compartments.

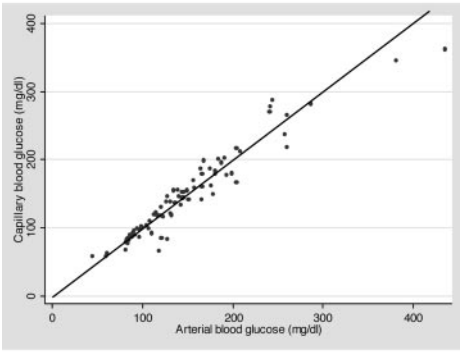
RESULTS: Mean blood glucose level measured in venous blood with a glucometer was 146.95 mg/dl with a median of 135 mg/dl and a range of 44 to 435 mg/dl. Glucose level in arterial sample was higher than in the venous sample by a mean of 8.25 mg/dl (5.88%) and a median of 5 mg/dl. The mean difference in glucose level between the capillary and arterial sample was 6.58% (10.55 mg/dl) and the mean difference between the capillary and the venous sample was 7.58% (12.58 mg/dl). The capillary sample had a consistently higher glucose level than the arterial or venous sample.

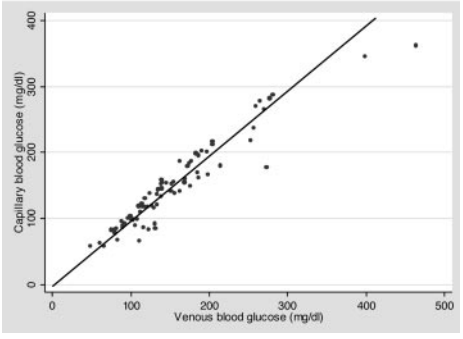
CONCLUSION: When glucose measurements are determined with a glucometer, the glucose level varies with the source of the blood sample. The difference between arterial sample and venous sample is minimal. If a capillary sample is used, then the difference in glucose level is increased.

CLINICAL IMPLICATIONS: Blood glucose levels in various vascular compartments, as determined by glucometer, differ and consistency in the source of the sample being tested is important.

Shock in Critical Care, continued







DISCLOSURE: Srinivas Chakravarthy, Grant monies (from sources other than industry) This study was supported by an award from The CHEST Foundation of the American College of Chest Physicians and Ortho Biotech Products, LP.; Grant monies (from industry related sources) The glucometer, chemistry strips and reagents were provided by Roche.

UNINFECTED SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS) OR FUTURE SEPSIS? DIFFERENCES IN EXTRACELLULAR MATRIX MODULATORS PRIOR TO ONSET OF CLINICAL SEPSIS

Steven B. Johnson MD* Grant Bochicchio MD Carl Shanholtz MD Alan Cross MD Jeff Hasday MD Michael Townes MD Richard Moore MD Thomas Scalea MD R. Adams Cowley Shock Trauma Center, Baltimore, MD

PURPOSE: Inflammation and sepsis induce changes in the extracellular matrix (ECM). ECM degradation and deposition is tightly controlled by matrix metalloproteinases (MMP) and their inhibitors, tissue inhibitors of metalloproteinase (TIMP) respectively. TIMP are multifunctional, participating in anti-apoptotic activity, B cell differentiation, and IL-10 production. We hypothesize that differential expression of TIMP-1 and MMP-9 occurs in SIRS patients that remain uninfected compared to those who subsequently become infected and that these differences occur prior to onset of clinical sepsis.

METHODS: Longitudinal blood samples were collected on critically ill non-infected SIRS patients and analyzed for MMP-9 and TIMP-1. SIRS patients who subsequently converted to sepsis (Pre-septic SIRS) were time matched to patients who remained uninfected (Non-septic SIRS). Comparisons between the 2 groups occurred at study entry, and at 60 hours prior (T-60), 36 hours prior (T-36), and 12 hours prior (T-12) to onset of microbiologically proven clinical sepsis. MMP-9 and TIMP-1 were measured by immunoassay. Data expressed as mean±SD.

RESULTS: 50 Pre-septic SIRS patients and 47 Non-septic SIRS patients were compared at each time point (see table). TIMP-1 levels were significantly higher in the pre-septic SIRS patients. MMP-9 levels were similar in both groups until Pre-septic elevated at T-12. MMP-9/TIMP-1 ratios were lower in the Pre-septic patients initially but sequentially increased becoming significantly elevated at T-12 prior to clinical sepsis.

CONCLUSION: ECM undergoes dynamic modulation with changes in MMP-9/TIMP-1 ratio prior to conversion from SIRS to sepsis. Elevated TIMP-1 levels occur early, more than 60 hours before clinical sepsis. In addition, TIMP-1 appears dissociated from MMP-9 suggesting alternative activation and functions in SIRS patients who subsequently convert to sepsis.

CLINICAL IMPLICATIONS: Earlier diagnosis of sepsis in SIRS patients may be possible by evaluating modulators of the extracellular matrix.

	MMP-9 (ng/ml)		TIMP-1 (ng/ml)		MMP-9/TIMP-1 Ratio	
	Non-septic	Pre-septic	Non-septic	Pre-septic	Non-septic	Pre-septic
Study entry	1199±936	1175±906	289±161	402±234**	5.2±4.7	3.6±3.3
T-60 Hrs.	1164±848	1342±1055	239±92	354±209	5.1±3.2	4.9±5.3
T-36 Hrs.	1115±834	1555±1518	245±152	378±249*	5.0±3.4	5.6±7.3
T-12 Hrs.	1344±1184	2052±1505*	235±122	418±305**	5.8±4.5	6.7±6.5#

* p<0.05 and ** p<0.01 compared to non-septic, #p<0.05 compared to study entry

DISCLOSURE: Steven Johnson, Grant monies (from industry related sources) Research Grant Support from BD Diagnostics, Baltimore Maryland; Glaxo SmithKline; Wyeth; Consultant fee, speaker bureau, advisory committee, etc. GlaxoSmithKline; Wyeth; Lilly.

THE SAFETY OF DROTRECOGIN ALFA (ACTIVATED): INDEPTH DATA ANALYSIS SUGGESTS SURVIVAL BENEFIT INDEPENDENT OF SERIOUS ADVERSE EVENT OCCURRENCES

Robert Levine MD* Stephen Lowry MD Jean-Francois Dhainaut MD Pierre-Francois Laterre MD Greg Beilman MD I. A. Fein MD Luiz Poli de Figueiredo MD Jonathan Janes David Nelson MS Joan Bailey BNS Frank Booth MD Michael Cobas Meyer MD University of Texas School of Medicine, Houston, TX

PURPOSE: To better understand treatment risks and benefits of drotrecogin alfa (activated) (DrotAA), a clinical evaluation committee evaluated all serious adverse events (SAEs), occurring across five clinical trials [conducted by a single sponsor (Eli Lilly and Company) and integrated into single database, INDEPTH (4459 patients)] in patients with severe sepsis.

METHODS: We examined all SAEs which occurred during infusion (n=277) from 1231 placebo and 3228 DrotAA patients. Investigators were blinded to treatment assignment.

RESULTS: Total SAE rates were similar. More bleeding but fewer non-bleeding SAEs occurred in patients receiving DrotAA. Approximately half of the SAEs during the 28-day study period were reported at a time when DrotAA (and also placebo) was not being infused and are considered likely unrelated, given the known short half-life of the drug. (See Table 1) SAEs occurred with similar frequency in both treatment arms and notably 93.8% of the DrotAA and 93.7% of the placebo treated patients did not experience an SAE during the infusion. Mortality was still lower in DrotAA treated patients compared to placebo in patients experiencing a bleeding or non-bleeding SAE. (See Table 2).

CONCLUSION: Although DrotAA is associated with an increased bleeding risk, it was also associated with fewer thrombotic events and the overall rate of SAEs was similar. Mortality was lower in DrotAA treated patients even in the presence of a bleeding or a non-bleeding event. Adjustment for the use of multiple studies with propensity scores did not affect these conclusions.

Shock in Critical Care, continued

CLINICAL IMPLICATIONS: Benefit of treatment with DrotAA outweighs the risks associated with adverse events and improves survival.

Table 1

SAEs During Infusion Period	DrotAA	Placebo	p Value**
All SAEs	199 (6.16%)	78 (6.34%)	0.832
Non Bleeding Events	113 (3.50%)	72 (5.85%)	<0.001
Arterial Thrombotic Events*	26 (0.81%)	22 (1.79%)	.0045
Bleeding Events	101 (3.13%)	9 (0.73%)	<0.001
CNS Bleeding	15 (0.46)	1(0.08)	0.087***

*MI, stroke without hemorrhage, other arterial thrombotic events

DISCLOSURE: Robert Levine, Consultant fee, speaker bureau, advisory committee, etc. Advisory panel fee.

CLINICAL IMPACT OF EARLY GOAL-DIRECTED ECHOCARDIOGRAPHY IN SHOCK PATIENTS PERFORMED BY NON-CARDIOLOGIST INTENSIVISTS

Anthony Manasia MD* Dragos Cucu MD John Oropello MD Rosanna DelGiudice RN Jerry Hufanda RN Ernest Benjamin MD Mount Sinai School of Medicine, New York, NY

PURPOSE: Circulatory shock is life-threatening requiring immediate therapeutic intervention. Real time assessment of cardiac function and volume provides information to guide fluid and vasopressor therapy. Early bedside transthoracic or transesophageal echocardiography performed by non-cardiologist intensivists has the potential to improve the management of patients with acute hemodynamic instability.* The purpose of this study is to determine the clinical impact of limited, goal-directed bedside echocardiography performed by non-cardiologist intensivists in ICU patients in shock.

METHODS: Eighteen (n=18) patients in shock admitted to the surgical and neurosurgical ICUs were enrolled after informed written consent was obtained. Shock was defined as hypotension (MAP<65 mmHg, or SBP<90 mmHg) or need of vasopressor therapy, associated with either hyperlactatemia, oliguria/anuria or an increase in serum creatinine. A treatment plan was instituted by the ICU team. Each patient then underwent a limited echocardiographic exam (transthoracic or transesophageal), to assess left ventricular function and to estimate cardiovascular volume status (preload). The echocardiographic exam was performed by an echo-trained intensivist not involved in the patient's care. A second echo exam was performed 24 hours later. Changes in medical management were recorded following each echo. Data were analyzed and presented in proportions using descriptive statistics.

RESULTS: The first echo changed the treatment plan in 38.8% (7/18) of the patients when compared to the initial management instituted by the primary ICU team. The treatment plan was changed in 11.7% (2/17) of patients following the second echo exam. The mean time from enrolling patients into the study to performing the first echo was 5.1±4.1 hours.

CONCLUSION: In evaluating patients in shock, an early limited, goal-directed echocardiographic exam performed by trained intensivists, provides new information and significantly changes medical management.

CLINICAL IMPLICATIONS: The performance of an early, limited, goal-directed echocardiographic exam by non-cardiologist intensivists, has the potential to improve the hemodynamic management of patients in shock.*J Cardiothoracic Vasc Anesth 12 (1) 10-15, 1998.

DISCLOSURE: Anthony Manasia, None.

Sleep-Disordered Breathing: CPAP and Beyond
10:30 AM - 12:00 PM

IMPACT OF UPPER AIRWAY RESISTANCE SYNDROME IN BARIATRIC SURGERY

John G. Park MD* Timothy I. Morgenthaler MD Eric J. Olson MD Mayo Clinic College of Medicine, Rochester, MN

PURPOSE: The clinical impact of upper airway resistance syndrome (UARS) continues to be debated. Reports suggest increased post-operative complications in those with untreated obstructive sleep apnea (OSA). Due to pathophysiologic similarities between UARS and OSA, we hypothesized that those with UARS would have increased complications and longer hospital length-of-stay (LOS) after bariatric surgery.

METHODS: We retrospectively reviewed all patients who underwent bariatric surgery and attended pre-operative overnight polysomnogram (PSG) at our institution between January and November of 2004. UARS was defined as greater than 10 respiratory-related arousals per hour of sleep with an apnea-hypopnea index less than 5. Among 285 bariatric surgeries, 156 underwent PSGs. Among these patients, 33 had UARS and 15 had normal polysomnogram results (normal controls). We subsequently compared complication rates, and hospital and intensive care unit (ICU) LOS between the two groups. We also compared the results within the UARS group between those who received continuous positive airway pressure (CPAP) versus those who did not.

RESULTS: Most subjects were female and there were no statistical differences in the mean age or body mass index (45.3 ± 5.9 kg/m2 versus 48.3 ± 10 kg/m2, p=0.29) between the two groups. There was no statistical difference in the hospital LOS (5.4 ± 2.3 vs 5.7 ± 2.3 days), but more patients in the UARS group spent days in the ICU (26/33 vs 7/15) and the ICU LOS was significantly higher in the UARS group (1.12 ± 0.97 vs 0.63 ± 0.77 days, p=0.03). There were no significant differences in the frequency of complications between the two groups (24% vs 20%) or in complication rates among UARS patients that received CPAP and those that did not.

CONCLUSION: UARS does not appear to contribute to increases in complications or total LOS in the hospital after bariatric surgery. CPAP use during recovery did not seem to significantly impact the outcome of bariatric surgery in those with UARS.

CLINICAL IMPLICATIONS: Aggressive peri-operative treatment of UARS may not be imperative in bariatric surgery.

DISCLOSURE: John Park, None.

PREDICTORS OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) COMPLIANCE AND SATISFACTION AFTER SPLIT-NIGHT PROTOCOL

Osama Elkhouli MD* Norman Wolkove MD Marc Baltzan MD Mount Sinai Hospital Center, Montreal, PQ, Canada

PURPOSE: Poor compliance and low satisfaction with continuous positive airway pressure (CPAP) are significant obstacles in the treatment of obstructive sleep apnea(OSA). We investigated the polysomnographic (PSG) and clinical predictors of compliance and satisfaction in patients treated with CPAP after a "diagnostic/titration split-night protocol" (SNP).

METHODS: We studied 122 consecutive patients 3-6 months after SNP. Satisfaction, compliance, and side effects of the CPAP were assessed using a questionnaire. Compliance was validated by examination of meter reading. PSG variables during the SNP were analyzed.

RESULTS: During SNP increased slow-wave sleep (SWS) during the titration was correlated with compliance (p=0.037). The obstructive apnea index (OAI) during the diagnostic part of the SNP was correlated with compliance (p = 0.021) and satisfaction (p= 0.011).Clinical correlates of long term compliance included increasing age, improvement in subjective daytime concentration, quality of life, vitality and mood (all p<0.01). Improvement in sleep quality and reduction of the Epworth score after CPAP were strong predictors for long term compliance and satisfaction with CPAP (p = 0.0001).Taking the CPAP mask off during sleep was negatively correlated with compliance (p=0.0003). Pain related to the CPAP was negatively correlated with satisfaction (p = 0.021).

CONCLUSION: High OAI during the diagnostic part of the SNP and increase of SWS during the titration part of the SNP can predict long term compliance and satisfaction with CPAP. However, clinical parameters including reduction in the Epworth score and improvement in the sleep quality are even better predictors of long term compliance and satisfaction with CPAP.

CLINICAL IMPLICATIONS: SNP sleep architecture and especially clinical parameters are of predictive value in estimation of long term compliance and satisfaction with CPAP.

DISCLOSURE: Osama Elkhouli, None.

Sleep-Disordered Breathing: CPAP and Beyond, continued

LONG-TERM EFFECT OF CPAP THERAPY ON BLOOD PRESSURE CONTROL IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

Tanveer Ahmed MD* Joe G. Zein MD Walid G. Younis MD Fazal Ali MD Maroun M. Tawk MD Gary T. Kinasewitz MD University of Oklahoma Health Sciences Center, Oklahoma City, OK

PURPOSE: Many patients with OSA are also hypertensive. We hypothesized that CPAP therapy will lead to a long-term improvement in blood pressure control as reflected by the need for less intense antihypertensive therapy.

METHODS: We identified 50 patients on therapy with moderate to severe OSA who began CPAP therapy between January 2003 and August 2004 and followed for 1 year at the Oklahoma City VA medical center by review of sleep lab logs. Blood pressures and medications were obtained from clinic and pharmacy records. Patients with a >5 mmHg decrease in blood pressure were considered responders and compared to non-responders. Data are presented as mean ± SEM. Comparisons were performed using ANOVA for continuous variables and the Pearson chi-square test for categorical variables. A p value <0.05 was considered statistically significant.

RESULTS: There were 32 responders and 18 nonresponders. A majority of both responders (77%) and nonresponders (74%) had severe OSA with an apnea-hypopnea index (AHI) > 30 events/h. Responders were older and had a higher pre-CPAP blood pressure than nonresponders (Table). The awake room air PaO2 was lower and the PaCO2 higher in nonresponders and their AHI and body mass index tended to be higher and their mean nocturnal O2 saturation lower. The blood pressure fell gradually after the institution of CPAP in the responders but was unchanged in the nonresponders. The improvement in the responders was greatest after 12 months of CPAP. The number of antihypertensive medications was similar in both groups at the start of CPAP therapy and after 12 months.

CONCLUSION: CPAP therapy produces a gradual reduction in blood pressure which is significant at 12 months. This benefit occurs without any change in antihypertensive therapy.

CLINICAL IMPLICATIONS: In the poorly controlled hypertensive patient with OSA, CPAP therapy will help lowers blood pressure while it treats the OSA.

Table 1

Variable	Responders (n=32)	Non-responders (n=18)	p Value
Age (years)	61.7±1.4	55.3±1.9	0.01
$PaCO_2$ (mmHg)*	41.9±1.8	52.6±2.6	0.005
PaO_2 (mmHg)*	82.3±3.6	55.7±5.1	0.0006
Mean nocturnal Oxygen saturation (%)	91.7±0.6	89.7±0.8	0.06
AHI	51.1±5.6	67.1±7.7	0.1
Antihypertensive medication (n)	2.4±0.2	2.2±0.3	0.7
Baseline MAP (mm Hg)	101.1±1.6	95.4±2.1	0.04
MAP at 12 months (mmHg)	86.9±2.1	98.2±2.5	0.001
BMI (kg/m^2)	36.0±1.5	38.6± 2	0.3

*PaO_2 and $PaCO_2$ were measured on room air

DISCLOSURE: Tanveer Ahmed, None.

EMPIRIC TREATMENT OF CLINICALLY DIAGNOSED OBSTRUCTIVE SLEEP APNEA USING AUTO-TITRATING CONTINUOUS POSITIVE AIRWAY PRESSURE

Fitzgerald E. Drummond MD* Peter Doelken MD Michael D. Frye MD Medical University of South Carolina, Charleston, SC

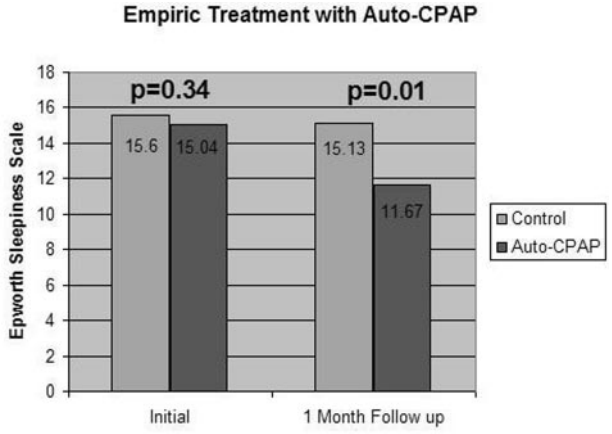
PURPOSE: To evaluate the efficacy and safety of empiric auto-adjusting CPAP to treat suspected OSA in veterans awaiting polysomnography.

METHODS: Consecutive patients referred for polysomnography were screened. Exclusion criteria were: known OSA, risk of central apnea, insomnia, narcolepsy, or severe comorbid disease. Inclusion criteria were positive findings in two of the following three categories: severe snoring, daytime sleepiness, and either hypertension or BMI>30. Eligible subjects were seen in clinic and randomized either to treatment with auto-adjusting CPAP or to usual care at the VA. Subjects completed the FOSQ quality of life indicator and the Epworth sleepiness scale at the initial visit and again after 4 weeks.

RESULTS: 338 patients were screened. 58 patients met entry criteria and were enrolled. Of these, 39 have completed the initial and follow up questionnaires, 24 in the treatment group and 15 in the control group. The groups did not differ significantly at the start of the study. At follow up, the mean Epworth scores in the treatment and control groups were 11.67 and 15.13 respectively (p=0.01). The mean FOSQ scores in the treatment and control groups were 15.14 and 13.43 respectively (p=0.055). There was a statistically significant improvement in the Epworth scores of patients treated with auto-CPAP. A trend toward improvement in FOSQ was observed that did not reach statistical significance. There were no adverse events documented. One patient withdrew for reasons unrelated to the study.

CONCLUSION: These data suggest that auto-CPAP significantly improved the Epworth scores of veteran patients likely to have OSA while awaiting polysomnography. This is an encouraging finding and warrants continuation of this trial to its planned enrollment of 300 subjects.

CLINICAL IMPLICATIONS: While the prevalence of OSA in the veteran population is likely higher than in the general population, the waiting time for polysomnography can be long. These data suggest empiric treatment while awaiting a polysomnogram may be safe and effective in select patients.



DISCLOSURE: Fitzgerald Drummond, None.

TOLERANCE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP) CORRELATES WITH NASAL AIRWAY ANATOMY, BUT NOT WITH CPAP PRESSURE OR SLEEP STUDY FINDINGS

Luc G. Morris MD* Omar E. Burschtin MD S. J. Setlur BS Kelvin C. Lee MD New York University School of Medicine, New York, NY

PURPOSE: Nasal continuous positive airway pressure (nCPAP) is an effective first-line therapy for sleep disordered breathing (SDB), but 25-50% of patients are unable to tolerate long term therapy. There have been few systematic investigations into potential causes of nCPAP intolerance. Recent studies have suggested that surgical improvement of nasal airway function also improves nasal CPAP tolerance. In this study we examined the correlation of long term CPAP tolerance with nasal airway measurements and other clinical variables, in patients with SDB.

METHODS: We prospectively enrolled 44 patients presenting to an academic sleep disorders center for polysomnography. In addition to undergoing standard diagnostic polysomnography, demographic information, body mass index (BMI), Epworth Sleepiness Scale, and acoustic rhinometry measurements of nasal cross-sectional area were recorded for each patient. Of the 34 patients ultimately titrated to nCPAP, follow-up telephone interviews were conducted to determine their tolerance of therapy after 18 months.

Sleep-Disordered Breathing: CPAP and Beyond, continued

RESULTS: Long term nasal CPAP tolerance data was available in 25 patients. When comparing CPAP tolerant and intolerant patients, there were no differences in age, gender, Epworth Sleepiness Scale, subjective nasal congestion, or neck circumference. Sleep study data revealed no differences in respiratory disturbance index, oxygen desaturation, sleep efficiency, or nasal CPAP pressure level. Only one factor correlated with CPAP tolerance: nasal cross-sectional area at the inferior turbinate (p=.03).

CONCLUSION: Nasal airway patency appears to be a major factor in nasal CPAP tolerance. The severity of SDB and the level of positive pressure do not affect CPAP tolerance. Other aspects of the history and physical exam, and sleep study results, were all unrelated to nCPAP tolerance.

CLINICAL IMPLICATIONS: Objective nasal airway measurements may prove important in the evaluation of the SDB patient. Such information may help clinicians predict which patients are likely to tolerate nasal CPAP therapy, and who may benefit from medical or surgical management of their nasal airway.

Parameter	CPAP Tolerant	CPAP Intolerant	p Value
Age	51	54	NS
% male	69	75	NS
BMI	33.6	28.9	NS
ESS	12.0	9.0	NS
RDI	30.2	35.2	NS
CPAP level	8.38	7.36	NS
O_2 saturation nadir	80.7	79.8	NS
CSA (baseline)	0.67	0.51	.03
CSA (decongested)	0.85	0.66	.05

CSA: nasal cross-sectional area at the inferior turbinate

DISCLOSURE: Luc Morris, Other Acoustic rhinometer provided by RhinoMetrics Corporation to Kelvin C. Lee, MD.

PREVALENCE OF SNORING AMONG YOUNG ADULT FEMALES WITH ATOPY

Maninder Kalra MD* David Bernstein MD Ameet Daftary MD Harpinder K. Kalra MD Grace LeMasters PhD Cincinnati Children's Hospital Medical Center, Cincinnati, OH

PURPOSE: Snoring is the primary symptom of sleep-disordered breathing and is associated with cardiovascular and metabolic morbidity(Young T,AJRCM 2002). The prevalence of habitual snoring, in a large cohort of 30-60 year old adults, has been reported to be 19% in males and 9% in females(Jennum P, J Sleep Res 1992). However, the effect of atopy on gender predisposition of snoring is not known(Young T,AJRCM 2002). The objective of this study was thus to determine the prevalence of snoring in a community based cohort of young adult females with atopy, and to identify risk factors for habitual snoring in this group.

METHODS: Mothers of all children (n=710) participating in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) were recruited for this study. A questionnaire survey of their snoring frequency as well as cigarette smoking was obtained. Atopic status was determined by a skin prick test to a panel of 15 aeroallergens (ALK America, Round Rock, Texas). Subjects with habitual snoring (defined as snoring $\geq$ 3 times per week) were compared to those who either did not snore or snored $<$3 times per week using chi-square test.

RESULTS: Data were available in 515 of the 710 females whose children were participating in CCAAPS study. The mean age of our cohort at the time of assessment for snoring was 29.8 years (S.D. 5.7). Of the 515 females, 257 (49.9%) never snored, 176(34.2%) snored at least one night per week, and 105 (20.4%) snored habitually. There was a significant association between habitual snoring and (1) positive cigarette smoking (34% vs. 18.2%) (p=0.001), (2) being African American (29.1% vs. 18.5%) (p=0.02).

CONCLUSION: We report a high prevalence of habitual snoring in young adult females with atopy. Cigarette smoking and being African American are risk factors for habitual snoring in this group.

CLINICAL IMPLICATIONS: Atopic adult females are at increased risk for sleep-disordered breathing. This high risk group should be targeted for screening to reduce morbidity from untreated sleep-disordered breathing.

DISCLOSURE: Maninder Kalra, University grant monies Dr.M Kalra is supported by CReFF grant, Cincinnati Children's General Clinical Research Center; Grant monies (from sources other than industry); This study was funded by NIEHS, grant # R01 ES 11170-01.