

Causal Link Possible Between ICU Hypoglycemia, ICU Death

Hypoglycemia Is Associated With Intensive Care Unit Mortality.

Hermanides J, Bosman RJ, et al:

Crit Care Med 2010; 38 (June): 1430-1434

Using the SOFA score to help estimate disease severity, analyses show that hypoglycemia in the ICU increases the risk of ICU death.

Background: Recent studies have conflicting results regarding ICU mortality associated with strict glucose control in the ICU. Intensive insulin therapy appears to be associated with a 6-fold increased risk of severe hypoglycemia in the ICU. It is possible that hypoglycemia in the ICU is a marker rather than a risk factor for severe illness or dying.

Objective: To determine if hypoglycemia in the ICU affects ICU mortality after adjusting for daily measures of disease severity and other confounding factors.

Design: Retrospective, database cohort study.

Participants: 5961 patients admitted to an 18-bed medical/surgical ICU in the Netherlands from 2004 to 2007.

Methods: All patients had been treated using a computerized insulin algorithm. The incidence rate of ICU death/1000 ICU days was calculated for patients with and without hypoglycemia as was the crude incidence rate ratio (IRR). Daily Sequential Organ Failure Assessment (SOFA) scores were subdivided into tertiles so that mortality rates could be compared for patients with and without hypoglycemia as a function of disease severity. Potential confounders accounted for in the analyses included sepsis, diabetes, and cardiothoracic surgery. Analyses also were adjusted for age and gender and were performed for various cutoff values of glucose levels.

Results: A median of 11 glucose values were collected daily for participants. In this study population, 6.4% of patients died in the ICU. Hypoglycemia was defined as ≤ 45 mg/dL, and 113 patients experienced ≥ 1 episode of hypoglycemia. The incidence ratio for ICU death was 40/1000 ICU days after a hypoglycemic event and 17/1000 ICU days without a hypoglycemic episode (crude IRR, 2.3; 95% CI, 1.8 to 3.1; $P < 0.001$). The risk of ICU death was increased for glucose levels up to 85 mg/dL. For all SOFA levels, the incidence ratios of ICU death were higher after experiencing hypoglycemia. The IRR for ICU death was 1.6 when the APACHE II score was used to correct for severity of disease and 2.1 when the SOFA score was used. The crude incidence ratio was 36/1000 ICU days when patients had only 1 episode of hypoglycemia and 42/1000 ICU days when patients had > 1 episode of hypoglycemia.

Conclusions: After adjusting for severity of disease using the SOFA score, hypoglycemia in the ICU increases the risk of ICU death. A causal relationship between hypoglycemia and ICU death is possible.

Reviewer's Comments: The dilemma intensifies. Several studies have suggested a benefit to tight glycemic control but this is offset by the occurrence of hypoglycemia. Perhaps reducing the level of tight control to 150 to 160 might be optimal. Alternative algorithms for the prevention of hypoglycemia might be useful as well. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Hypoglycemia, ICU, Mortality, Marker, Risk Factor

Print Tag: Refer to original journal article

COPD Helplessness Index Is Valid Predictor of COPD Exacerbation

The COPD Helplessness Index: A New Tool to Measure Factors Affecting Patient Self-Management.

Omachi TA, Katz PP, et al:

Chest 2010; 137 (April): 823-830

Identifying hopelessness in chronic obstructive pulmonary disease patients may reduce exacerbations and lower costs.

Objective: To evaluate the validity of the COPD Helplessness Index (CHI) in predicting chronic obstructive pulmonary disease (COPD)-related hospitalizations and visits to the emergency department (ED).

Participants/Methods: A cohort of 1212 patients with COPD were identified by telephone interview and followed in the research clinic. All had to be members of Kaiser Permanente, aged 40 to 65 years, live within 30 miles of the research center, and have been recently treated for COPD. COPD was defined as treatment for this disease at least once in the past 12 months and at least 2 prescriptions for COPD in that time period. The CHI was adapted from the Arthritis Helplessness Index. Generic physical health-related quality of life (HRQL) and respiratory HRQL were measured by questionnaires. Anxiety was assessed as was COPD severity. The prospective validity of the CHI was associated with COPD emergency health care use. (See the journal article for a description of the questionnaires and the methods of obtaining this information as well as statistical methodology.)

Results: Mean age of participants was 58.2 years, and 57% were women. A table is presented showing other characteristics of the group. CHI scoring varied from 0 to 52. Higher CHI scores correlated with worse health status for QOL, psychological overlay, and severity of COPD as assessed by the Body-Mass, Obstruction, Dyspnea, Exercise Index. A total of 76 hospitalizations and 244 ED visits for COPD occurred over 2.1 years. For every standard deviation increase in the CHI score, the risk of emergency health care use increased by 31%. Surprisingly, the CHI was more predictive of emergency care in those with less severe COPD as opposed to the more severe cases.

Conclusions: The CHI is a valid predictor of emergency health-related care in COPD patients, and its use should be considered in trying to prevent acute exacerbations of COPD.

Reviewer's Comments: This is a very nice study. Whether one uses the CHI or another measure of hopelessness, it is clear those patients who have given up and do not participate in self-management experience more exacerbations and generate higher costs. This is a preventable situation. (Reviewer-Allan R. Goldstein, MD).

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Keywords: COPD Helplessness Index, Self-Management, Measuring Tool

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Agree to Disagree -- Portables vs Polysomnography

Impact of Clinical Assessment on Use of Data From Unattended Limited Monitoring as Opposed to Full-In Lab PSG in Sleep Disordered Breathing.

Masdeu MJ, Ayappa I, et al:

J Clin Sleep Med 2010; 6 (February 15): 51-58

The more severe the sleep-disordered breathing, the more likely that clinicians using either unattended portable monitoring or attended polysomnography will agree on the diagnosis and therapy.

Objective: To ascertain whether multiple sleep clinicians agreed when presented with clinical data with data obtained from unattended limited monitoring (ULM) versus full polysomnography (PSG).

Participants/Methods: 66 patients with complaints referable to sleep-disordered breathing (SDB) and 19 volunteers for 2 nights of ULM followed by PSG were included in the study. Questionnaires and data were presented to 4 sleep-trained clinicians for diagnosis and treatment recommendation. Comparisons were made between clinicians using ULM or PSG and within clinicians comparing both modalities.

Results: For diagnosis, agreement between clinician pairs using a history plus PSG ranged from 74% to 86% compared 66% to 85% for clinicians using a history plus ULM. Agreement for treatment using a history plus PSG was 74% to 86% versus 58% to 77% for treatment using a history plus ULM. The highest respiratory disturbance index (RDI) predicted highest agreement between clinicians and fell off sharply at the lowest RDI for both sets of tools and for individual clinicians using either tool set.

Conclusions: Sleep clinicians have diagnostic disagreements, even when the highest standard (history plus PSG) is available. Regardless of the tools used, agreement was high when the SDB index was elevated and lower when it was in the mild-to-moderate range.

Reviewer's Comments: When patients have severe SDB, looking at data from either unattended studies or attended PSG provide similar and robust agreement between clinicians. However, mild SDB results in low agreement, regardless of the objective tool used (ULM or PSG). The authors suggest that other nonobjective factors are considered by clinicians in making diagnostic and therapeutic decisions. The American Academy of Sleep Medicine Clinical Guidelines for Portable Monitoring recommend moving to attended PSG if an ULM study is negative. These problems of intra-clinician agreement are magnified in centers where portable monitoring is common, but a severely positive unattended portable study is an unambiguous labor-saver in a sleep lab with high volume requirements and limited resources, such as a government system-based laboratory. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep-Disordered Breathing, Polysomnography, Unattended Limited Monitoring

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CT-ANPB, Thoracoscopy Have Unique Applications for ANPB

Medical Thoracoscopy vs CT Scan-Guided Abrams Pleural Needle Biopsy for Diagnosis of Patients With Pleural Effusions: A Randomized, Controlled Trial.

Metintas M, Ak G, et al:

Chest 2010; 137 (June): 1362-1368

CT-guided Abrams needle pleural biopsy is the diagnostic approach recommended for patients with pleural thickening observed on CT. However, medical thoracoscopy should be used for patients with suspected benign pleural pathologies.

Background: When the cytology examination of exudative pleural effusions is nondiagnostic, then an Abrams needle pleural biopsy (ANPB) is recommended. However, when performed blindly, ANPB is diagnostic in only 50% of patients with malignant effusions. To increase the efficacy, needle guidance via medical thoracoscopy has been performed routinely at many clinics. However, the diagnostic sensitivity of the needle biopsy is approximately 80% with real-time CT-guided ANPB (CT-ANPB).

Objective: To determine and compare the diagnostic sensitivity of ANPB when the needle is guided by thoracoscopy versus CT.

Design: Prospective, randomized, parallel study conducted in Turkey between January 2006 and January 2008.

Participants: 124 patients with exudative pleural effusions who required pleural tissue sampling.

Methods: All patients underwent CT scan and then were randomly assigned to either CT-ANPB or thoracoscopy. For CT-ANPB, the most probable lesion area was marked on the patient's skin, as determined by the original CT scan of the thorax.

Results: Thoracoscopy and CT-ANPB were each performed on 62 different patients. The 2 groups were similar for gender, age, distribution of diagnoses, and distribution of malignant cases. For patients with malignant or tuberculous pleural effusions, the diagnostic sensitivity did not differ significantly for the 2 procedures (thoracoscopy, 94.1%; CT-ANPB, 87.5%). A diagnosis could not be achieved in 6 patients undergoing CT-ANPB, but thoracoscopy was able to reach a specific diagnosis in 4 of these patients. A diagnosis could not be achieved in 2 patients undergoing thoracoscopy; however, a specific diagnosis was reached clinically in 1 patient, and the remaining patient was diagnosed via thoracoscopy at the 6-month follow-up when the signs of a malignant disease became abundant. For patients with malignant effusions, the diagnostic sensitivity was 86.8% for CT-ANPB and 95.2% for thoracoscopy (difference not statistically significant). In patients with pleural thickness <1 cm and those with pleural thickness >1 cm, diagnostic sensitivities were not significantly different for the 2 methods. Complications in the CT-ANPB group included hemorrhage (n=1) and pneumothorax (n=1). In the thoracoscopy group, percutaneous emphysema around the entry site occurred frequently.

Conclusions: CT-ANPB is recommended as the primary diagnostic approach for patients with pleural thickening or lesions observed on CT. However, medical thoracoscopy is recommended as the primary diagnostic approach for patients with pleural fluid visible only on CT and for patients suspected of having benign pleural pathologies (other than tuberculosis).

Reviewer's Comments: This study points out strengths and limitations of these 2 procedures. Those with thickening or lesions visible on CT can have CT-guided procedures, while the remaining patients have to undergo thoracoscopy. It is not surprising that a surgical specimen is necessary when the lesions are benign since the path is often very subtle. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Exudative Pleural Effusions, Abrams Needle Pleural Biopsy, Thoracoscopy, CT Guidance

Print Tag: Refer to original journal article

COPD is Under-Diagnosed

Do Symptoms Predict COPD in Smokers?

Ohar JA, Sadeghnejad A, et al:

Chest 2010; 137 (June): 1345-1353

Symptoms are less valuable in predicting chronic obstructive pulmonary disease by spirometry than are age and smoking history.

Objective: To show that chronic obstructive pulmonary disease (COPD) is under-diagnosed and that symptoms of airway obstruction (AO) add little to age and smoking in the predictive value of spirometry.

Participants/Methods: Subjects were recruited from work-related physical exams between 1980 and 2008. Evaluation included questionnaire, chest x-rays, and pulmonary function tests. Cigarette smoking was quantified by pack-years. Symptoms of cough, sputum, dyspnea on exertion, and wheeze were evaluated, and all medications were identified. Diagnoses of asthma, COPD, chronic bronchitis, or emphysema were established. COPD was defined as an FEV₁/FVC ratio <70% in smokers aged ≥40 years. Long-term smokers were defined as having smoked for ≥20 pack-years. Never-smokers or those who smoked <20 pack-years were considered non-smokers. Three groups were established based on spirometry: subjects with COPD (FEV₁/FVC ratio <70%), unaffected smokers with normal spirometry, and restricted smokers. Exclusion criteria were significant pneumoconiosis, mesothelioma, active lung cancer, and any disorder with a predicted life expectancy of <1 year. Variables evaluated were age, pack-years, cough, sputum, wheeze, and dyspnea. Pulmonary diagnoses were based on patient reports. Statistical methods were also described.

Results: Smokers with obstruction were older, smoked more, and had more symptoms than did the other 2 groups. Of 1269 patients with obstruction, 86% were stage II to IV of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). BMI was greater in restricted smokers. Of symptomatic smokers, 92% had symptoms. Symptoms were also present in 76% of smokers with normal and 86% of smokers with restricted spirometry. Asymptomatic smokers with obstruction were GOLD stage II in 62% and GOLD stage III to IV in 10%. Never smokers had a 17% incidence of obstruction; 79% of these subjects had symptoms. Mean FEV₁ for nonsmokers with obstruction was 66.6%, and mean age was 68.2 years. Of 178 nonsmokers with obstruction, 78 never smoked and 100 had a mean pack-year history of 10.5. Those with symptoms had multiple complaints (65% of the group). Cough and sputum was the most common combination. COPD was under-diagnosed in the entire cohort. Those with a previous diagnosis of COPD were more symptomatic, smoked more, were older, and had a lower FEV₁. Those with AO but without a diagnosis of COPD had an 80% incidence of GOLD II or greater. The odds ratio for COPD was greater for smoking history than for symptoms. Presence of symptoms poorly predicted COPD in smokers with AO.

Conclusions: AO is common in long-term smokers aged ≥40 years and is not readily recognized. Symptoms are high in smokers but not sensitive, specific, or predictive of AO.

Reviewer's Comments: This study confirms that spirometry should be considered based on smoking history and age. Waiting for symptoms may be too late to effectively treat a patient. Again, early diagnosis is quality care. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Age, Smoking History

Print Tag: Refer to original journal article

Fat Chance of Snoozing -- Sleep Duration, Obesity

Sleep Duration and Five-Year Abdominal Fat Accumulation in a Minority Cohort: The IRAS Family Study.

Hairston KG, Bryer-Ash M, et al:

Sleep 2010; 33 (March 1): 289-295

Visceral and subcutaneous fat measurements as well as body mass index increases are found in selected U.S. minorities aged <40 years with either long or short sleep duration.

Background/Objective: The authors measured changes in CT-derived visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) measurements to determine whether these changes were associated with sleep duration.

Design/Participants: Longitudinal epidemiologic study of African-Americans (n=332) and Hispanics (n=775) aged 18 to 81 years in 3 U.S. communities.

Methods: The authors examined the relationship between VAT, SAT, and sleep duration.

Results: Body mass index (BMI) and CT of the abdomen were obtained at baseline and 5 years, with sleep duration assessed by questionnaire at baseline (≤ 5 hours, 6 to 7 hours, and ≥ 8 hours). The association between sleep duration and 5-year fat accumulation was examined, adjusting for age, race, gender, activity, calories, smoking, education, and other factors. Age and sleep duration predicted change in fat measures ($P < 0.01$). In subjects aged <40 years, ≤ 5 hours of sleep was associated with greater accumulation of BMI (1.8 kg/m²; $P < 0.001$), SAT (41 cm²; $P < 0.001$), and VAT (13 cm²; $P > 0.01$), compared to 6 to 7 hours of sleep time. Short sleep was associated with the greatest accumulation of fat.

Conclusions: Extremes of sleep duration were related to increases in BMI, SAT, and VAT in persons aged <40 years within this ethnic minority cohort.

Reviewer's Comments: Before this study, precise measures of fat had not been used to correlate short or long sleep duration. The authors chose these 2 ethnic groups because they have a disproportionately high incidence of metabolic disorder (eg, diabetes, insulin resistance), and they note that short sleep is more common in the United States, with minorities particularly affected. Whether we should thereby encourage young persons of color to observe 7 to 8 hours of sleep opportunity and to avoid extremes to help avoid obesity is an open question. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep Disorders, Obesity

Print Tag: Refer to original journal article

Dreamers Breathe -- Nightmare Recall Inversely Proportional to OSA Severity

The Nightmares of Sleep Apnea: Nightmare Frequency Declines With Increasing Apnea Hypopnea Index.

Pagel JF, Kwiatkowski C:

J Clin Sleep Med 2010; 6 (February 15): 69-73

Patients with more severe apnea-hypopnea index report a lower nightmare frequency, suggesting that significant obstructive sleep apnea (OSA) suppresses nightmare recall, which may be a consequence of REM sleep suppression in those with severe OSA.

Objective: To clarify the association of nightmare recall with objective obstructive sleep apnea (OSA) in a sleep laboratory population.

Participants/Methods: 393 subjects underwent clinical polysomnography, including completion of a questionnaire with questions including dream and nightmare recall frequency. Patients had an average age of 50.5 years (range, 13 to 82 years) with 33% of the sample female. Reported dream and nightmare recall was rated as infrequent when reported at less than once monthly, or frequent when reported greater than once weekly.

Results: Average apnea-hypopnea index (AHI) was 34.9 ± 32.0 , indicating a high frequency of severe OSA (AHI >30). Both AHI and apnea index (AI) were significantly greater for the group reporting infrequent nightmare recall ($P=0.000$). As the AHI index increased, the proportion of subjects with frequent nightmare recall decreased in a linear pattern. Reported dreams, as opposed to nightmares, were not significantly correlated to AHI.

Conclusions: Individuals with more severe AHI report a lower nightmare frequency, suggesting that significant OSA suppresses nightmare recall, which may be a consequence of REM sleep suppression in individuals with severe OSA.

Reviewer's Comments: A question often heard in a CPAP clinic serving mental health patients is, "Will my nightmares get better with this?" Those patients, this study suggests, will not be the ones with severe OSA in the first place. The authors suspect that REM suppression in OSA patients is the reason patients report nightmares with decreasing frequency at higher AHIs. Why nightmares and not simple dreams are suppressed by OSA is not clear. Another unanswered question is whether treatment of OSA with CPAP will produce the inverse effect in a given individual, ie, increased nightmare recall. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep Apnea, Nightmare Recall, Parasomnia

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Dyspnea With ADLs in Patients With COPD Is Related to Dynamic Hyperinflation

Dynamic Hyperinflation During Daily Activities.

Hannink JD, van Helvoort HA, et al:

Chest 2010; 137 (May): 1116-1121

Dynamic hyperinflation occurs independent of GOLD stage during real-life daily activities. However, the combination of static and dynamic hyperinflation increases with increasing airflow obstruction.

Objective: To compare the effect of dynamic hyperinflation (DH) on dyspnea with activities of daily living (ADL) in COPD Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages II through IV.

Participants/Methods: 32 clinically stable patients with COPD GOLD stages II through IV were identified in the outpatient clinic. Exclusions included long-term oxygen therapy, respiratory insufficiency, asthma, exercise-limiting comorbidity, or an exacerbation within 4 weeks of the study. Respiratory physiologic studies were measured in the patients' homes by Oxycon Mobile. Patients were instructed to perform an ADL that causes the most dyspnea and perform that ADL until dyspnea occurred that limited them or for a total of 10 minutes. Breathlessness was measured by a 10-point scale; disability by a 0 to 4 scale; and symptoms, functional state, and mental state by a 0 to 6 scale. The Oxycon Mobile is described and the physiologic testing and studies performed are reviewed. Key studies are inspiratory capacity maneuvers performed at rest (IC_{rest}), total lung capacity (TLC), end-expiratory lung volume (Δ EELV) change. These studies allowed for measurement of DH. Statistical methods are described.

Results: Age, gender, body mass index (BMI), and smoking histories were comparable between COPD GOLD stages II through IV. Only 3 patients were not receiving long-acting bronchodilators. GOLD IV patients showed lower IC_{rest} and IC_{rest}/TLC ratios than GOLD II to III patients. Based on the scoring scales, patients with more severe disease were more disabled. GOLD IV patients reached maximum ventilatory capacity but had lower CO₂ production and O₂ uptake. EELV occurred in all GOLD stages. However, the change in EELV was least in GOLD IV consistent with greater resting hyperinflation in that group. DH seemed greater in GOLD III than GOLD IV. Inspiratory reserve volume was smaller in GOLD III to IV than GOLD II. GOLD IV had the highest dyspnea level and the shortest ADL time. The change in EELV was related to IC_{rest}, IC_{rest}/TLC, ventilation, and tidal volume. The change in EELV was not related to FEV₁.

Conclusions: DH occurs in all GOLD stages with less DH in GOLD IV than GOLD II to III. Disability is greater in the higher GOLD stages. Static hyperinflation determines to some degree the DH in performing ADLs. Dyspnea reserve limit and maximal ventilatory capacity were not reached by GOLD II to III. This probably represented lower operating lung volumes.

Reviewer's Comments: This study neatly explains the physiology involved in the dyspnea associated with ADLs in patients with COPD. Paying attention to respiratory patterns and instructing patients on how to breathe may be an important aspect of the care of patients with COPD. In addition, the effectiveness of medication may better be measured by lung volumes and not spirometry. (Reviewer-Allan R. Goldstein, MD).

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Keywords: COPD, Dynamic Hyperinflation, Dyspnea, Activities of Daily Living

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Short Sleep, Weight Creep -- Is There a Link?

A Twin Study of Sleep Duration and Body Mass Index.

Watson NF, Buchwald D, et al:

J Clin Sleep Med 2010; 6 (February 15): 11-17

In this study, short sleep was associated with elevated body mass index (BMI) after adjustment for genetics and shared environment, suggesting an environmental cause of the association between sleep duration and BMI.

Objective: To assess the relative importance of genetic and environmental contributions to the connection between sleep duration and body mass index (BMI).

Participants: Subjects were from the University of Washington Twin Registry, a community-based sample of U.S. twins.

Methods: Twins reported height, weight, and perceived sleep duration. A generalized estimating equation model assessed overall and intra-twin pair effects of sleep duration on BMI. A structural equation model was used to assess genetic and non-genetic contributions to BMI and sleep duration.

Results: 423 monozygotic, 143 dizygotic, and 46 indeterminate twin pairs comprised 1224 twins studied. Mean age was 36.9 years; 69% were female. Multivariate adjusted analysis of subjects demonstrated elevated mean BMI (26.0 kg/m²) in short-sleeping twins (<7 hours/night) compared to twins sleeping 5.0 to 8.9 hours/night (BMI 24.8 kg/m²; $P < 0.01$). The intra-twin pair analysis revealed similar results with the short-sleeping twins having mean BMI 25.8 kg/m² compared to 24.9 kg/m² for the 7.0 to 8.9 hours/night sleep duration group ($P = 0.02$). Intra-twin monozygotic pair analysis also demonstrated elevated BMI in the short-sleeping twins (25.7 kg/m²) compared to the 7.0 to 8.9 hours/night reference group and longer-sleeping twins (≥ 9 hours/night) in the analysis of all twins or the overall intra-twin analyses. The heritability of sleep duration was 0.31 ($P = 0.08$) and BMI 0.76 ($P = 0.01$). Bivariate genetic analysis did not reveal definite evidence of shared genetics between sleep duration and BMI ($P = 0.28$).

Conclusions: Short sleep was associated with elevated BMI after adjustment for genetics and shared environment, suggesting an environmental cause of the association between sleep duration and BMI.

Reviewer's Comments: The results of this study suggest that we clinicians have our work cut out for us in addressing short sleepers, because we can no longer ascribe the condition to genetic factors. The authors postulate self-imposed sleep restriction as a likely cause in many subjects. This article underlines the importance of discussing sleep habits and duration with all obese patients, whether or not obstructive sleep apnea is present. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep Disorders, Obesity

Print Tag: Refer to original journal article

OSAS Promotes CCV Formation

Occurrence of Coronary Collateral Vessels in Patients With Sleep Apnea and Total Coronary Occlusion.

Steiner S, Schueller PO, et al:

Chest 2010; 137 (March): 516-520

Coronary collateral vessel development in patients with occluded coronary arteries is promoted in patients with obstructive sleep apnea syndrome.

Background: Intermittent phases of hypoxia are thought to contribute to alterations of the cardiovascular system.

Objective: To assess whether obstructive sleep apnea syndrome (OSAS) is associated with increased coronary collateral vessel (CCV) formation in patients with total coronary occlusion.

Participants/Methods: 34 patients with total coronary occlusions in any vessel were stratified by apnea-hypopnea index (AHI; >10 = OSAS; <10 = non-OSAS). Collateral vessels were scored by visual analysis, analyzed, and given a Cohen and Rentrop grading system score.

Results: There were no significant differences between groups concerning the prevalence of age, gender, presence of hypertension, smoking, or diabetes. There was no difference in left ventricular systolic function ($P=0.29$) or left ventricular end-diastolic pressure ($P=0.41$). OSAS patients demonstrated a higher Rentrop score compared with non-OSAS patients (1.61 ± 1.2 vs 2.4 ± 0.7 ; $P=0.02$).

Conclusions: CCV development in patients with occluded coronary arteries is promoted in patients with OSAS.

Reviewer's Comments: Augmentation of coronary collateralization is almost intuitive in a population that experiences a saw-tooth pattern of arterial oxygen desaturation each and every night, as do patients with untreated OSAS. Angiogenesis is a response to hypoxia, mediated by vascular endothelial growth factor. The authors postulate that this finding of improved collateralization may explain why patients with OSAS have declining relative mortality after age 50 years. The main take-home point of this article, however, is that OSAS has an apparent mechanism of provoking ischemia (namely, hypoxemia). Similarly, collateralization of coronary vessels is a clear marker of the body's response to cardiac ischemia in the setting of OSAS, particularly in the setting of gross coronary vascular obstruction. (Reviewer-A. Gray Bullard, MD).

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Keywords: Obstructive Sleep Apnea, Coronary Artery Disease

Print Tag: Refer to original journal article



Early Successful Anticoagulation Reduces Hospital, 30-Day Mortality in PE

Early Anticoagulation Is Associated With Reduced Mortality for Acute Pulmonary Embolism.

Smith SB, Geske JB, et al:

Chest 2010; 137 (June): 1382-1390

There is an association between early anticoagulation and reduced mortality rate for patients who present with a pulmonary embolism.

Objective: To determine if there is a time-sensitive interval for diagnosis and treatment in pulmonary embolism (PE) that might affect overall outcome.

Design/Participants: Retrospective study of patients who presented to the emergency department (ED) of a tertiary care center.

Methods: All diagnoses of PE were confirmed by either CT or angiography. All patients were initially treated with IV heparin. Patients in whom heparin was contraindicated were excluded, as were those who had arrived with a prior diagnosis of PE. Standard criteria were used for identification of PE on CT or angiography. The primary outcome of the study was in-hospital and 30-day all-cause mortality.

Results: 400 patients met entrance criteria. Median age was 68 years, and 49% were male. Almost 20% required ICU admission. Median follow-up time was 1400 days. Diagnosis was made on average 2.4 hours after arrival in the ED. Of patients, 260 were diagnosed in the ED, and all of them plus 20 more received heparin. On average, it took just under 11 hours to arrive at a therapeutic drug level from the time of ED arrival. Four patients died prior to receiving adequate dosing of heparin. In-hospital mortality rate was 3%, and 30-day mortality rate was 7.7%. Patients who received heparin in the ED had a lower mortality rate (1.4%) than did those who did not (6.7%) and at 30 days (4.4% vs 15.3%). In addition, those who were therapeutic within 24 hours had a lower mortality rate (5.6% vs 14.8%). Patients who died in the hospital took a longer time to be anticoagulated than did those who survived. Patients with cancer and those with chronic obstructive pulmonary disease also had higher mortality rates.

Conclusions: There was an association between early anticoagulation and reduced mortality rate for patients with PE.

Reviewer's Comments: This is a rather well done retrospective study. The data strongly suggest that patients need to be identified early with PE and treatment started as soon as possible. We also have to consider overdiagnosing PE since the treatment is not without its adverse effects. Most centers can easily get CT scans right away. Evaluating renal function sometimes delays imaging. Patients with comorbidities that can present similarly often appear to confuse the clinician sufficiently to delay the workup. Perhaps establishing an algorithm for evaluation of these patients might be of use. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Early Anticoagulation, Reduced Mortality, Diagnosis

Print Tag: Refer to original journal article

Theophylline Appears to Reduce Inflammation in Lungs of COPD Patients

Treatment Effects of Low-Dose Theophylline Combined With an Inhaled Corticosteroid in COPD.

Ford PA, Durham AL, et al:

Chest 2010; 137 (June): 1338-1344

In this study, theophylline reduced sputum markers of inflammation like neutrophil count and interleukin-8 in COPD patients, but quality of life was not improved.

Objective: To evaluate the effectiveness of the combination of theophylline plus an inhaled corticosteroid (ICS) versus theophylline alone for treatment of chronic obstructive pulmonary disease (COPD).

Participants/Methods: 30 patients with COPD were enrolled and had a run-in period of 2 weeks. All ICSs were discontinued. Patients were randomized to receive either both active drugs or active theophylline plus a placebo ICS. Patients underwent each arm of the treatment for 4 weeks. At the end of the trial, an open-label trial began. Sputum, lung function tests, and quality-of-life (QOL) measurements were evaluated throughout the trials.

Results: 30 patients made up the cohort after patients were removed for missing data or for inability to tolerate withdrawal of the ICS as well as adverse reactions to active medications. On average, patients demonstrated moderate obstruction. Peak plasma theophylline levels were therapeutic in both arms. The data showed no significant reduction in absolute sputum neutrophils but a significant reduction ($P < 0.05$) in sputum total eosinophil counts following treatment with fluticasone propionate (FP) plus theophylline. In addition, the data showed a significant reduction in expression of sputum interleukin-8 following treatment with FP plus theophylline compared with theophylline treatment alone. There was no significant difference in QOL between arms.

Conclusions: Combination therapy with an ICS plus theophylline may result in attenuated airway inflammation in patients with COPD.

Reviewer's Comments: Obviously, it is a bit disappointing in that there was no benefit in QOL in patients who received theophylline when compared to those who received an ICS alone. However, both cellular components and cytokine data suggest a significant reduction in inflammation. Pulmonary function tests also showed some benefit, but this was not statistically significant. Perhaps the problem with the study is duration of follow-up. It might be necessary to continue a treatment like this for months or even years before the reduction in inflammation could show a benefit to patients with respect to QOL or lung function improvement. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Treatment, Theophylline, Inhaled Corticosteroid

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6MWD May Not Reveal Severity of PAH Impairment

Characterization of Pulmonary Arterial Hypertension Patients Walking More Than 450 m in 6 Min at Diagnosis.

Degano B, Sitbon O, et al:

Chest 2010; 137 (June): 1297-1303

Because patients with pulmonary arterial hypertension (PAH) and “near-normal” baseline 6-minute walk distances >450 m benefit from PAH treatments, these patients should be included in future randomized controlled trials of PAH.

Background: Most randomized controlled trials of pulmonary arterial hypertension (PAH) exclude patients with a baseline “near-normal” 6-minute walking distance (6MWD) >450 m. As a result, few data are available regarding characteristics and outcomes associated with this cohort of patients.

Objective: To describe characteristics of and outcomes associated with PAH patients who have a baseline near-normal 6MWD >450 m.

Design: Retrospective record review.

Participants: 49 patients with a near-normal 6MWD >450 at the time of PAH diagnosis and matched PAH patients with a 6MWD ≤450 m.

Methods: Analysis was performed to evaluate the impact of patient characteristics and to examine the relationship between baseline 6MWD and survival.

Results: Patients with a near-normal 6MWD were classified into the World Health Organization (WHO) functional class II (FC II, n=23) or FC III (n=26). Despite their functional class, these patients were similar for age, gender, height, weight, and 6MWD. However, those with FC III had more severe hemodynamic impairment than did those in FC II. In patients with near-normal 6MWD, PAH treatments were initiated, and the first evaluation was performed about 4.7 months later. This evaluation showed that, in these patients, FC improved significantly but 6MWD did not. In the matched controls with baseline 6MWD ≤450 m, treatment was initiated and the first evaluation was performed approximately 4.6 months later. In this group, both FC and 6MWD improved significantly. Improved survival was not associated with 6MWD in patients with baseline near-normal 6MWD, but it was associated with higher 6MWD levels in patients with baseline 6MWD ≤450 m. Patients with 6MWD >450 m were younger, taller, and weighed less than did patients with 6MWD ≤450 m. In addition, patients with baseline 6MWD >450 m tended to have lower body mass indices (BMIs), while patients with baseline 6MWD ≤450 m were more frequently in WHO FC III.

Conclusions: The baseline 6MWD may be >450 m in PAH patients with severe hemodynamic impairment. Patients with near-normal 6MWD tend to be younger and taller and to have lower BMIs than do PAH patients with a baseline 6MWD ≤450 m. PAH treatment may help improve hemodynamic parameters and WHO FC in patients with baseline 6MWD >450 m, although it may not significantly improve the 6MWD. The authors suggest that, because PAH patients with baseline near-normal 6MWD benefit from PAH treatments, these patients should be included in future randomized controlled trials of PAH.

Reviewer's Comments: Interesting study in that it suggests that hemodynamic status and functional status are not always well correlated. This implies that evaluation of both is necessary to determine who might benefit from treatment. Patients with near-normal or normal 6MWD should not be overlooked as potentially benefitting from an intervention. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Near-Normal 6-Minute Walk Distance, Patient Characteristics & Treatment Responses

Print Tag: Refer to original journal article

Obesity Not Risk Factor for Misdiagnosis of Asthma

A Comparison of Obese and Nonobese People With Asthma: Exploring an Asthma-Obesity Interaction.

Parkhale S, Doucette S, et al:

Chest 2010; 137 (June): 1316-1323

In a study of Canadian subjects, obese subjects with asthma were more likely to be male, have hypertension, have a history of gastroesophageal reflux disease, and have a lower FEV₁ when compared to individuals of normal weight with asthma.

Background: In North America, the incidence of asthma has increased 75% during recent decades, as has the incidence of obesity. Most recent studies have concluded that the risk of a new diagnosis of asthma is significantly higher in obese individuals than in normal-weight individuals. However, whether obesity is linked to an increased severity of asthma remains controversial.

Objective: To describe characteristics of obese versus normal-weight individuals who had asthma proven by a diagnostic algorithm and to determine if asthma symptoms were more severe in obese patients than in normal-weight subjects with asthma.

Design: Secondary analysis of data from a study determining the proportion of Canadian adults who were obese versus those who were of normal weight who had an incorrect diagnosis of asthma.

Participants: 496 Canadian patients with physician-diagnosed asthma who were aged ≥ 16 years and who were either obese (body mass index [BMI] ≥ 30) or of normal weight (BMI 18 to 25).

Methods: Participants were randomly selected, and asthma diagnosis was confirmed using a sequential lung function testing algorithm. Characteristics of obese and normal-weight individuals with asthma were compared, and characteristics associated with a misdiagnosis of asthma also were assessed.

Results/Conclusions: The asthma diagnosis was confirmed in 70% of subjects. On univariate analysis, obese patients with asthma were older at the time of first diagnosis, had more prevalent dyspnea and wheeze during the prior 12 months, and had significantly lower lung function than did normal-weight patients with asthma. However, obese and normal-weight patients with asthma were similar for their use of asthma medications, urgent health care use for asthma, highest level of education, and environmental exposure to cigarette smoke, fumes, dust, and pets. Obese subjects with asthma had more gastroesophageal reflux disease (GERD), diabetes, and hypertension than did the normal-weight subjects with asthma. Although the total score for health-related quality of life was similar for obese and non-obese subjects with asthma, the activity subscale score was higher in normal-weight subjects with asthma. On multivariate analysis, obese subjects with asthma were more likely to be male, have hypertension, have a history of GERD, and have a lower FEV₁. Obesity did not appear to be related to receiving a misdiagnosis of asthma (OR of misdiagnosis in obese patients, 1.06). However, among subjects who visited emergency departments or walk-in clinics or who had unscheduled visits to family physicians, obese patients were more likely to be misdiagnosed as having asthma when compared to non-obese subjects.

Reviewer's Comments: Obese patients with asthma have slightly different characteristics than do non-obese patients. Fortunately, it did not appear to result in the misdiagnosis of the disorder unless they were presenting acutely to the emergency department where they might have a more limited database to evaluate patients. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Asthma-Obesity Interaction

Print Tag: Refer to original journal article

Incidence of Swallowing Dysfunction High With PDT

Swallowing Dysfunction in Nonneurologic Critically Ill Patients Who Require Percutaneous Dilatational Tracheostomy.

Romero CM, Marambio A, et al:

Chest 2010; 137 (June): 1278-1282

Approximately 40% of ventilator-dependent tracheostomized patients with a non-neurologic critical illness present with swallowing dysfunction, which is associated with a significant delay in decannulation.

Background: The risk of nosocomial pneumonia resulting from aspiration is significantly increased in patients requiring translaryngeal prolonged intubations. Percutaneous dilation tracheostomy (PDT) currently is the method of choice for critically ill patients. During fiberoptic endoscopic evaluation of swallowing (FEES), aspiration of saliva is seen in approximately one third of tracheostomized critically ill patients.

Objective: To determine the incidence of swallowing dysfunction in non-neurologic critically ill patients with a PDT for prolonged mechanical ventilation.

Design: Prospective observational study performed at a teaching hospital in Chile.

Participants: 40 patients who required PDT because of prolonged mechanical ventilation met the study's inclusion criteria. All patients were admitted between July 2006 and June 2008.

Methods: 2 trained intensivists placed the PDT while patients remained in the ICU. At 3 to 5 days after discontinuing mechanical ventilation, FEES was performed by an otolaryngologist with experience in the evaluation of swallowing. FEES was completed using a flexible fiberoptic rhinolaryngoscope.

Results: Mean patient age was 65 years. Mean APACHE II score was 21 ± 2 , and mean SOFA score was 9 ± 1 . Before PDT, patients were intubated and on mechanical ventilation for a mean of 20 days. FEES was well tolerated and was performed at a mean of 43 ± 13 days of translaryngeal intubation. Swallowing dysfunction was identified in 15 of 40 patients (38%). Silent aspiration was found in 11 of 15 patients (73%). Patient age, number of days of translaryngeal intubation before PDT, and duration of mechanical ventilation were similar for patients with and without swallowing dysfunction. The tracheostomy tube was successfully removed in all patients, but time to decannulation was 19 ± 11 days after FEES in those with swallowing dysfunction and was 2 ± 4 days after FEES in those without swallowing dysfunction. The length of stay in the critical care unit was a median of 69 days in patients with swallowing dysfunction versus a median of 47 days in patients without swallowing dysfunction.

Conclusions: The incidence of swallowing dysfunction in non-neurologic critically ill patients who undergo PDT because of prolonged mechanical ventilation is approximately 40%. Decannulation was significantly delayed in these patients. The authors recommend performing FEES before decannulation or before initiating oral feeding in these patients.

Reviewer's Comments: Not surprising that the combination of prolonged intubation followed by PDT might induce a problem in swallowing. Swallowing evaluation in these patients is probably crucial in order to prevent significant aspiration and a recurrence of ventilatory failure. However, not sure how reliable a FEES study would be in someone who is cannulated. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Percutaneous Dilatational Tracheostomy, Swallowing Dysfunction, Incidence

Print Tag: Refer to original journal article

Perivascular Cuffs Have Big Impact on Lung Compliance

Perivascular Fluid Cuffs Decrease Lung Compliance by Increasing Tissue Resistance.

Lowe K, Alvarez DF, et al:

Crit Care Med 2010; 38 (June): 1458-1466

Perivascular cuff formation reduces dynamic compliance and increases lung "stiffness" by increasing tissue resistance to volume expansion. However, perivascular cuffs do not impact airway resistance.

Background: The pulmonary endothelial cell barrier is disrupted during acute lung injury (ALI). This can cause extravascular fluid accumulation in the lung interstitium, which ultimately decreases pulmonary compliance. The barrier function of the endothelium is not homogenous throughout the lung. For example, the capillary endothelium forms a tighter barrier than does the extra-alveolar arterial and venous endothelium. The permeability of these 2 different variations of endothelium also responds differently to certain stimuli. The impact of perivascular cuffs on lung compliance is not clearly understood.

Objective: To determine how perivascular cuffs influence pulmonary compliance in patients with ALI or acute respiratory distress syndrome (ARDS).

Design: Prospective, randomized, controlled animal-based study.

Methods: 120 intact, sedated, and mechanically ventilated CD40 rats were divided into groups that received rolipram before, after, or not at all with thapsigargin or dimethyl sulfoxide (controls). Assessments were made for arterial blood gas and respiratory mechanics at baseline and again 2 more times after various treatments.

Results: Thapsigargin induced perivascular cuff formation around extra-alveolar vessels but not around capillary segments, and it did not induce alveolar edema. Thapsigargin was associated with a decreased cardiac output (reduced stroke volume via reduced systolic function), but it did not impact blood gases. Therefore, extra-alveolar perivascular cuff formation probably does not result from decreased systolic function. Pretreatment with rolipram prevented the perivascular cuff formation induced by thapsigargin. In studies of lung compliance, thapsigargin reduced dynamic compliance while rolipram pretreatment abolished this decrease in lung compliance. Therefore, perivascular cuff formation reduces dynamic compliance. Perivascular cuffs also were shown to increase lung "stiffness" by increasing tissue resistance to volume expansion. However, perivascular cuffs did not impact airway resistance.

Conclusions: In patients with ALI/ARDS, perivascular cuffs that form along extra-alveolar vessels decrease lung compliance by increasing tissue resistance, but they do not impact airway resistance. Rolipram prevents perivascular cuff formation, therefore it prevents the decreases in lung compliance seen with perivascular cuffs. Further studies are needed to determine the clinical application of using rolipram in patients with ALI/ARDS.

Reviewer's Comments: It has long been suggested that accumulation of water around the terminal bronchi could lead to significant functional impairment of the lungs. Rolipram appears to curtail this. Therefore, it might improve lung function and make it easier to vent patients with ALI. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Acute Lung Injury, Acute Respiratory Distress Syndrome, Perivascular Cuffs, Lung Compliance

Print Tag: Refer to original journal article

Talc-Related Lung Injury Seen in Few Patients

Lung Injury Following Thoracoscopic Talc Insufflation: Experience of a Single North American Center.

Gonzalez AV, Bezwada V, et al:

Chest 2010; 137 (June): 1375-1381

The incidence of talc-related lung injury was approximately 2.8% after using Sclerosol for thoracoscopic talc insufflations, but no cases of acute respiratory distress syndrome were reported.

Background: Pleurodesis is commonly performed for malignant pleural effusions, recurrent pneumothorax, and selected cases of nonmalignant pleural effusions. Talc is considered to be the most effective and least expensive of the various sclerosing agents available for chemical pleurodesis. However, reports have been conflicting regarding the occurrence of lung injury after using talc for pleurodesis.

Objective: To report the incidence of lung injury related to talc use in patients who underwent thoracoscopic talc insufflation (TTI) at a single institution during a 13-year study interval.

Design/Participants: Medical chart review of all patients who underwent TTI between January 1994 and July 2007 at the Lahey Clinic in Massachusetts.

Methods: Throughout the study period, TTI was performed using a single, commercially available sterile talc (Sclerosol®) delivered in single-use pressurized spray canisters. This product was the only talc approved by the United States Food and Drug Administration. Patient records were reviewed to determine outcomes, among other important information.

Results: During the 13-year study interval, 138 patients underwent 142 TTI procedures, which were performed mainly for recurrent pleural effusions. Of the pleural effusions seen, 75.5% were malignant pleural effusions. For patients with malignant pleural effusions, median survival was 5.5 months, and mean survival was 9.5 months. When TTI was performed for benign pleural effusions or pneumothorax, mean survival was >3 years.

Results: Within 72 hours after TTI, respiratory deterioration was reported for 12 procedures (8.5%). Eight of these lung injury cases may have been related to talc use, although this was not a definitive diagnosis. Therefore, charts were reviewed for these 8 cases. A definitive diagnosis of talc reaction was established for 4 cases, and an alternate diagnosis could not be excluded for the remaining 4 cases. Considering only the 4 cases with no alternate diagnosis, the incidence of talc-related injury was 2.8%. No association was found between talc dose and the occurrence of talc-related lung injury. Patients with respiratory deterioration after TTI had respiratory symptoms and increased oxygen requirements. No cases of acute respiratory distress syndrome were reported after TTI. Of the patients who died after TTI, all had advanced underlying malignancy.

Conclusions: Using Sclerosol for TTI may cause talc-related lung injury in a small proportion of patients. However, the authors recommend the use of Sclerosol for performing TTI in the U.S.

Reviewer's Comments: Of all agents available for sclerosing, talc is the most widely used. These data suggest that the incidence of adverse reactions is relatively small, especially considering the patient population. One must also note the short survival times after the procedure. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Pleurodesis, Talc-Related Lung

Print Tag: Refer to original journal article

Married Folks at Lower Risk of Hospitalization for Sepsis

Marital Status and the Epidemiology and Outcomes of Sepsis.

Seymour CW, Iwashyna TJ, et al:

Chest 2010; 137 (June): 1289-1296

Married patients have a lower incidence of hospitalization for sepsis than do widowed, single, and legally separated patients, and they have a lower risk of in-hospital mortality than do single and divorced men and single women.

Background: Many demographic factors, such as age, male gender, and black race, have been associated with an increased incidence of sepsis. Treating patients with sepsis places a large burden on health care resources. To reduce this burden, we need to understand more about social factors that increase the incidence of sepsis. Currently, how a patient's marital status affects the risk and outcomes for patients with sepsis is not known. However, we do know that, in general, being unmarried increases the risk of disease and death for both men and women.

Objective: To determine if marital status is associated with the incidence of hospitalization for sepsis and with hospital mortality related to sepsis.

Design: Population-based cohort of hospital discharge data for 876,963 adults hospitalized in 91 New Jersey hospitals in 2006.

Methods: Data from the Healthcare Cost and Utilization Project 2006 State Inpatient Database for New Jersey were analyzed. Categories of marital status included married, widowed, divorced, single, and legally separated.

Results: The database contained 37,524 hospitalizations for sepsis. Among these patients, 40% were married, 7% were divorced, 26% were widowed, 2% were legally separated, and 26% were single. In 2006, the incidence of hospitalization for sepsis was 5.8/1000 in the general study population, 21.5/1000 among widowed patients, 6.1/1000 for single patients, 5.3/1000 for separated patients, 4.6/1000 for divorced patients, and 4.6/1000 for married patients. After adjusting for age, race, and ethnicity, the greatest incidence rate ratio of hospitalization for sepsis was seen among single individuals when compared to married individuals. Other factors associated with hospitalization for sepsis included male gender, advanced age, Hispanic ethnicity, and non-white race. When investigating hospital mortality associated with sepsis, the highest mortality risk was seen for single and divorced men and for single women when compared to married men. This was true even after accounting for sociodemographic factors and patient comorbidity.

Conclusions: The risk-adjusted incidence of hospitalization for sepsis is greater among widowed, single, and legally separated patients than among married individuals. Among patients hospitalized with sepsis, the odds of in-hospital mortality are greater for single and divorced men and for single women than for married patients. These results suggest that marital status is one of the social factors impacting the epidemiology and outcomes of sepsis.

Reviewer's Comments: Yet another benefit of marriage. It appears that married people fare better than do single people if they are hospitalized for sepsis. Widowed subjects, especially those aged >70 years, have a very high mortality for many diseases; therefore, it's not surprising that there is an adverse effect on sepsis as well. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Sepsis, Marital Status, Risks, Outcomes

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Age-, Sex-, and Race-Based Differences Among Patients Enrolled Versus Not Enrolled in Acute Lung Injury Clinical Trials.

Cooke CR, Erickson SE, et al:

Crit Care Med 2010; 38 (June): 1450-1457

Equivalent enrollment fractions among women and racial/ethnic groups were achieved by the Acute Respiratory Distress Syndrome Network (ARDSNet) trials of acute lung injury. However, the likelihood of enrollment became less as age increased.

Background: Clinical trials of critical illness often underrepresent racial/ethnic minorities, women, and the elderly. Although in 1993, the National Institutes of Health (NIH) Revitalization Act mandated that NIH-sponsored research include minorities and women, these populations remain underrepresented in clinical trials of cancer, cardiovascular disease, and HIV therapies. In addition, we must be mindful that the burden of critical illness tends to be higher in racial/ethnic minorities and the elderly.

Objective: To characterize the participation of women, racial/ethnic minorities, and the elderly in clinical trials of acute lung injury (ALI) and to determine the reasons cited for omitting certain groups from these studies.

Design: Cross-sectional analysis of pooled screening logs from 3 randomized multicentered trials conducted by the Acute Respiratory Distress Syndrome Network (ARDSNet).

Participants: 17,459 ALI patients who were intubated, receiving mechanical ventilation, and screened for inclusion in 1 of 3 ARDSNet studies.

Methods: "Enrollment fraction" was defined as the number of patients enrolled in a clinical trial divided by the total number of patients screened for enrollment. The age and gender of patients was obtained from the screening logs. A patient's race/ethnicity was determined by direct patient examination, medical records, and consulting with family members, resulting in 1 of the following assigned classifications: (1) white non-Hispanic, (2) black non-Hispanic, (3) Hispanic, (4) Asian or Pacific Islander, (5) American Indian/Alaskan Native, or (6) other.

Results: When comparing enrolled versus non-enrolled patients, the authors found that enrolled patients were more likely (1) to be younger, female, and black or Hispanic, (2) to have pneumonia, sepsis, or aspiration as the predisposing risk factor for ALI, (3) to have lower PaO₂/Fio₂ ratios, and (4) to be cared for in a medical rather than surgical ICU. The odds of enrolling any racial/ethnic group were similar to the odds for enrolling white patients. However, in some instances, women appeared to be more likely to be enrolled than men. In addition, the likelihood of enrollment in a study became less as age increased, which appeared to be related to an age-associated increase in comorbid conditions. Blacks, Hispanics, and American Indian/Alaskan Native patients were more likely to be excluded because of an inability to consent or absence of a surrogate.

Conclusions: Equivalent enrollment fractions among women and racial/ethnic groups were achieved by the ARDSNet trials evaluated in this study.

Reviewer's Comments: It is important to have a representative cohort of patients in a research project if we are going to be able to extrapolate the data to a larger cross section of the population. Many drugs we use in the elderly have never been tested on anyone aged >65 years, leading to the possibility that they might be as effective in this group. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Acute Lung Injury Studies, Study Populations, Likelihood of Enrollment

Print Tag: Refer to original journal article

ECMO Survival Benefit Unclear for H1N1-Related ARF

A Systematic Review to Inform Institutional Decisions About the Use of Extracorporeal Membrane Oxygenation During the H1N1 Influenza Pandemic.

Mitchell MD, Mikkelsen ME, et al:

Crit Care Med 2010; 38 (June): 1398-1404

No recommendation can be made for using extracorporeal membrane oxygenation to treat H1N1-associated respiratory failure, but it may be considered alongside other rescue therapies when hypoxemia persists despite optimal mechanical ventilation.

Background: Based on the published experience of hospitals in Australia and New Zealand, extracorporeal membrane oxygenation (ECMO) appears to be a viable rescue therapy for patients with refractory hypoxemia resulting from H1N1-associated respiratory failure. Nonetheless, there are no published evidence-based clinical guidelines regarding the use of ECMO in adults with acute respiratory failure (ARF) or adults with influenza.

Objective: To review the literature regarding use of ECMO in adults with refractory hypoxemia resulting from H1N1-associated respiratory failure.

Design: Systematic literature review.

Methods: 19 potential reports were identified, but after screening for eligibility, only 6 studies were included in this review (including 3 randomized controlled trials).

Results: Only 1 study has been published specifically evaluating use of ECMO in influenza-related ARF. It compared 68 H1N1 patients treated with ECMO to 133 patients on mechanical ventilation. Patients receiving ECMO were selected based on the severity of their condition and were not randomly assigned to this therapy. Patients were mechanically ventilated for a median of 2 days before being placed on ECMO. In these patients, lung injury was considered severe because the level of hypoxemia was severe. Of ECMO patients, 81% required at least 1 rescue therapy. The mortality rate was 23% in ECMO patients and was 13% in non-ECMO patients. During the southern hemisphere's winter of 2009, the incidence of H1N1 cases requiring ECMO was 2.6 per million population in New Zealand and Australia. A meta-analysis was performed for 3 randomized controlled trials with patients having various etiologies for ARF and none reporting influenza or viral pneumonia as the specific cause. In the ECMO group, the relative risk of death or disability at 6 months was 0.69 (95% CI; 0.05 to 0.97), and the relative risk of just death at 6 months was 0.73 (95% CI, 0.52 to 1.03).

Conclusions: Because of insufficient evidence in the existing literature, a recommendation cannot be made for use of ECMO for managing refractory hypoxemia resulting from H1N1-associated respiratory failure. Nonetheless, ECMO may be considered alongside other rescue therapies for patients whose hypoxemia persists despite optimal mechanical ventilation. Further studies are needed.

Reviewer's Comments: ECMO has long been a tool with a lot of intuitive appeal but no real data to support its use. It is too expensive and risky to use as a primary means of oxygenation. Therefore, it suffers from the fate of being used on patients who are almost unsalvageable, leading to association with bad outcomes. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: H1N1-Associated Respiratory Failure, Acute Respiratory Failure, Extracorporeal Membrane Oxygenation, Adults

Print Tag: Refer to original journal article

Are Subsequent PEF Measurements Worthwhile in the ED?

The Utility of Serial Peak Flow Measurements in the Acute Asthmatic Being Treated in the ED.

Henderson SO, Ahern TL:

Am J Emerg Med 2010; 28 (February): 221-223

The improvement in peak expiratory flow that is seen after the first emergency department inhaled treatment appears to describe most of the total improvement seen in mild to moderate asthmatic patients.

Background: Peak expiratory flow (PEF) measurements are more commonly used in the emergency department (ED) than is FEV₁ because of its portability, low cost, and ease of use. It can be a prognostic tool to help predict which patients can be discharged. Prior work has suggested that the change between a person's baseline and first posttreatment PEF measurement accounted for most of the response seen during the patient's ED course.

Objective: To evaluate changes in serial pretreatment and posttreatment PEF values of acute asthmatics in the ED.

Design/Participants: Prospective study, not randomized, involving mild to moderate asthmatics in a large inner-city ED. Patients required a history of asthma, to be aged 18 to 55 years, to have a minimal arrival pulse oximetry of 92% upon ED arrival, and to have clinical signs of acute asthma exacerbation. Exclusion criteria included other cardiopulmonary comorbidities, temperature >100°F, etc.

Methods: PEF (best of 3 trials) was measured before treatment (baseline PEF) and post-inhaled treatments (eg, PEF posttreatment [TX] 1, 2, 3). Beta agonists were given every 20 minutes (as per protocol), usually a total of 3 to 4 treatments. Outcome variables were PEF measurements. Analysis focused on degree of pre- and post-PEF change between each treatment.

Results: 100 total patients were used (43 males); 68% were Latino. The study calculated the total change in PEF values from baseline to post TX 3, and the percent of change after each of the 3 treatments. The change from PEF baseline (pretreatment) to posttreatment (TX 1) represented 86% of the total PEF improvement. The change from post TX 1 to post TX 2 represented 7.5% of the total PEF improvement, and change from post TX 2 to post TX 3 was 8.6%.

Conclusions: The PEF improvement seen after the first ED inhaled treatment appears to describe most of the total improvement seen in mild to moderate asthmatics...and the most important. Subsequent PEF measurements provided little additional value.

Reviewer's Comments: As per the authors, no correlation between outcome and PEF percent of predicted was made or implied, nor was the study done to assess the reliability of common asthma classification schemes but only to evaluate improvements between serial PEF values in response to drug therapy. This article may be useful for people seeing patients in the ED and trying to improve the efficiency of their management. Serial PEF may not be needed after each treatment, but perhaps after the first or last treatment. However, this was a specific, narrow group of patients, and often we see patients who have multiple other problems. Furthermore, more data using controlled studies, broader patient groups, and outcome measures are needed before one can decide how many PEF measurements are actually needed. (Reviewer-Ricky Bajaj, MD).

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Keywords: Peak Expiratory Flow Measurements, Acute Asthma

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