Sedatives in CPAP Titration

Sedative Use During Continuous Positive Airway Pressure Titration Improves Subsequent Compliance: A Randomized, Double-Blind, Placebo-Controlled Trial.

Lettieri CJ, Collen JF, et al:

Chest 2009; 136 (November): 1263-1268

CPAP is subsequently used a higher percentage of nights for more hours per night among patients premedicated with eszopiclone prior to CPAP titration study.

**Background/Objective:** Initial interactions with continuous positive airway pressure (CPAP) may predict subsequent compliance with CPAP. In a previous retrospective study, the authors found that bed premedication with non-benzodiazepine sedative-hypnotic agents during CPAP titration polysomnography independently predicted short-term compliance. To validate these findings, the authors conducted a prospective clinical trial to confirm whether or not premedication with eszopiclone prior to CPAP titration would improve short-term CPAP compliance.

**Design:** Randomized, double-blind, placebo-controlled trial.

**Methods:** Subjects received 3 mg of eszopiclone or matching placebo prior to undergoing CPAP titration. The authors compared the quality of CPAP titrations and objective measures of compliance between the 2 groups during the first 4 to 6 weeks of therapy.

**Results:** Of the 117 subjects, 98 completed the protocol, with 50 subjects in the eszopiclone group and 48 subjects in the placebo group. Compared with placebo, premedication with eszopiclone significantly improved mean sleep latency (87% ± 5.8% vs 80% ± 10.5%, respectively; \( P =0.002 \)) and mean total sleep time (350 minutes ± 33.6 minutes vs 319 minutes ± 48.7 minutes, respectively; \( P =0.007 \)). A trend toward improved sleep latency and the number of residual obstructive events observed at final CPAP pressure during polysomnography was noted. Among subjects treated with eszopiclone on the night of the titration study, CPAP was used on a higher percentage of nights (75.9% vs 60.1%; \( P =0.005 \)) and for more hours per night (4.8 hours vs 3.9 hours; \( P =0.03 \)).

**Conclusions:** On the night of CPAP titration, premedication with eszopiclone improved the quality of titration and lead to significantly greater short-term compliance.

**Reviewer's Comments:** Because sleep studies are so expensive in general and CPAP titration studies in particular, it is important to optimize factors leading to successful titration and subsequent compliance. Until now, most sleep specialists recommended that patients only take sedatives that they usually take prior to a sleep study, but most preferred not to routinely add a hypnotic premedication for the study. This study supports premedication with eszopiclone with initial CPAP titration study. (Reviewer-A. Gray Bullard, MD).

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Keywords: Obstructive Sleep Apnea, CPAP Titration, Eszopiclone, Compliance

Print Tag: Refer to original journal article
Modafinil Ameliorates Sleepiness When CPAP Withdrawn Suddenly in OSA

Modafinil Effects During Acute Continuous Positive Airway Pressure Withdrawal: A Randomized Crossover Double-Blind Placebo-Controlled Trial.

Williams SC, Marshall NS, et al:

Am J Respir Crit Care Med 2010; 181 (April15): 825-831

Neurocognitive function and sleepiness may improve in patients who take modafinil when they are withdrawn suddenly from use of CPAP.

Background: Obstructive sleep apnea (OSA) can have significant impact on the quality of life of individuals. It is also one of the leading causes of motor vehicle accidents. Compliance with treatment is, at times, not very good because continuous positive airway pressure (CPAP) is difficult to endure for long periods of time. When patients travel, it is often difficult to bring the CPAP device with them as it is somewhat cumbersome. Therefore, these patients often find themselves without the benefit of CPAP for several days in a row, and because of this, they suffer with the daytime somnolence associated with OSA.

Objective: To determine whether modafinil, a medication known to enhance wakefulness, might be able to be used in order to bridge the gap between removal of CPAP and reinstatement.

Methods: The participating patients were studied at a sleep laboratory where they were admitted for 3 consecutive nights. CPAP was used during the first night, and then only nasal airflow was used during the subsequent 2 nights. Before sleep, the patients were trained on a driving simulator and a psychomotor vigilance test. On the evenings without CPAP, a nasal airflow device was used to quantify the significance of the sleep apnea. On the days without CPAP, the patients received 200 mg of modafinil or placebo. Patients repeated the protocol after approximately 5 weeks during which time they were using CPAP at home. After breakfast on the day that they received medication, they underwent the 20-minute driving simulation and the psychomotor tests.

Results: 23 patients were recruited for the study. Interestingly, there was no difference in the sleep architecture during the first night without CPAP, but there was a significant difference during the second night. Patients who received active medication had improved steering variability and performed overall significantly better on the driving simulator than patients who received placebo.

Reviewer's Comments: Obviously, this is a significant study, but it suffers from a very small patient population. The modafinil significantly improved the neurocognitive performance of patients who were unable to use CPAP the previous night. Unfortunately, neurocognitive function is only 1 of the side effects associated with patients with sleep apnea. I do not think that the authors in any way, shape, or form are advocating the replacement of CPAP with a drug like the modafinil. However, in the circumstance where a patient might be unable to use CPAP for a day or 2, the use of this medication might significantly improve their mental function and driving ability and thereby improve quality of life and potentially prevent significant injury. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: OSA, CPAP Withdrawal, Modafinil

Print Tag: Refer to original journal article
Treatment of psychological symptoms improves asthma control in adult patients. Therefore, the physician must take the time to completely evaluate the patient and teach him/her about asthma and its triggers.

**Objective:** To determine the prevalence and risk factors of psychological stress in asthma patients.

**Methods:** Data collected by the National Health Interview Survey (NHIS) between 2001 and 2007 were used. Patients were included if they were ≥18 years of age, had lifetime or current asthma, psychological distress, and other covariates. Demographics included race/ethnicity, age group, educational level, marital status, employment status, and income level. Health-related factors considered were smoking habit, alcohol use, body mass index, and chronic health conditions. The Kessler 6 Nonspecific Psychological Distress Scale and the Health and Activities Limitation Index were used to further evaluate the patients. Statistical methods are described.

**Results:** 187,000 patients were reviewed. Asthma patients tended to be female, non-Hispanic black, family income below federal poverty level (FPL), not working, not married, current smokers, and obese. The incidence of psychological distress was 7.5%, more than twice the 3% average of the U.S. population. Whereas 8.4% of the U.S. population has ≥3 health-related comorbidities, 21.5% of this group had ≥3 comorbidities. As psychological distress increased, activity and quality of life (QOL) decreased. Psychological stress interfering with QOL was more frequent in women aged 35 to 64 years, Hispanics, those with some high school education, those below the FPL, previously married individuals, and those not working. Nonworking adults and adults below the FPL had psychological distress that was 4 and 5 times the average, respectively. Psychological distress was higher in current smokers, obese individuals, patients with former alcohol use, or those having at least 3 comorbid health conditions. Effects of body mass index and marital status were not significant.

**Conclusions:** Psychological distress adds to the symptoms of asthma and makes treatment more difficult. Patients at greatest risk are those who are current smokers, not working, below the FPL, Hispanic, and those with ≥3 comorbidities.

**Reviewer’s Comments:** This study documents what we see in clinical practice. Asthma in adults rarely presents as a single problem. Successful treatment requires time to fully evaluate the patient and treat the whole patient, not just the asthma. Patients who go to the emergency department, are admitted to the hospital, or have unscheduled office visits should be considered to need pulmonary consultation. Asthma can be controlled if the physician has time to completely evaluate the patient and teach the patient about asthma and its triggers. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Psychological Distress, Prevalence, Risk Factors

Print Tag: Refer to original journal article
Short Sleep Makes Men Fat

**Association of Short Sleep Duration With Weight Gain and Obesity at 1-Year Follow-Up: A Large-Scale Prospective Study.**

Watanabe M, Kikuchi H, et al:

Sleep 2010; 33 (February): 161-167

Short sleep duration is associated with weight gain and the development of obesity over 1 year in men, but not in women.

**Objective/Participants:** To investigate the association between short sleep duration and elevated body mass index (BMI) and obesity in a large sample of Japanese adults over a short period.

**Methods:** 35,247 company employees of an electric power company in Japan were evaluated at workplaces distributed throughout Japan. The participants’ measured height and weight, as well as self-reported sleep duration, were obtained at annual health checkups in 2006 and 2007. Sleep duration was assessed by questionnaire. Reference sleep duration was 7 to 8 hours. Short sleep duration was defined as <5 hours of sleep and 5 to 6 hours of sleep, while long sleep duration was defined as ≥9 hours.

**Results:** Compared to the reference sleep duration, short sleep duration (<5 hours and 5 to 6 hours) and long sleep duration were associated with an increased risk of weight gain among men after adjustment for covariates. Among men with a BMI <25 at baseline, 5.8% became obese (BMI ≥25) 1 year later. A higher incidence of obesity was observed among the groups with shorter sleep duration. The adjusted odds ratio for development of obesity was 1.91 for men who slept <5 hours and 1.50 for men who slept 5 to 6 hours. No significant association between sleep duration and weight gain was observed for women.

**Conclusions:** Short sleep duration was associated with weight gain and the development of obesity over 1 year in men but not women.

**Reviewer’s Comments:** This study demonstrated no relation between short sleep duration and weight gain and obesity on 1-year follow-up in women, although the cross-sectional analysis did show a significant association. Previous studies have also shown a significant association between short sleep duration of <7 hours and BMI compared with sleeping time of 7 to 8 hours in both men and women. However, this study is limited by reliance on questionnaire and the absence of objective measurement of sleep duration (eg, polysomnography). Also, the data may not be generalizable across ethnic groups. The mechanism of weight gain in sleep deprivation is postulated to be related to orexin (hypocretin) produced by neurons in the hypothalamus which regulate feeding and wakefulness. The decrease in leptin and increase in ghrelin with short sleep duration may act to increase orexin activity, leading to higher food intake. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep Duration, Insufficient Sleep, Obesity

Print Tag: Refer to original journal article
In women with asthma, obstetrical and fetal outcomes are negatively affected by cigarette smoke.

 Objective: To estimate the effect of active and passive cigarette smoke on obstetrical and neonatal outcome.

 Design: Secondary analysis of 2 separate studies done on pregnant women with varying severity of asthma.

 Methods: One study was observational and included 906 women in each group of mild or moderate/severe asthma. The second study compared the use of beclomethasone by inhalation versus oral theophylline in moderate asthma. Data were collected between December 1994, and February 2000. The observational study included an equal percentage of smokers in both arms. Exclusion criteria are clearly defined. A questionnaire was used to define if the pregnant woman was an active smoker and if she was exposed to household passive smoke. In the interventional study, urinary cotinine was measured. Obstetrical outcomes were determined by chart review. Patients were evaluated by spirometry, symptom log diary, asthma exacerbations, hospitalizations, emergency department visits, unscheduled office visits, and treatment with oral steroids. Methods of analysis are described.

 Results: 2,210 asthmatic women were enrolled (87 were lost to follow-up). Of these, 18% were current smokers and reported a median number of 6 cigarettes smoked per day (maximum, 40 cigarettes smoked per day). Among the nonsmokers, 36% reported passive household tobacco smoke exposure, while 46% reported no passive smoke exposure. Smokers were more likely to be white and use marijuana or cocaine; they were less likely to have private health insurance. Nonsmokers with household exposure were younger than those in the other groups. Smokers had more symptomatic days and more restriction of daily activities. No differences in asthma exacerbations or hospitalizations were noted between smokers and nonsmokers, and no significant differences in spirometry were found between groups. Obstetrical and neonatal outcomes revealed the following. Asthmatic women who smoked had a higher incidence of small for gestational age (SGA) and perinatal mortality. Percentage-wise, there were more than twice as many perinatal deaths than in the nonsmoking, nonexposed group. Both pre-eclampsia and SGA were related to maternal smoking. Cotinine levels were highest in current smokers, and were twice as high in nonsmokers with passive exposure as opposed to nonsmokers without household exposure. There was a negative correlation between increasing cotinine levels and birth weight. Perinatal death rate and cotinine levels were unrelated.

 Conclusions: Cigarette smoking has an adverse effect on the fetus as represented by SGA and neonatal mortality. Passive household exposure seems less dangerous.

 Reviewer's Comments: This study proves the danger of smoking in pregnant asthmatics. I am also concerned as to whether or not marijuana or cocaine use contributes to the observed outcomes. Pregnant women, in my opinion, should be screened for cigarette use and recreational drug use. Maybe neonatal death or deformity is "mother induced" and not doctor caused. Despite the data, household smokers should be encouraged to quit cigarettes and protect the mother and fetus from harm. (Reviewer-Allan R. Goldstein, MD).
OSA Patients Have Ventilatory Control Instability

Increased Propensity for Central Apnea in Patients With Obstructive Sleep Apnea: Effect of Nasal Continuous Positive Airway Pressure.

Salloum A, Rowley JA, et al:

Am J Respir Crit Care Med 2010; 181 (January 15): 189-193

Ventilatory control instability is reversible with the use of continuous positive airway pressure.

**Background/Objective:** There is increasing evidence of increased ventilatory control instability in individuals with obstructive sleep apnea (OSA), but whether the hypocapnic apnea threshold is altered is unknown. The authors compared the apnea threshold, CO\(_2\) reserve, and controller gain between subjects with and without OSA matched for age, sex, and body mass index.

**Methods:** Hypocapnia was induced via nasal mechanical ventilation for 3 minutes. Cessation of mechanical ventilation resulted in hypocapnic central hypopnea or central apnea, depending upon the magnitude of the hypocapnia. The apnea threshold was defined as the measured end-tidal CO\(_2\) partial pressure (PETCO\(_2\)) at which the apnea closest to the last hypopnea occurred. The CO\(_2\) reserve was defined as the change in PETCO\(_2\) between the end-tidal CO\(_2\) pressure during normal breathing and the apnea threshold. Controller gain was defined as the ratio of change in minute ventilation between control and hypopnea or apnea to the change in end-tidal CO\(_2\) pressure.

**Results:** 11 pairs of subjects were studied. There was no difference in apnea threshold between the 2 groups. However, the CO\(_2\) reserve was smaller in the subjects with OSA compared with the control subjects (\(P <0.001\)). The controller gain was increased in the subjects with OSA compared with the control subjects (\(P <0.001\)). Controller gain decreased and CO\(_2\) reserve increased in 7 subjects restudied after using continuous positive airway pressure for 1 month.

**Conclusions:** Ventilatory control instability is higher in subjects with OSA and is reversible with the use of continuous positive airway pressure (CPAP).

**Reviewer’s Comments:** It is important to parse what the investigators are saying about OSA patients: Ventilatory control, as defined here, is not simply the mechanically disordered sleep ventilation of OSA subjects. Rather, the investigators refer to the medullary ventilatory drive and control mechanism. These findings are relevant to the pathogenesis of complex sleep apnea (emergence or persistence of central sleep apnea upon alleviation of upper airway obstruction with nasal CPAP). (Reviewer-A. Gray Bullard, MD).

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Keywords: OSA, Central Apnea, CPAP

Print Tag: Refer to original journal article
Objective: To determine the optimal choice of chest tube size for the treatment of pleural infection.

Methods: The Multi-Center Intrapleural Streptokinase Trial (MISTI) determined that the use of streptokinase intrapleurally did not improve outcome in pleural infection when compared to placebo. Using the same 454 patients, the effect of chest tube size on outcome was reviewed. Patients with macroscopic purulence, positive bacterial culture, positive Gram stain for bacteria, or a pH <7.2 were included. Outcome measures were death, need for thoracic surgery, length of hospital stay, chest x-ray improvement, FEV₁ and FVC at 3 months, and adverse events. Chest tube size and method of insertion were at the discretion of the treating physician. Care of the chest tube and pressures used are described. Pain experienced by the patient, while the tube was in place and on removal, was recorded. The method of analysis is described.

Results: At 12 months, there was no difference in deaths or need for thoracic surgery related to tube size. Increased mortality was related only to low albumin despite previous literature suggesting risk factors to also be related to bacteria cultured, urea level, age, low diastolic blood pressure, and hospital-acquired infection. No difference in death or the need for thoracic surgery between those who received streptokinase or placebo was found. Length of hospital stay, FEV₁, FVC, or residual on chest x-ray did not change based on tube size. The method of tube insertion did not affect outcome. At 12 months, there was a difference in death or need for surgery favoring the smaller tubes. Pain was rated greater by the patient on insertion and while in place (but not on removal) with larger chest tubes. Adverse events and tube displacement did not vary based on tube size.

Conclusions: Smaller bore chest tubes, properly maintained, have no increase in death or need for thoracic surgery and are associated with less pain.

Reviewer’s Comments: This is a very nice study and should be heeded. Reduction of pain without sacrificing quality or outcome is great for the patient. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Pleural Infection, Chest Tube Size

Print Tag: Refer to original journal article
Sildenafil in COPD

Hemodynamic and Gas Exchange Effects of Sildenafil in Patients With Chronic Obstructive Pulmonary Disease and Pulmonary Hypertension.

Blanco I, Gimeno E:

Am J Respir Crit Care Med 2010; 181 (February 1): 270-278

In patients with COPD and PH, sildenafil improves pulmonary hemodynamics; however, it also lowers arterial oxygenation at rest.

**Background:** Pulmonary hypertension (PH) frequently develops in patients with chronic obstructive lung disease (COPD). In patients with COPD, PH generally first appears during sleep and exercise. Subsequently, the PH may be present at rest. The presence of PH in patients with COPD has a number of adverse effects. These patients have more frequent exacerbations, consume greater health-care dollars, and have a shorter survival.

**Objective:** To evaluate hemodynamic and gas exchange effects of sildenafil in patients with PH and COPD.

**Design:** Prospective, randomized dose comparison of effects of single doses of sildenafil.

**Methods:** The acute effects of a single dose of sildenafil on pulmonary hemodynamics and gas exchange in patients at rest and with submaximal exercise were evaluated. Twenty patients with COPD agreed to participate. Right heart catheterization was performed to confirm the presence of PH. One patient had severe PH with mean pulmonary artery pressure of 61 mm Hg. In the remaining patients, the mean pulmonary artery pressure ranged from 21 to 34 mm Hg.

**Results:** At rest, sildenafil produced significant vasodilatation in both pulmonary and systemic circulation. There was a greater effect in pulmonary circulation. The mean pulmonary artery pressure fell 6 mm Hg. Gas exchange worsened after sildenafil. During exercise, sildenafil produced significant pulmonary vasodilatation. The mean pulmonary artery pressure fell 11 mm Hg. During exercise, gas exchange did not worsen after sildenafil.

**Conclusions:** Sildenafil improved pulmonary hemodynamics at rest and with exercise. There was deterioration in oxygenation at rest due to increased V/Q mismatching. During exercise, however, there were no adverse effects on gas exchange. There was no difference between the 20- and 40-mg doses of sildenafil.

**Reviewer's Comments:** It would certainly seem worthwhile to evaluate in a double-blind randomized trial the effects of chronic sildenafil administration in patients with COPD and PH. In particular, it would seem appropriate to study those patients whose PH seems "out of proportion." The effects of sildenafil on gas exchange may be different in other forms of chronic lung disease. In 16 patients with idiopathic pulmonary fibrosis and PH, sildenafil caused pulmonary vasodilatation and resulted in an improvement in gas exchange. (Reviewer-Richard A. Nusser, MD).

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Keywords: COPD, Hemodynamics, Gas Exchange

Print Tag: Refer to original journal article
Activated Protein C in Sepsis -- Does It Help?

Activated Protein C and Hospital Mortality and Septic Shock: A Propensity-Matched Analysis.

Lindenauer PK, Rothberg MB, et al:

Crit Care Med 2010; 38 (April): 1101-1107

In patients presenting with septic shock, early treatment with activated protein C may reduce hospital mortality.

**Background:** Severe sepsis is a significant medical problem encompassing about 10% of all admissions to the ICU. Mortality ranges from 30% to 50%, and the annual cost in the United States is estimated at $17 billion. Obviously, any therapeutic intervention that could reduce the risk of mortality in this devastating sickness would be of significant importance. Activated protein C has undergone 2 large randomized trials. The first one demonstrated approximately a 6% absolute reduction in mortality but a 1.5% increase in the risk of bleeding. In the second study in which patients were enrolled who were not necessarily severely ill, no obvious benefit was seen.

**Objective:** To analyze the benefit of activated protein C in a propensity-matched analysis.

**Participants:** Patients were included in the study if they were aged ≥18 years. All patients had a principal or secondary diagnosis of sepsis. Patients were excluded if they developed sepsis after hospital day 2. Patients were also excluded if they were transferred from another facility.

**Methods:** Standard laboratory and demographic data were obtained for all patients. Medical records were viewed to determine whether patients received activated protein C within the first 2 days of hospital admission. Any patients who received at least 24 hours of infusion were considered to have been treated with activator protein C. The primary outcome was in-hospital mortality.

**Results:** 404 hospitals participated in the study, which was retrospective in nature; 33,000 patients met the eligibility criteria. Almost 50% of patients required mechanical ventilation. The median length of stay was 9 days. On average, patients stayed 4 days in the ICU and received vasopressors for approximately 2 days. Only 5% of patients received activated protein C. Patients who received the drug tended to be a bit younger, were more likely to be Caucasian, were more likely to be married, and had fewer co-morbidities. Patients who received activated protein C had a 6% absolute reduction in mortality. This was not associated with an increased risk of bleeding.

**Conclusions:** In patients presenting with septic shock, early treatment with activated protein C may reduce hospital mortality.

**Reviewer's Comments:** This study, similar to the first trial, demonstrated approximately a 6% overall absolute reduction in mortality. Unlike the first study, there was no significant increased risk of hemorrhage. The patient population in this study was similar to the population in the first study. However, the second study, which did not demonstrate an improvement, had significantly more patients who were not quite as sick. These more recent data, therefore, suggest that activated protein C can offer a modest but significant improvement in outcomes in patients with severe sepsis. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Severe Sepsis, Activated Protein C

Print Tag: Refer to original journal article
Guidelines for Managing Subsolid Pulmonary Nodules

Subsolid Pulmonary Nodules and the Spectrum of Peripheral Adenocarcinomas of the Lung: Recommended Interim Guidelines for Assessment and Management.

Godoy MCB, Naidich DP:

Radiology 2009; 253 (December): 606-622

There are 2 types of subsolid nodules, pure ground-glass nodules and part solid-part ground glass nodules; these 2 types have different pathologic and prognostic implications.

**Background:** It seems logical that the earlier a lung cancer is diagnosed, the better chance it can be cured. With the advent of CT and multi-detector CT, it was hoped that screening utilizing these modalities would produce a decline in lung cancer mortality. Whether screening for lung cancer with multi-detector CT scans will achieve this goal remains a highly controversial question. What is clear is that screening for lung cancer will detect many unsuspected nodules. In the initial report of the Early Lung Cancer Action project, most nodules discovered on screening were solid nodules. Only 19% of nodules found were characterized as subsolid nodules.

**Objective/Design:** Review of the recent literature to develop guidelines for the management of subsolid nodules.

**Discussion:** Adenocarcinoma is the most common type of lung cancer. Bronchoalveolar cell carcinoma exhibits a unique growth pattern along the alveolar septa without stromal invasion. Atypical adenomatous hyperplasia is defined as focal lesion often ≤5 mm in diameter in which involved alveoli are lined by monotonous slightly atypical epithelial cells with dense nuclear chromatin, inconspicuous nucleoli, and scant cytoplasm. In 1995, Japanese pathologist Noguchi proposed a histological classification for small peripheral adenocarcinomas that included 6 subtypes (A through F) that were based on the patterns of tumor growth. Despite the close correlation between CT appearance and pathology, considerable overlap exists. There are a number of studies in the literature suggesting that the percentage of ground-glass opacity in a lesion corresponds to the bronchoalveolar cell component of the lesion. Mean doubling time for adenocarcinomas is longer than other cell types.

**Results:** The greater the bronchoalveolar cell component of the lesion, the more favorable the prognosis. It is not always easy to accurately measure the size of subsolid nodules. Sometimes an increase in attenuation of the lesion without any change in overall size may reflect significant interval change. The role of PET scanning to assess lesions with predominantly ground-glass opacity has yet to be established. There appears to be a very limited role for transbronchial or transthoracic needle biopsy in the management of subsolid nodules. Due to recent data documenting the markedly improved 5-year survival of patients with subsolid nodules, studies have been undertaken to evaluate the efficacy of partial wedge resections and segmentectomies for subsolid nodules.

**Conclusions:** The optimal time and duration of follow-up imaging studies for patients with subsolid nodules remains to be determined. Improved methods are needed to accurately measure poorly or irregularly marginated lesions.

**Reviewer's Comments:** This article did a superb job of collating a wealth of information on subsolid nodules, and pulmonary physicians will find it well worth reviewing. (Reviewer-Richard A. Nusser, MD).

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Keywords: Lung Cancer, CT

Print Tag: Refer to original journal article
Swallowing assessments are recommended after prolonged intubations.

**Background:** The risk of oropharyngeal dysphagia appears to be elevated in patients on prolonged ventilation. Whether this dysphagia is caused by the endotracheal tube (ET), the underlying medical condition, or some combination of the two is unknown.

**Objective:** To determine the incidence of post-ET dysphagia in various diagnostic groups to determine if dysphagia is associated with the duration of intubation and to describe patient characteristics associated with dysphagia.

**Design:** Systematic literature review.

**Methods:** The authors reviewed articles that reported on oropharyngeal dysphagia in adults (age >18 years) who underwent endotracheal intubation while hospitalized. Articles assessing patients with neurogenic or head and neck diagnoses or with tracheotomies were excluded.

**Results:** 14 articles were accepted for analysis. Swallowing assessments were conducted between 24 and 48 hours after intubation in 6 studies. In studies using chest radiographs to assess swallowing, the radiographs were taken at 2 minutes, 30 minutes, and 1 hour after oral contrast ingestion. In all 14 studies, the dysphagia frequency ranged from 3% to 62% after extubation. In patients with prolonged intubation (>48 hours), the dysphagia frequency ranged from 10% to 56%. One of the 14 studies showed that longer intubation times were recorded for those without dysphagia (mean, 288 hours) than for those with dysphagia (mean, 254 hours). This finding could not be corroborated in the other studies. Evidence in the 14 studies was insufficient for reporting the frequency of dysphagia across a range of intubation durations. No single diagnosis was associated with an increased risk of dysphagia. The surgical and medical risk factors associated with dysphagia included congestive heart failure, functional status, hypercholesterolemia, increased ICU or hospital length of stay, multiple intubations, increased operative time, perioperative transesophageal echocardiography, and sepsis. Factors that were not associated with dysphagia included smoking status, urgency of surgery, APACHE scores, chronic obstructive pulmonary disease, circulatory shock, gastroesophageal reflux, hypertension, ICU readmission, and myocardial infarction.

**Conclusions:** The dysphagia frequencies ranged from 3% to 62%, and this wide range most likely results from the variations in study designs seen in the 14 studies analyzed. No single diagnosis was linked to an increased risk of dysphagia after extubation. The authors recommend swallowing assessments for patients undergoing prolonged intubation durations. Further studies are needed to determine the effects of prolonged intubation and various medical comorbidities on the risk of dysphagia in intubated patients.

**Reviewer's Comments:** Nutrition is a key factor to a patient’s eventual recovery. Using the gastrointestinal tract is the way to go. Post-intubation dysphagia appears to be a problem, but its magnitude is uncertain even after a review of the literature, perhaps because the definition of dysphagia varies so much. (Reviewer-Eric H. Gluck, MD, JD).
Although the LAS has decreased lung transplant waiting list mortality and time, the system needs reviewing because elevated LAS scores are linked to decreased survival in the first year after transplant.

**Background:** In an effort to improve lung allocation and transplant outcomes, the lung allocation score (LAS) was implemented. This score balances expected survival on the lung transplant waiting list (medical urgency) and expected survival during the first year after lung transplantation, placing a greater emphasis on waiting list survival than on post-transplant survival. Since its implementation, the LAS has been associated with decreased waiting list mortality, decreased waiting list time, no effect on survival, higher rates of primary graft dysfunction, and increased ICU stays.

**Objective:** To determine the postoperative morbidity and mortality rates associated with extremely high LAS at the time of lung transplantation.

**Design:** Retrospective analysis of data from the Thoracic Registry of the United Network for Organ Sharing.

**Participants:** Lung transplant recipients aged ≥12 years who underwent lung transplantation for end-stage pulmonary disease between April 2006 and December 2007.

**Methods:** All patients were subclassified into 1 of 3 groups based on their LAS: LAS <50 (low LAS); LAS 50 to 75 (intermediate LAS); and LAS ≥75 (high LAS). The maximum LAS was 100. Using these various designations, postoperative survival at 1 year, length of stay during transplant hospitalization, and in-hospital complications were determined. The in-hospital complications included primary graft failure (PGF) at 30 days, dialysis, antibiotic-treated infection, airway dehiscence, and stroke.

**Results:** 3161 patients had low LAS, 411 had intermediate LAS, and 197 had high LAS. Survival at 90 days and 1 year was significantly worse for high LAS recipients than for low LAS recipients. An elevated LAS was associated with decreased survival, regardless of the cause of lung disease requiring transplantation. Patients with high LAS were more likely to require dialysis or develop infection than were those with low LAS. However, the rates of PGF, airway dehiscence, and stroke were not significantly different between the 3 LAS categories. Length of stay during transplant hospitalization was longer for patients with high LAS than for those with low LAS.

**Conclusions:** An elevated LAS is associated with decreased survival rates during the first year after transplantation, higher morbidity rates, and a longer length of stay during transplant hospitalization. Survival is worse for increasing LAS for all causes of lung disease requiring transplantation, but especially for patients with chronic obstructive pulmonary disease and pulmonary fibrosis. A review of the LAS system is needed to help improve long-term transplant survival.

**Reviewer's Comments:** This study sort of points out the obvious. While we want to wait to the last possible time to transplant a patient, once he/she reaches a critical condition, multisystem effects probably take affect and result in poorer outcomes. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Lung Allocation Score, Survival, Outcomes

Print Tag: Refer to original journal article
When compared with sputum eosinophil counts, fractional concentrations of nitric oxide do not appear to be a reliable alternative for investigating occupational asthma.

**Background:** In patients with moderate to severe asthma, treatment based on sputum eosinophil counts is associated with a reduction in asthmatic exacerbations as compared to treatment based on symptoms and spirometry. However, sputum induction can be a time-consuming test that is not readily available. Exhaled nitric oxide is considered to be a surrogate marker for eosinophilic inflammation in asthma, and these tests are readily available.

**Objective:** To determine if changes in fractional concentrations of exhaled nitric oxide (FENO) levels correlate with sputum eosinophil counts after exposure to offending agents in patients with occupational asthma (OA).

**Design:** Comparison of testing results conducted at a hospital in Canada and a second hospital in Belgium.

**Methods:** Inhaled corticosteroids (ICS) were given once daily in Canada but were discontinued 72 hours before the specific inhalation challenge (SIC) in Belgium. Long-acting β-2 agonists were stopped 72 hours before SIC in both hospitals. For each patient, the sputum cell counts and FENO levels were determined at 24 hours after exposure to a sham agent (control day) and again at 7 and 24 hours after exposure to the offending agent. The SIC was considered positive if FEV1 decreased ≥20% after exposure to the offending agent.

**Results:** Of the 68 adult patients entered into the study, 46 had a negative SIC, 26 had a positive SIC (had OA), and 1 had undetermined results. Baseline sputum eosinophil counts and FENO levels were higher in SIC-positive patients than in SIC-negative patients. At 24 hours after exposure to the offending agent, SIC-positive patients showed increases in both the sputum eosinophil counts and FENO levels, whereas SIC-negative patients did not show these increases. Overall, after exposure to the offending agent, the increase in sputum eosinophil counts occurred 7 hours after exposure, while the increases in FENO levels occurred 24 hours after exposure in SIC-positive patients. Treatment with ICS did not appear to affect sputum eosinophil counts in SIC-positive patients, but it may have suppressed FENO levels at 1 of the 2 hospitals.

**Conclusions:** Both sputum eosinophil counts and FENO are increased in patients with a positive SIC after exposure to occupational agents. These increases are not seen in SIC-negative cases. However, increases in sputum eosinophil counts occur more quickly and to a greater magnitude than do increases in FENO levels in SIC-positive patients. Therefore, sputum eosinophil counts appear to be more reliable for interpreting SICs than are FENO levels.

**Reviewer’s Comments:** We are always looking for a more reliable indicator of airway reactivity. It would appear from this study, that sputum eosinophilia is very reliable in this patient population and relatively easy to come by. (Reviewer-Eric H. Gluck, MD, JD).
Air pollution levels are positively associated with the prevalence and incidence of asthma in children. The incidence of asthma is highest during the first year after birth, but it then remains relatively constant until age 8 years.

Background: The prevalence of respiratory symptoms as they relate to exposure to traffic-related pollutants change rapidly during childhood. Existing birth cohort studies may not have analyzed the incidence of asthma over long enough study intervals to assess the long-term effects of traffic-related pollutants on childhood asthma.

Objective: To report the incidence of asthma as it relates to traffic-related pollutants in children during the first 8 years after birth.

Design: Reporting of data from the prospective 8-year birth cohort study of the Dutch Prevention and Incidence of Asthma and Mite Allergy Study.

Methods: Long-term average concentrations of NO₂, fine particles <2.5 µm in diameter (PM₂.₅), and soot were determined at the birth address of each child. Additional data were collected about local traffic, road, and population density for each address, which were used to make regression models for estimating ambient air pollution concentrations for each participant. On each child's birthday, parents completed questionnaires about their children's respiratory health. These responses were assessed for information on asthma, allergies, and related symptoms. At age 8 years, a sample of children underwent testing for bronchial hyperresponsiveness (BHR).

Results: 3863 children were included in this study. The annual prevalence of asthma ranged from 3% to 6% and decreased with age. During the first year after birth, the incidence of asthma was highest (6.1%), but then, it remained relatively constant until age 8 years (range, 1.4% to 2.4%). Air pollution levels were positively associated with the prevalence and incidence of asthma and with the prevalence of asthma symptoms, wheeze, sneezing, and runny/blocked nose. There was little variation in the effects of air pollution on asthma as the children aged. Air pollution was not associated with BHR. The NO₂, PM₂.₅, and soot levels were each associated with a significant increase in the incidence and prevalence of asthma.

Conclusions: Traffic-related air pollution levels outside the homes of children are positively associated with the incidence and prevalence of asthma in children up to age 8 years. This exposure to traffic-related pollutants may cause asthma in children.

Reviewer's Comments: This study corroborates a study that we reported some time ago from Toronto in that asthma prevalence was related to the distance a child lived from a high traffic area. The problem is in determining the solution. Less traffic is not likely, and moving is only a possibility for a select group of these patients. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Traffic-Related Pollutants, Asthma Initiation

Print Tag: Refer to original journal article
Persistent Airway Injury Plagues 9-11 Rescue Workers

Obstructive Airways Disease With Air Trapping Among Firefighters Exposed to World Trade Center Dust.

Weiden MD, Ferrier N, et al:

Chest 2010; 137 (March): 566-574

For FDNY rescue workers who helped after the 9/11 terrorist attack on the World Trade Center, persistent airway injury is the main pathophysiologic abnormality linked to decreased lung function.

**Background:** After terrorists crashed 2 commercial jets into the World Trade Center (WTC) in New York City and caused the collapse of 3 skyscrapers in 2001, many rescue workers for the New York City Fire Department (FDNYC) have reported new or increased respiratory symptoms. Whether restrictive interstitial or obstructive lung disease was the underlying cause for these changes is not known.

**Objective:** To report the authors’ experience with FDNY rescue workers exposed to particulates and combustion by-products at the September 11 (9/11) WTC collapse who reported for pulmonary evaluation during the first 7 years after the attacks.

**Participants:** Rescue workers employed by FDNY who participated in rescue and recovery efforts were included. Exposure levels were ranked as high (rescue worker arrived during morning of 9/11), intermediate (arrived after morning of 9/11 but within first 2 days), and low (arrived between days 3 and 14).

**Methods:** All patients completed a questionnaire and underwent spirometry and chest radiography examinations. Patients were referred for pulmonary subspecialty evaluations based on symptoms, functional impairment, or abnormalities in spirometry or chest radiographs. Three acceptable spirograms were obtained for each participant. Patients also underwent pulmonary function tests (PFTs), and some underwent chest CT scans.

**Results:** Of 13,234 FDNY rescue workers at the WTC scene, 1720 participated in the study. Subspecialty evaluation was needed for 19% of those with high-intensity exposure, for 13% of those in the intermediate-exposure category, and for 6% in the low-exposure category. In patients referred for pulmonary evaluation, FEV₁ and FEV₁/FVC declined significantly during the first year after 9/11 when compared with spirometry from the year before 9/11. The mean time between pre–9/11 and post–9/11 PFTs was 48 months. The median FEV₁ was 93% predicted, the median FVC was 98% predicted, and the median FEV₁/FVC was 0.78. After adjusting for other factors, the decline in FEV₁ was significantly associated with increased patient response to bronchodilators, increased response to methacholine (hyperreactivity), and increases in predicted percent residual volume. These findings indicated that airway injury was the predominant underlying physiologic abnormality. Of the 982 patients who underwent CT scan, 26% had bronchial wall thickening, 12% had emphysema, 4% had evidence of sarcoidosis, and <1% had pulmonary fibrosis.

**Conclusions:** These test results reveal that the predominant underlying pathophysiologic abnormality of decreased lung function was persistent airway injury and obstruction for FDNY rescue workers helping during the 9/11 rescue efforts at the WTC.

**Reviewer’s Comments:** I present this paper not for the specific information regarding the exposure to select New Yorkers after 9/11, but for the possibility that we all might encounter individuals with a similar smaller scale exposure. These data suggest that airway reactivity is the predominant injury. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Rescue Workers, World Trade Center Collapse, Exposure, Pulmonary Function

Print Tag: Refer to original journal article
Patients with OSA have better CCV development than do non-OSA patients. However, whether OSA is a causative factor for CCV augmentation is not yet known.

**Background:** Obstructive sleep apnea (OSA) is associated with both harmful and protective effects. An example of a protective effect is that the recurring cycles of hypoxemia-reoxygenation may precondition the heart for ischemic events, such as infarction. In general, coronary collateral vessels (CCVs) may potentially provide an alternate source of blood flow (and thus oxygen supply) when the original vessels fail to supply enough blood. Angiogenesis is an adaptive response to hypoxia, and the development of CCVs is mediated by vascular endothelial growth factor (EGF). As it happens, vascular EGF is upregulated in OSA. However, whether the development of CCVs is triggered by sleep apnea in patients with both OSA and coronary artery disease (CAD) is not known.

**Objective:** To determine the extent of CCVs in patients with OSA and total chronic coronary occlusion.

**Participants:** 190 patients with suspected OSA and CAD who were screened for total coronary artery occlusion of at least 1 vessel via elective coronary angiography were included.

**Methods:** After undergoing overnight polygraphy, patients were classified as having OSA or not having OSA (controls). Because of CAD symptoms and/or pathologic exercise test results, all patients underwent selective coronary angiography. Two cardiologists evaluated the coronary angiograms and retrospectively scored the CCVs according to the Cohen and Rentrop grading system (0=no visible filling of epicardial vessel; 3=complete filling of epicardial vessel).

**Results:** Of the 190 participants, 34 had total coronary occlusion. Of these 34 patients, 15 were classified as having OSA. Among the 34 patients with total coronary occlusion, those with OSA had poorer control of arterial hypertension than did those without OSA. Eight OSA patients (53%) and 11 non-OSA patients (58%) had previous myocardial infarction. OSA patients had better CCV development (Rentrop Score, 2.4) than did non-OSA patients (Rentrop Score, 1.61). The 2 groups did not differ significantly in left ventricular systolic function or left ventricular end-diastolic pressure.

**Conclusions:** The development of CCVs is augmented in patients with OSA and total coronary occlusion. However, whether OSA is a causative factor for CCV augmentation is not yet known.

**Reviewer's Comments:** A minor benefit, but not sure if this just keeps the individual equal to his non-OSA counterparts or has some survivor benefit. It would seem likely that treating OSA as soon as it is discovered will still offer significant benefit to patients. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Obstructive Sleep Apnea, Coronary Hypoxia, Coronary Collateral Vessels

Print Tag: Refer to original journal article
Background: Initially, acute respiratory distress syndrome (ARDS) was reported only in mechanically ventilated ICU patients. However, a recent study identified a substantial population of acute lung injury (ALI) and ARDS patients in the respiratory isolation wards of a tertiary care facility.

Objective: To determine the incidence and outcomes associated with ALI and ARDS on a hospital-wide basis (not just ICU wards) at 1 health-care institution.

Design: Retrospective cohort study.

Participants: All ALI and ARDS patients (n=156) seen between October 2003 and October 2005 at a Department of Veterans Affairs (VA) medical center in the U.S. were included.

Methods: The patients' medical records were reviewed by a critical care physician. Information was acquired regarding history of chronic lung conditions, tobacco use, exposure to blood products, and times of ICU admission, and/or initiation of ventilator support. ALI cases were identified and classified as MV-ALI (invasive mechanical ventilation [MV] initiated for respiratory failure within ± 72 hours of ALI onset), MV-Other (invasive MV initiated for >72 hours by time that ALI criteria were satisfied or for reasons other than respiratory failure), ICU-NoMV (ICU admission within 72 hours after ALI onset but no invasive MV), and NoICU (no ICU admission).

Results: After record review, 74 cases were classified as MV-ALI, 15 cases were classified as MV-Other, 41 cases were classified as ICU-NoMV, and 26 cases were classified as NoICU. The 4-week mortality rate was 50% in MV-ALI patients (37 of 74 patients), 40% for MV-Other patients (6 of 15 patients), 22% for ICU-NoMV patients (9 of 41 patients), and 46% for No-ICU patients (12 of 26 patients). The main 2 reasons patients did not go to an ICU were because the physician never presented the patient to the ICU (77%) or because the patient had advanced directives limiting care (35%). The 2 main reasons patients were not intubated were that the providers judged intubation to be unnecessary (84%) and because the patient had advanced directives precluding intubation (28%).

Conclusions: Using the consensus definitions of ALI and ARDS for patients throughout a VA hospital, 89 ALI patients were ventilated and 26 were treated outside the ICU. Although the 4-week mortality rate was lower among nonintubated ALI patients, these patients still had a substantial 4-week mortality rate (22%). Further studies are needed to help identify appropriate treatment interventions for various subsets of ALI patients.

Reviewer's Comments: More and more patients are receiving noninvasive ventilation for a myriad of reasons; ALI is no exception. It is not surprising that there are a number of patients who meet the criteria for ALI who do not end up in the ICU. Limiting advanced directives are sure to play a significant role. (Reviewer-Eric H. Gluck, MD, JD).
Silver-Coated ETs Block Bacterial Adherence, Growth

Activity of a Silver-Coated Endotracheal Tube in Preclinical Models of Ventilator-Associated Pneumonia and a Study After Extubation.

Rello J, Afessa B, et al:

Crit Care Med 2010; 38 (April): 1135-1140

ETs coated with silver ions dispersed in a proprietary polymer appear to reduce bacterial adherence and biofilm formation, and the silver ions appear to have antimicrobial activity.

**Background:** Biofilm formation on endotracheal tubes (ETs) begins within hours after intubation, and bacterial contamination becomes abundant by 96 hours. ETs with biofilm formation are potential sources of bacterial inoculation leading to ventilator-associated pneumonia (VAP). ETs coated with silver ions dispersed in a proprietary polymer are designed to block bacterial adherence and provide broad-spectrum antimicrobial activity.

**Objective:** To report the outcomes of 4 sequentially conducted studies assessing the performance of these silver-coated ETs in preventing bacterial adherence and biofilm formation during ventilation.

**Results:** Study 1 – In Vitro Silver Elution Model: The residual silver concentrations in the silver-coated ETs were assessed after prolonged in vitro exposure to simulated body fluids. Samples of 3 silver-coated ETs were incubated in saline elution media. After 21 days of incubation, the residual silver concentrations were 20% of the initial concentrations. Study 2 – In Vitro Bacterial Adherence Model: The abilities of 18 bacterial isolates and 3 Candida isolates to adhere to ETs were assessed. Samples of uncoated and silver-coated ETs were incubated in a radiolabeled microorganism suspension for 2 to 4 hours. Seven isolates showed equivalent levels of adherence to the uncoated and silver-coated ETs, 12 isolates showed greater levels of adherence to the uncoated ETs, and both *Enterobacter cloacae* and *Candida glabrata* showed greater adherence to silver-coated ETs. Study 3 – Rabbit Intubation Model: Using 6 rabbit models, the colonization of *Pseudomonas aeruginosa* was determined at 16 hours after intubation in uncoated ETs, silver-coated ETs, and the adjacent trachea. *P. aeruginosa* heavily colonized the uncoated ETs and adjacent trachea in 6 of 6 rabbits, and it colonized the silver-coated ETs and adjacent trachea in 2 of 6 rabbits. On sampling the lungs, *P. aeruginosa* was isolated in 4 of 6 rabbits intubated with uncoated ETs and in 0 of 6 rabbits intubated with silver-coated ETs. Study 4 – In Vitro Assessment of ETs After Extubation: After extubation, the colonization of pathogenic microorganisms was determined in silver-coated ETs (mean intubation, 4.3 days) and uncoated ETs (mean intubation, 6.8 days). Colonization was detected in 0 of 9 silver-coated ETs and in 3 of 7 uncoated ETs. The silver-coated tubes were associated with less colonization and less biofilm formation. In addition, the microorganisms were dead in the silver-coated ETs and were predominantly alive in uncoated ETs.

**Conclusions:** The silver coating on ETs may block the processes contributing to the early pathogenesis of VAP. More studies are needed.

**Reviewer’s Comments:** A mechanical barrier to adherence of bacteria may well prevent VAP. These animal studies are quite intriguing but certainly would be premature to assume this would work in humans, especially since the trials were of such short duration. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: VAP, Endotracheal Intubation, Biocompatible Coated Materials

Print Tag: Refer to original journal article
During ARDS recruitment maneuvers, the potential for alveolar recruitment is 6% in patients with focal morphology (aeration loss mainly in lower lobes) and 18% in those with nonfocal morphology (diffuse/patchy aeration loss).

**Background:** In patients with acute respiratory distress syndrome (ARDS), recruitment maneuvers (RMs) are used to re-inflate collapsed alveoli through an intentional, transient increase in transpulmonary pressure. Oxygenation increases significantly in patients with a positive response to RM. Nonresponders to RM have more pronounced side effects, including short-term acute hypotension, hypoxemia, and barotraumas. Previous studies have shown that ARDS patients with focal aeration loss respond to RMs with limited alveolar recruitment and significant alveolar hyperinflation, and that ARDS patients with diffuse or patchy aeration loss respond to RMs with significant alveolar recruitment without significant alveolar hyperinflation.

**Objective:** To determine if response to RMs can be predicted by the pulmonary distribution pattern of aeration loss (lung morphology) seen during zero end-expiratory pressure (ZEEP).

**Design:** Prospective study.

**Participants:** 19 adults with early acute lung injury/ARDS in the ICU of a university hospital.

**Methods:** Patients underwent assessment during ZEEP, during RMs (positive end-expiratory pressure of 40 cm H$_2$O applied for 40 seconds), and 5 minutes after RMs. Patients were assessed for respiratory mechanics, hemodynamics, and gas exchange. Lung morphologies determined via CT scans were classified as either focal (aeration loss mainly in lower lobes) or nonfocal (diffuse or patchy aeration loss).

**Results:** Of the 19 patients, 9 patients had focal and 10 had nonfocal lung morphologies at ZEEP. During this study, PaCO$_2$ and pH did not change significantly under various testing conditions, but PaO$_2$ and oxygenation increased significantly during RMs. Nonfocal lung morphology was associated with significantly increased PaO$_2$. However, focal lung morphology was not associated with any significant improvements in arterial oxygenation. The potential for alveolar recruitment during RMs was 6% in patients with focal morphology and was 18% in those with nonfocal morphology. During RMs, greater hyperinflation was seen in patients with focal lung morphology than in those with nonfocal morphology.

**Conclusions:** In patients with early ARDS, response to RMs can be predicted by the regional distribution of aeration loss at ZEEP. In patients with focal lung morphology, hyperinflation was predominant over recruitment during RMs, and alveolar recruitment did not persist beyond the RMs. In patients with nonfocal lung morphology, alveolar recruitment was predominant over hyperinflation during RMs, and it persisted beyond RMs. Therefore, focal lung morphology is associated with a significantly increased risk for hyperinflation and limited alveolar recruitment during RMs.

**Reviewer’s Comments:** Nice study that reiterates what we had already surmised. Focal injuries to the lung are typically not PEEP sensitive or capable of being recruited since the pressure goes down the pathway of least resistance. This will inflate the relatively normal lungs and leave the injured lung without change. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Recruitment Maneuvers, Hyperinflation, Alveolar Recruitment

Print Tag: Refer to original journal article