Objective: To determine the effect of hypoxia on coagulation and inflammation in patients with chronic obstructive pulmonary disease (COPD).

Participants: 20 patients with confirmed COPD were recruited from the clinic. All patients had obstructive lung disease, but they all had an FEV\textsubscript{1} of >50%.

Methods: Patients were randomized to receive either medical air or a nitrogen combination through a 40% of venturi mask to simulate hypoxia. The hypoxic challenge simulated an oxygen fraction of about 15%, which would be similar to what would be found in an aircraft cabin at high altitude. Venous blood samples were taken to measure coagulation and inflammatory markers. Standard laboratory techniques were used. Specifically, samples were analyzed for thrombin-antithrombin complex, prothrombin activation fragments, D-dimer, von Willebrand factor, and interleukin (IL)-6.

Results: All 20 patients completed the study. Patients in both the hypoxic challenge and the control group were similar in terms of age, sex, and smoking history. All patients in the test group tolerated the hypoxic episode. Baseline levels for coagulation profile were similar in both groups. Patients who received medical oxygen had no change in heart rate, respiratory rate, or oxygen saturation over the study period. Similarly, there were no changes in markers of coagulation. In the hypoxic group, the heart rate increased and oxygen saturation was lower at the end of the study compared with baseline. Thrombin-antithrombin complex was increased, as were fragments of prothrombin after the study was completed. IL-6 also increased from baseline in patients who received hypoxic challenge. There was no difference between the levels of D-dimer or von Willebrand factor in patients who received the hypoxic challenge.

Conclusions: A 2-hour hypoxic challenge in patients with COPD resulted in coagulation activation in conjunction with an increase in systemic inflammation.

Reviewer's Comments: These data demonstrate that, in addition to the immobility associated with being in an aircraft cabin, there is significant activation of coagulation factors most likely as a function of hypoxia. One difference here is that barometric pressure was not reduced, as it would be in an airplane. In addition, the authors did partition the immobility factor from the inflammatory factor. Long-haul truck drivers have a high prevalence of deep vein thrombosis, but they are not exposed to hypoxia. Further study is definitely in order to determine whether, in fact, a prophylactic use of anticoagulant might be appropriate in patients with COPD who plan to take long airplane trips. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Hypoxia, Coagulation Markers, Systemic Inflammation, Comorbidity

Print Tag: Refer to original journal article
Objective: To determine whether an association exists between cephalometric measurements between the sella and hyoid (S-H) and severity of obstructive sleep apnea (OSA).

Design/Methods: Retrospective study of patients treated with a mandibular advancement splint for sleep-disordered breathing from June 2000 to May 2005 at the orthodontic department of a British hospital; 106 consecutive patients were treated. Lateral cephalograms were obtained prior to mandibular advancement splint therapy.

Results: Mean S-H distance was 125.5 mm (range, 103.0 to 148.0 mm; median 126.0). Four of 8 patients (50%) with severe OSA had an S-H distance of >120 mm, as did 38 of 50 (76%) with mild to moderate OSA (apnea-hypopnea index [AHI], 5 to 30), and 17 of 22 (77%) without OSA. No significant correlation between S-H distance and severity of apnea was found (Pearson correlation coefficient, –0.034; 95% CI, –0.25, 0.18).

Conclusions: No correlation between OSA severity and cephalometric S-H distance was noted.

Reviewer’s Comments: A previous study on this subject demonstrated significant correlation between S-H distance >120 mm and severe OSA. The present study confirmed no correlation between OSA severity and cephalometric S-H distance. As many of us who have used soft-tissue cephalometrics in clinic in the past during evaluation of patients with OSA (partly because these are easy to obtain as a simple radiograph), it is important to note that use of cephalometric S-H distance as a routine screening test cannot be recommended. There is, however, a reasonable use of cephalometrics in patients with maxillomandibular disproportion and other facial deformities associated with OSA, and oral surgeons use the technique extensively in their practices. (Reviewer: A. Gray Bullard, MD).

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Keywords: Obstructive Sleep Apnea, Severity, Cephalometric Measurement

Print Tag: Refer to original journal article
The term “health care-associated pneumonia” does not reliably predict drug-resistant pathogens.

**Objective:** To determine the validity of the concept that the term health care-associated pneumonia (HCAP) accurately identifies infection with drug-resistant pathogens.

**Participants/Methods:** All patients aged >18 years admitted with respiratory failure requiring mechanical ventilation within 24 hours of admission were included. Cases were identified between January 2004 and December 2007. Cases were limited to those patients with evidence of bacterial infection. Exclusions were patients transferred from other hospitals. Presence of pneumonia was determined by typical signs and symptoms of pneumonia as well as a chest x-ray consistent with that diagnosis. Bacterial infection was defined by a positive culture of blood, pleural fluid, or lower airway secretions. A positive urine antigen for *Streptococcus pneumoniae* or *Legionella* was also considered as evidence of a bacterial infection. HCAP was defined as 1 of the following: recent hospitalization (90 days), admission from a long-term care facility, chronic hemodialysis or wound care, immunosuppression, and/or treatment with broad-spectrum antibiotics within the last 30 days. Immunosuppression included patients with AIDS, malignancy undergoing chemotherapy, and other patients being treated with immunosuppressants. The primary end point was presence of a resistant pathogen. Rates of methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* (PA), and extended-spectrum beta-lactamase (ESBL) organisms were measured. Demographics, severity of illness, and comorbidities were measured. APACHE II and the PaO$_2$/FiO$_2$ ratio were used to determine severity of illness. Statistical analysis methods are described.

**Results:** 190 subjects were studied. Mean age was 61 years, and 54% were men. Resistant pathogens were identified in nearly 33% of patients. MRSA, PA, and ESBL were identified in 18.4%, 13.2%, and 1.0%, respectively. Diagnosis of *S pneumoniae*, MRSA, and *Legionella* was made in 14.2%, 12.6%, and 2.6%, respectively. No difference in demographics or severity of illness was found between resistant and non-resistant groups. There was also no difference in comorbidities. Having at least 2 criteria for HCAP was a positive prognosticator for a resistant pathogen. Other positive factors were immunosuppression, admission from a long-term care facility, and chronic obstructive pulmonary disease with recent antibiotic treatment. A clinical scoring system was developed and described. A score of ≥2 was found to have a 40% predictive chance of a drug-resistant pathogen. However, 17.5% of patients without the studied predictive factors had a drug-resistant organism.

**Conclusions:** The present criteria for determining drug-resistant pathogens in HCAP are not accurate and need refining.

**Reviewer’s Comments:** Assumption that HCAP accurately predicts drug-resistant pathogens is not established in the literature and may expose patients to more toxic drugs that are costly and do not improve outcome. (Reviewer-Allan R. Goldstein, MD).

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**Keywords:** Health Care-Associated Pneumonia, Resistant Pathogens, Relationship

**Print Tag:** Refer to original journal article
Stroke or TIA -- Your Patient's Ticket to Polysomnography

Frequency of Sleep Apnea in Stroke and TIA Patients: A Meta-Analysis.

Johnson KG, Johnson DC:
J Clin Sleep Med 2010; 6 (April 15): 131-137

Patients with a cardioembolic etiology of stroke have a lower percentage of sleep-disordered breathing than do those with other causes of stroke.

Objective: To ascertain the frequency of sleep-disordered breathing (SDB) in stroke and transient ischemic attack (TIA) patients using a meta-analysis.

Methods: 29 clinical research articles through December 2008 examining SDB, stroke, and TIA were obtained using online clinical searches. The authors obtained the frequency of SDB in terms of the apnea-hypopnea index (AHI). Weighted averages were calculated using a random-effects model (95% CI).

Results: By meta-analysis of 2343 ischemic or hemorrhagic stroke and TIA patients, the frequency of SDB with an AHI >5 was 72%. With an AHI >20, frequency of SDB was 38%. Only 7% of SDB was primarily central sleep apnea. No significant differences in SDB were noted by the event type, timing after stroke, or monitoring method. Males had a higher percentage of SDB (AHI >10) than did females (65% vs 48%; \( P = 0.001 \)). Patients with a recurrent stroke had a higher percentage of SDB (AHI >10) than did those with initial strokes (74% vs 57%; \( P = 0.013 \)). Patients with an unknown cause of stroke had higher percentages of SDB than other causes. Patients with a cardioembolic cause of stroke had a lower percentage of SDB than other causes.

Conclusions: SDB is very common in stroke, regardless of the type of stroke or timing after stroke, and tends to be obstructive rather than central. Clinical history alone does not identify the majority of patients with SDB, so the authors conclude that sleep studies should be considered in all of these patients.

Reviewer's Comments: There is a growing body of evidence now that all patients with cerebrovascular disease, notably stroke and TIA, should have sleep studies. Now we learn that it is not necessary to have symptoms directly referable to apnea in order to justify proceeding with polysomnography. Generally, approved Medicare indications for polysomnography are locally determined by carriers, but for patients with stroke or TIA as an indication, a common policy reads, "Patients with...stroke/TIA...who have nocturnal symptoms suggestive of a sleep-related breathing disorder or otherwise suspected of having sleep apnea." A reasonable person might determine from the present article that the symptom of a stroke or TIA is itself a symptom suggestive of a SDB disorder, so that there should be no practical roadblock in implementing the practice of considering all such patients for polysomnography, as the authors recommend. As always, of course, consult your Medicare carrier and insurance companies for local policy. (Reviewer-A. Gray Bullard, MD).

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Keywords: Sleep Apnea, Stroke, Transient Ischemic Attack, Frequency

Print Tag: Refer to original journal article
Patients Decline Surgery for Stage I-II Lung Cancer for Multiple Reasons

Factors Associated With Decisions to Undergo Surgery Among Patients With Newly Diagnosed Early-Stage Lung Cancer.
Cykert S, Dilworth-Anderson P, et al:

JAMA 2010; 303 (June 16): 2368-2376

Reasons other than comorbidities are a significant cause for patients declining potentially curative lung resection.

Objective: To identify potentially modifiable factors causing patients to decline lung surgery for cancer and to explore racial disparities.

Participants/Methods: Patients from 5 communities in North and South Carolina were enrolled between December 2005 and December 2008. All patients were aged ≥21 years, had a lung lesion that had a 60% likelihood of being cancer, and had a lung lesion that was clinically classified as stage I-II. Patients were surveyed and the following were determined: demographics, patient perception of patient-physician communication, perceived certainty of diagnosis, attitudes about lung cancer, religiosity, access to a regular source of care, and decision makers. Patients were followed up by chart review for 4 months. Form of therapy was determined. Comorbid illnesses were identified. Statistical analysis methods were described.

Results: 437 patients were initially enrolled; 47 others (75% white) declined participation. Fifty-one patients were excluded for a variety of reasons, all of which are described. The final study evaluated 386 patients. Of patients, 60% were referred by pulmonologists or thoracic surgeons; another 16% were referred by oncologists. Of patients, 67% had biopsy-proven disease at enrollment, and 62% of these went on to surgery. Of patients with CT-probable disease, and 62% agreed to surgery. Of early biopsy/later surgery patients, 88% had tissue-confirmed disease. Of patients, 62% had lung cancer surgery as defined by the primary outcome (66% of white patients vs 55% of black patients). This gap was noted despite the average age of black patients being 4 years less than that of white patients. Of 145 patients who did not have surgery, the following was found: 10.3% declined, 29.0% were nonsurgical candidates due to comorbid illness, 27.0% were still being followed at 4 months, and 3.0% died. Factors associated with no surgical treatment were black race, age ≥73 years, religiosity, and ≥2 comorbid factors. Potentially reversible factors for declining surgery were as follows: patient felt that lung cancer diagnosis was <90% certain, overall quality of life would worsen, patient perception of lower-quality communication, and a mental component. Lack of a regular source of medical care was a significant factor for declining surgery in black patients. Lower income seemed to be a factor for no surgery in white patients.

Conclusions: Many patients decline potentially curative surgery for stage I-II lung cancer for reasons other than age or comorbidities. Lack of communication and poorer understanding were important factors in patient decision-making.

Reviewer's Comments: The importance of taking time with each patient to explain lung cancer and the potential for cure with maintaining a good quality of life cannot be overstressed. Patients trust our ability but need their fears allayed. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Potentially Curable Lung Cancer, Declining Surgery, Reasons

Print Tag: Refer to original journal article
Objective: To determine whether rescue breathing performed by lay personnel being directed over the phone during cardiopulmonary resuscitation (CPR) would improve outcomes.

Design/Participants: Randomized controlled trial of bystanders performing CPR for out-of-hospital cardiac arrest.

Methods: During each arrest, the bystander was directed by a dispatcher. The bystander was randomly directed to either perform compressions alone or compressions with rescue breathing. Standard protocols were followed. The primary outcome was survival to hospital discharge. Secondary outcome was neurological function at the time of discharge.

Results: Almost 2000 patients were enrolled in the study: 981 received chest compression, while 960 received chest compression plus rescue breathing. Average age in both groups was 63 years. More than 70% of cardiac arrests were felt to be due to cardiac causes. Respiratory and overdose causes were the next 2 most common reasons for arrest. There was no difference in presence of pulse at the end of CPR in either group. In addition, there was no difference in survival at discharge in either group. Survival rates were 11.0% in the chest compression plus breathing group and 12.5% with chest compression alone. Two sites evaluated neurological outcome. There were about 500 patients in this part of the study. Patients with good neurological outcomes averaged 14.4% in chest compression alone and 11.5% in chest compression plus rescue breathing. This did not reach statistical significance. In circumstances where there was a shockable rhythm present at the end of emergency medical service (EMS) care, there was a statistically significant difference with improvement seen with chest compression alone. This was not true for non-shockable rhythms. There was also a statistical improvement with compression alone when the EMS response was <6 minutes after a witnessed arrest.

Conclusions: Chest compression alone did not increase the survival rate, although there was a trend toward better outcomes in some subgroups. The results do support a strategy for CPR that emphasizes chest compression and minimizes the role of rescue breathing.

Reviewer's Comments: Obviously, no difference between groups would be important in a public health situation. It is so much easier to train individuals to do chest compression alone than to couple that with the appropriate timing for rescue breathing. Oftentimes, this results in a significant reduction in chest compression. It would appear from these data that this strategy will become the standard strategy in the future. (Reviewer-Eric H. Gluck, MD, JD).
Treating obstructive sleep apnea with continuous positive airway pressure improves blood pressure in hypertensive patients, even if excessive daytime sleepiness is initially absent.

**Objective:** To examine the effect of 1 year of continuous positive airway pressure (CPAP) treatment on blood pressure in asymptomatic hypertensive patients with obstructive sleep apnea (OSA).

**Design:** Spanish, multicenter controlled trial.

**Participants/Methods:** 359 patients with OSA were randomized to CPAP (n=178) or to conservative therapy (n=181). Blood pressure was measured at 3 months, 6 months, and 12 months post-therapy. Included subjects had an apnea-hypopnea index (AHI) of >19 events/hour, Epworth Sleepiness Scale score <11, and were either being treated for hypertension or had systolic pressure >140 and diastolic pressure >90 mm Hg.

**Results:** Average age of the cohort was 56 ± 10 years, body mass index 32 ± 5, AHI 45 ± 20 events/hour, and Epworth Sleepiness Scale score 7 ± 3. CPAP treatment decreased systolic blood pressure by 1.89 mm Hg (95% CI, –3.9, 0.11 mm Hg; \( P =0.0654 \)) and diastolic blood pressure by 2.19 mm Hg (95% CI, –3.46, –0.93 mm Hg; \( P =0.0008 \)). Using CPAP for > 5.6 hours per night predicted the greatest reduction in blood pressure. AHI and decrease in Epworth Sleepiness Scale score were related to CPAP compliance.

**Conclusions:** In asymptomatic OSA patients (no daytime sleepiness), CPAP therapy for 1 year is associated with a small blood pressure decrease. The reduction is seen only in individuals using CPAP for >5.6 hours nightly.

**Reviewer’s Comments:** Oftentimes, we disregard patients with mild to moderate OSA in terms of considering them as candidates for CPAP therapy, especially if they are not sleepy during the day. In this situation, neither the doctor nor the patient see the point of initiating a therapy involving placing a mask on the face at night, possibly for the rest of the patient’s life. Now we know that there are measurable improvements in hypertension that occur as a result of therapy in these asymptomatic patients. Only a long-term randomized study in these patients could determine whether this degree of blood pressure reduction translates to improvement in morbidity and mortality. (Reviewer-A. Gray Bullard, MD).

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**Keywords:** Obstructive Sleep Apnea, Continuous Positive Airway Pressure, Hypertension
Use of low-dose oral steroids in a chronic obstructive pulmonary disease exacerbation is safe as initial therapy.

Objective: To compare outcomes between patients treated with low-dose oral steroids and those treated with higher doses of IV steroids in patients with chronic obstructive pulmonary disease (COPD) exacerbation.

Design/Methods: Retrospective study involving 414 hospitals that were geographically diverse, small to midsize, predominantly non-teaching, serving urban areas, and whose billing data were available. Patients were admitted to the study between January 1, 2006, and December 1, 2007. All were aged ≥40 years and had diagnoses of COPD with exacerbation or respiratory failure associated with COPD or emphysema. All were treated with steroids for the first 2 days of hospitalization. Patients were excluded if receiving very low or very high doses of oral or IV steroids (dosages are described). Patients were excluded if admitted directly to the ICU, had pneumonia, or had a pulmonary embolism. Only patients admitted by medical specialties or sub-specialties were included. Patients transferred from other hospitals were excluded. Patients were categorized as high or low dose. Other forms of treatment were identified. Hospital demographics were also recorded. Steroid treatment was recorded, and patients were identified. Primary outcomes were mechanical ventilation after 2 days, death in hospital, and 30-day readmission for COPD. Secondary outcomes were cost and length of stay. Statistical analysis was described.

Results: Almost 80,000 patients met criteria: 90% had COPD and 10% had respiratory failure. Median age was 69 years, 61% were women, 73% were white, and Medicare was the most common insurance. Hypertension, diabetes mellitus, congestive heart failure, and depression were the most common comorbidities. Of patients, 17% had 1 admission for COPD in the past year and 12% had ≥2; 60% were admitted to non-teaching hospitals and 80% directly from the emergency department. Median length of stay was 4 days, median costs were $5021, and 30% were hospitalized for at least 6 days. In addition, 1.2% required mechanical ventilation, 1.4% died, and 9.0% were readmitted for COPD within 30 days. A total of 92% were initially treated with IV steroids and 8% with oral steroids. Total doses are presented. Patients receiving oral steroids were older, more likely to be white, less likely to have private insurance, had more comorbidities, and received fewer ancillary medications. Treatment failure outcomes were the same in both groups. Length of stay and costs were less in the oral steroid group.

Conclusions: Oral steroids are a reasonable alternative to IV steroids in the treatment of acute exacerbations of COPD.

Reviewer’s Comments: We must keep in mind that oral medications are effective in select patients. Not all patients with COPD exacerbations must have IV steroids. Knowledge of the patient should guide clinical decisions. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Exacerbation, Oral Steroids, Safety, Route of Administration

Print Tag: Refer to original journal article
Walking Has Some Advantages for COPD Testing

Advantages of Endurance Treadmill Walking Compared With Cycling to Assess Bronchodilator Therapy.

Zhang X, Waterman LA, et al:

Chest 2010; 137 (June): 1354-1361

Although both cycle ergometry and treadmill walking are good tests for assessing response to bronchodilator therapy in patients with chronic obstructive pulmonary disease, treadmill walking may help these patients achieve greater test benefits.

**Background:** Most individuals agree that walking is a more familiar daily activity than is cycling. Yet, cycle ergometry is the preferred test for evaluating exercise capacity and response to bronchodilators in patients with chronic obstructive pulmonary disease (COPD). The main reason cited for discontinuing a cycle ergometry test is leg discomfort, while breathlessness is the main reason cited for discontinuing a walking test.

**Objective:** To determine if treadmill walking is superior to cycle ergometry for evaluating response to bronchodilator therapy in patients with COPD.

**Design:** Randomized, 2x2, double-blind, placebo-controlled crossover study.

**Participants:** 20 patients with COPD, a ≥10 pack-year history of smoking, and an FEV₁ ≤80% predicted after bronchodilator therapy.

**Methods:** Initially, baseline pulmonary function tests were completed, and spirometry was repeated after inhalation of albuterol. On the next 2 visits, patients inhaled albuterol and then performed a symptom-limited incremental test on the treadmill or cycle ergometer. After a 1-hour rest, patients underwent a 10-minute constant-load exercise test at 85% of peak oxygen consumption. On visits 4 through 7, patient response to nebulized arformoterol (ARF) or saline inhalation was assessed via spirometry and the determination of lung volumes, followed by a constant-load endurance exercise test. Patients rated breathlessness and leg discomfort throughout their exercise tests.

**Results:** After bronchodilator use, endurance times improved more on treadmill walking (80% improvement) compared with cycle exercise (65% improvement). Nonetheless, these differences in endurance time were not significantly different for the 2 exercise modes. Treadmill walking was associated with a significantly lower slope of breathlessness time and a significantly attenuated magnitude of oxygen desaturation after ARF inhalation versus normal saline. These changes were not observed with cycle exercise. On treadmill walking, bronchodilator therapy shifted the test's symptom limitation from breathlessness to leg discomfort. Both cycle exercise and treadmill walking were associated with similar inspiratory capacities after ARF.

**Conclusions:** Response to bronchodilator therapy may be assessed with either treadmill walking or cycle ergometry in patients with COPD. However, treadmill walking is associated with improvements in endurance time, altered perceptual responses regarding exercise limitations, and attenuation of oxygen desaturation after bronchodilator therapy. In addition, compared to cycling, walking is a more familiar daily activity for most people. Therefore, the authors believe that treadmill walking may help patients with COPD achieve greater test benefits.

**Reviewer's Comments:** These data suggest that we don't have to invest in expensive exercise equipment to determine if our patients are responding to therapy. A simple walking test or treadmill works as well as cycle ergometry. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Bronchodilator Therapy, Measuring Response, Walk Test vs Cycle Ergometry

Print Tag: Refer to original journal article
Serum high mobility group box-1 protein is an additional measure of inflammation that is regularly seen with obstructive sleep apnea.

**Objective:** To evaluate whether the inflammatory marker high mobility group box-1 protein (HMGB1) is elevated in patients with obstructive sleep apnea (OSA), and to evaluate its relation to endothelial function by measuring levels of nitric oxide (NO) and its derivatives (NOx) before and after nasal continuous positive airway treatment in individuals with OSA syndrome.

**Participants/Methods:** 30 subjects with moderately severe or severe OSA willing to use continuous positive airway pressure (CPAP) treatment and 20 healthy subjects were studied. Serum levels of HMGB1 and an NO derivative (NOx) were measured, and subjects underwent polysomnography. The studies were repeated 2 months after nasal CPAP treatment.

**Results:** The serum level of HMGB1 was higher but NOx lower than those levels in normal subjects. HMGB1 levels correlated negatively with NOx levels in individuals with OSA. HMGB1 and NOx returned to normal levels when measured 2 months after CPAP therapy.

**Conclusions:** OSA syndrome patients had elevated HMGB1 levels and reduced NOx levels. These levels normalize after CPAP treatment.

**Reviewer's Comments:** Markers of oxidative stress are elevated OSA, including cytokines such as interleukin-6, and are thought to be related to endothelial function and pro-coagulopathy. Factors leading to production of these inflammatory mediators include nuclear factor-kappaB and activator protein-1. Serum levels of HMGB1 are increased in a variety of inflammatory disorders. Inside the cell, HMGB1 binds to DNA as a transcription factor, whereas outside the cell, it acts as a pro-inflammatory cytokine. OSA is associated with inflammation secondary to chronic intermittent hypoxia. NO is released by endothelial cells as a consequence of oxidative stress damage. This study demonstrates elevated levels of HMGB1 as a robust indicator of this inflammatory process, as evidenced by correspondingly low NO levels, and normalization of these abnormalities with CPAP therapy. Perhaps these tests may be used in the future in conjunction with CPAP downloads to confirm efficacy of total therapy in selected patients with severe OSA. (Reviewer-A. Gray Bullard, MD).

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**Keywords:** Sleep Apnea, Continuous Positive Airway Pressure, Serum Markers

**Print Tag:** Refer to original journal article
Loss of slow-wave sleep and rapid eye movement sleep may be important factors in the association between sleep loss and central obesity.

**Objective:** To assess associations between sleep duration, sleep stages, and central obesity in women.

**Methods:** The study used polysomnography and measurement of anthropomorphic variables.

**Results:** Sleep duration remained inversely related to waist circumference and sagittal abdominal diameter ($P = 0.001$) after adjusting for compounding variables. Duration of slow-wave sleep ($P = 0.025$) and rhythm sleep ($P = 0.002$) were both inversely related to waist circumference after adjustments. Moreover, duration of rhythm sleep was inversely related to sagittal abdominal diameter ($P < 0.0001$). Associations were stronger in women aged < 50 years.

**Conclusions:** There is an inverse relationship between short sleep duration and central obesity in women. Loss of slow-wave sleep and rapid eye movement (REM) sleep may be important factors in the association between sleep loss and central obesity.

**Reviewer's Comments:** The authors note a relationship between short sleep duration and central obesity in women, most pronounced in women aged <50 years. Both loss of slow-wave sleep and REM sleep were associated with central obesity and may reflect the relationship between sleep duration and central obesity. Short sleep duration may promote obesity by way of lifestyle: lack of sleep leads to daytime fatigue, which can in turn lead to a vicious cycle of short sleep duration, inactivity, and weight gain. Less time for sleep leaves more time for feeding. Stress and emotional disturbance may be the link between sleep duration and obesity, as both have been associated in other studies. As we consider centrally obese women we see in our pulmonary practices for shortness of breath or symptoms of sleep apnea, inquiry regarding short sleep seems a reasonable topic for conversation. (Reviewer-A. Gray Bullard, MD).

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Keywords: Short Sleep, Sleep Stages, Obesity, Polysomnography

Print Tag: Refer to original journal article
Massive Database Analysis Supports Early Antibiotics in COPD Exacerbations

Antibiotic Therapy and Treatment Failure in Patients Hospitalized for Acute Exacerbations of Chronic Obstructive Pulmonary Disease.
Rothberg MB, Pekow PS, et al:

JAMA 2010; 303 (May 26): 2035-2042

U.S. national hospital data indicate that early antibiotic treatment for COPD exacerbation is associated with improvement in a composite measure of treatment failure.

**Background:** Treatment guidelines for COPD exacerbation recommend antibiotic treatment for patients with purulent sputum, increased sputum, and/or increased dyspnea. Evidence supporting these recommendations stems from 11 small randomized trials demonstrating that antibiotics can reduce mortality and treatment failure. However, approximately 50% of COPD exacerbations do not have an identifiable bacterial etiology, and some recent studies have failed to identify a benefit deriving from antibiotics.

**Objective:** To compare outcomes of patients treated with antibiotics in the first 2 hospital days with those treated later or not at all.

**Design:** Retrospective cohort study.

**Participants:** Patients aged ≥40 years hospitalized from January 2006 to December 2007 for acute COPD exacerbations at 413 acute care facilities throughout the U.S. Patients admitted directly to the ICU were excluded.

**Methods:** Inpatient data were examined for U.S. hospitals participating in the Premier's Perspective database. Acute COPD exacerbation was identified by ICD-9-CM codes. Antibiotic treatment was defined as ≥2 consecutive days of antibiotics initiated on hospital day 1 or 2. The main outcome measure was a composite measure of treatment failure, defined as initiation of mechanical ventilation after hospital day 2, inpatient mortality, or readmission for acute COPD exacerbation within 30 days of discharge. **Results:** Of 84,621 patients, 79% received ≥2 consecutive days of antibiotics. Treated patients were less likely than nontreated patients to receive mechanical ventilation after hospital day 2 (1.07%; 95% CI, 1.06% to 1.08% vs 1.80%; 95% CI, 1.78% to 1.82%), had lower rates of inpatient mortality (1.04%; 95% CI, 1.03% to 1.05% vs 1.59%; 95% CI, 1.57% to 1.61%), and had lower rates of readmission for COPD exacerbation (7.91%; 95% CI, 7.89% to 7.94% vs 8.79%; 95% CI, 8.74% to 8.83%). Patients treated with antibiotics had a higher rate of readmission for *Clostridium difficile* infection (0.19%; 95% CI, 0.187% to 0.193%) than did those who were not treated (0.09%; 95% CI, 0.086% to 0.094%). After multivariate adjustment, including the propensity for antibiotic treatment, the risk of treatment failure was lower in antibiotic-treated patients (odds ratio, 0.87; 95% CI, 0.82 to 0.92). A grouped treatment approach and hierarchical modeling to account for potential confounding yielded similar results. Analysis stratified by risk of treatment failure found similar magnitudes of benefit across all subgroups.

**Conclusions:** Early antibiotic treatment was associated with an improved outcome among patients hospitalized for acute COPD exacerbation regardless of the risk of treatment failure.

**Reviewer's Comments:** This study reports that antibiotics are associated with a 13% decrease in the risk of a composite measure of treatment failure in COPD exacerbation. The investigators were unable to show that this benefit was restricted to patients with specific clinical presentations. Although this study is limited by its retrospective design and identification of study subjects with administrative data, its conclusions are buttressed by its tremendous size and by its careful propensity analysis. Future prospective confirmatory trials appear warranted. (Reviewer-Michael B. Fessler, MD).

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**Keywords:** Exacerbation, Antibiotics

**Print Tag:** Refer to original journal article
Ventilation Modes Have Similar Outcomes

Outcomes of Patients Ventilated With Synchronized Intermittent Mandatory Ventilation With Pressure Support: A Comparative Propensity Score Study.

There is no difference in outcome in patients ventilated with synchronized intermittent mandatory ventilation with pressure support compared to assist-control ventilation.

**Background:** Data showing real benefits of one mode of mechanical ventilation over another are sparse. Significant factors driving mode choice are the provider's comfort and familiarity with particular modes and an element of faith.

**Objective:** To compare outcomes in patients mechanically ventilated with either synchronized intermittent mandatory ventilation (SIMV; with pressure support, SIMV-PS) or assist-control (A/C) ventilation.

**Design:** Secondary analysis of observational study.

**Participants:** Mechanically ventilated adults from 349 ICUs in 23 countries. Patients were included if they received exclusively A/C or SIMV-PS ventilation during their ICU stay. Those receiving neuromuscular blockade were excluded.

**Methods:** A propensity score for use of SIMV-PS was developed to account for inability to randomize modes in this observational study. Multivariate analysis was performed to assess factors associated with the likely use of SIMV-PS. Patients were stratified into quintiles by propensity score. Effect on end points was assessed for each quintile based on likelihood of receiving SIMV-PS. The primary outcome was hospital mortality, and secondary outcomes included sedative use, days of mechanical ventilation, ICU length of stay, and ICU mortality.

**Results:** Of 4968 patients, 1228 were mechanically ventilated with A/C exclusively and 350 with SIMV-PS. Those in the SIMV-PS group were more common in the U.S./Canada, had lower Sequential Organ Failure Assessment scores, and were more likely surgical or trauma patients. Those ventilated with A/C tended to have sepsis and cardiovascular failure, and to require mechanical ventilation due to asthma or coma. There was no effect of mode of mechanical ventilation on hospital mortality across propensity score for SIMV-PS use (odds ratio, 1.04; 95% CI, 0.77 to 1.42; P =0.78). Of SIMV-PS patients, 245 (70%) were weaned successfully compared to 638 (52%, P <0.001) in the A/C group. There was no difference in reintubation or tracheostomy rates.

**Conclusions:** SIMV-PS was used more often for less severely ill medical and surgical patients. Also, there was no difference in mortality or duration of mechanical ventilation between modes when accounting for baseline differences in groups.

**Reviewer's Comments:** Although hampered by its observational design, this study suggests no difference in meaningful outcomes related to use of SIMV-PS mode versus A/C. The authors found continued wide use of SIMV-PS in postoperative and trauma patients in particular. Sicker patients were more often ventilated with A/C. Not evaluated in this study was the managing physician's discipline of training, but one could speculate differences in mode use based on medical intensivist training versus anesthesia or surgical training. This study design has numerous opportunities for confounders to color the conclusions. Cohorts differed by diagnoses, by severity of illness, and probably by the type of unit and training of their intensivists. Adjustment or propensity scores still cannot convincingly allow comparison of apples and oranges. It seems that the best mode of ventilation for a given patient population remains unclear. (Reviewer-Jeffrey B. Hoag, MD, MS).

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Keywords: Synchronized Intermittent Mandatory Ventilation, Pressure Support

Print Tag: Refer to original journal article
Background: Preservation of the coupling between cerebral metabolic demand and cerebral blood flow (CBF) is extremely important. However, after cardiac arrest, the effect of mild induced therapeutic hypothermia on CBF is unknown. A study by Lemiale and colleagues showed reduced CBF and oxygen extraction during the first 24 hours of hypothermia and an increase in CBF when the patient was rewarmed. Under normothermic conditions, CBF is affected by changes in PaCO$_2$, but whether this cerebrovascular reactivity to PaCO$_2$ is preserved after cardiac arrest in patients treated with mild hypothermia is unknown.

Objective: To determine if treatment with mild hypothermia after cardiac arrest impacts the coupling between CBF and cerebral oxygen extraction in comatose patients and to determine if mild therapeutic hypothermia impacts cerebrovascular reactivity to changes in PaCO$_2$.

Design: Prospective observational study.

Participants: 10 comatose patients who were successfully resuscitated and treated with mild hypothermia after cardiac arrest.

Methods: Patients were admitted to the ICU at a university hospital in the Netherlands. Mild hypothermia (32°C to 34°C) was induced by rapid infusion of cold Ringer's lactate followed by external cooling with 2 water-circulating blankets. Patients were held at this body temperature for 24 hours. Cerebrovascular reactivity to changes in PaCO$_2$ was evaluated on ICU admission and again at 6, 12, 18, and 24 hours by monitoring the mean flow velocity in the middle cerebral artery (MFVMCA) and by measuring jugular bulb oxygenation (SjbO$_2$).

Results: Five of 10 patients died in the ICU as a consequence of postanoxic brain damage. CBF was lower in patients treated with mild hypothermia, as reflected by decreased MFVMCA. However, SjbO$_2$ was normal. Decreased MFVMCA and normal SjbO$_2$ suggest a decreased cerebral metabolism. Cerebrovascular reactivity to PaCO$_2$ changes was preserved during hypothermia.

Conclusions: After resuscitation for out-of-hospital cardiac arrest, treatment with mild hypothermia lowers CBF and preserves metabolic coupling. During the first 48 hours after cardiac arrest, cerebrovascular reactivity to PaCO$_2$ changes remains intact. Cerebral oxygenation does not appear to be compromised. Mild therapeutic hypothermia appears to be a safe strategy for treating cardiac arrest for 24 hours after resuscitation.

Reviewer's Comments: Hypothermia reduces blood flow to the brain post-arrest but the oxygen needs are still coupled allowing the brain to maintain adequate metabolism. Since the purpose appears to help avoid exposure to toxic byproducts of hypoxia, this strategy should work without creating further problems. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Cardiac Arrest, Mild Induced Hypothermia, Cerebral Blood Flow, Cerebral Oxygenation

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Biomass Smoke Exposure Increases Worldwide Risk of COPD

Risk of COPD From Exposure to Biomass Smoke: A Metaanalysis.
Chest 2010; 138 (July): 20-31

Exposure to biomass smoke increases the risk of chronic obstructive pulmonary disease (COPD). Because biomass fuels are used in >50% of the world’s households, interventions targeting biomass smoke could help reduce the worldwide incidence of COPD.

Background: Although cigarette smoking is the main risk factor for the development of chronic obstructive pulmonary disease (COPD), the effect of exposure to smoke from wood and other biofuels (animal dung, crop residues, etc) on the development of COPD remains unclear.

Objective: To perform a meta-analysis of the literature to determine if exposure to biomass smoke is associated with the development of COPD and to assess the effect of various factors on the development of COPD.

Design: Meta-analysis of literature published in the MEDLINE database, the Latin American and Caribbean Literature in Health Sciences Database, and EMBASE.

Methods: The authors performed a meta-analysis of 4 case-control studies and 11 cross-sectional studies that included 34,969 healthy controls and 3719 COPD patients. Various models were used for the analysis.

Results: The risk of COPD was significantly higher in individuals exposed to biomass smoke (OR, 2.44) compared with those who were not. Exposure to biomass smoke increased the risk of COPD in smokers (OR, 4.39), in nonsmokers (OR, 2.55), in Asian populations (OR, 2.31), and in non-Asian populations (OR, 2.56). When stratified by gender, the results showed that exposure to biomass smoke increased the risk of COPD in both men (OR, 4.30) and women (OR, 2.73). When evaluating 2 specific COPD subgroups, the exposure to biomass smoke increased the risk of both chronic bronchitis (OR, 2.57) and COPD (OR, 2.77). As the duration of exposure to biomass smoke increased, so did the risk of developing COPD.

Conclusions: The risk of COPD is significantly higher in individuals exposed to biomass smoke compared with those who are not. Exposure to biomass smoke increases the risk of COPD in smokers, nonsmokers, Asian populations, non-Asian populations, men, and women. Because biomass fuels are used in >50% of the world's households, interventions targeting biomass smoke could help reduce the worldwide incidence of COPD.

Reviewer’s Comments: In the U.S., the use of biomass fuels was very popular about 10 years ago and some popularity still persists today. These data suggest that it is not a benign exposure. Questions regarding this type of exposure should be included in a history of someone with airflow obstruction. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Risk Factors, Biomass Smoke, Exposure vs Risk

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A new quantitative PCR assay for the rapid detection of methicillin-resistant *Staphylococcus aureus* (MRSA) in patients with ventilator-associated pneumonia should allow for early discontinuation of empiric MRSA antibiotic coverage.

**Background:** In patients with ventilator-associated pneumonia (VAP), 48 to 72 hours are required before culture and sensitivity results can be obtained. During this time, physicians must administer empiric broad-spectrum antibiotics to help reduce mortality. Because methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most frequent VAP pathogens, empiric antibiotics must include MRSA coverage. However, broad antibiotic coverage promotes the development of resistance. Therefore, physicians need a rapid test to determine if MRSA is present in each VAP case so that the use of MRSA antibiotic coverage and the development of resistance can be limited.

**Objective:** To develop a quantitative polymerase chain reaction (qPCR) assay for the rapid detection of MRSA in mini-bronchoalveolar lavage (mini-BAL) samples from patients with VAP.

**Methods:** A qPCR was developed to detect the *mecA* gene that confers methicillin resistance in *S. aureus* and *S. epidermidis*. After the assay was developed, it was validated using 50 patients from 2 different hospitals.

**Results:** The qPCR system developed by the authors was useful for the rapid exclusion of MRSA in mini-BAL samples from patients with VAP. The test required about 8 hours before results could be obtained. Using a cut-off value of ≥421 for the qPCR, the test's sensitivity was 100%, specificity was 80%, positive predictive value was 36%, and negative predictive value was 100%. The overall correct classification rate was 82%. All the incorrectly classified samples were false-positives.

**Conclusions:** In patients with VAP, unnecessary MRSA antibiotic coverage can be limited by the use of a qPCR based partially on measuring *mecA* copy numbers in mini-BAL samples. The test developed by these authors is highly accurate, but further refinement is needed before widespread use. The test should allow for early discontinuation of empiric MRSA antibiotic coverage in patients with VAP.

**Reviewer's Comments:** These data suggest that treatment can be avoided for MRSA if the results are negative. However, there were a lot of false-positives. The results are ready in 8 hours, which do not meet the Centers for Medicare & Medicaid Services guidelines for antibiotic initiation. Perhaps this 8-hour delay could change outcomes. However, once the results are back, the antibiotic could be stopped. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Ventilator-Associated Pneumonia, Methicillin-Resistant *Staphylococcus aureus*, Rapid Detection
In patients with pulmonary sarcoidosis, the most useful markers for assessing lymphocytic alveolitis appear to be soluble interleukin-2 receptor, lysozyme, and KL-6, while KL-6 appears to be predictive of increased parenchymal infiltration.

**Background:** Several serum markers have been suggested to reflect pulmonary sarcoidosis activity, including serum amyloid A (SAA), soluble interleukin-2 receptor (sIL-2R), lysozyme, angiotensin-converting enzyme (ACE), and KL-6. However, no published studies have compared the usefulness of these various markers for reflecting lymphocytic alveolitis or for predicting disease progression in sarcoidosis.

**Objective:** To compare the use of SAA, sIL-2R, lysozyme, ACE, and KL-6 as parameters reflecting lymphocytic alveolitis and predicting increased parenchymal infiltration indicative of disease progression in sarcoidosis.

**Design:** Retrospective analysis of clinical data from a sarcoidosis referral center in Japan.

**Participants:** 43 patients seen between 1990 and 2006 who had newly diagnosed pulmonary sarcoidosis based on clinical findings and histologic evidence of noncaseating epithelioid cell granulomas.

**Methods:** Patients were not receiving any medications and did not have any comorbidities at presentation. Bronchoalveolar (BAL) fluid cells were analyzed, and serum levels of the following markers were determined: SAA, sIL-2R, lysozyme, ACE, and KL-6. Clinical data collected at presentation and during follow-ups were analyzed. A comparative analysis was performed to determine which markers were most predictive of increased parenchymal infiltration (disease progression).

**Results:** The levels of sIL-2R, lysozyme, and KL-6 were significantly higher in patients with parenchymal infiltration than in those without infiltration. The number of BAL lymphocytes and the number of total cells on BAL were significantly higher in patients with parenchymal infiltration than in those without. Active lymphocytic alveolitis may have been reflected by sIL-2R, lysozyme, and KL-6 because they were significantly correlated with the total cells, lymphocytes, and CD4+ T lymphocytes in BAL fluid. On univariate analysis, increased parenchymal infiltration correlated with sIL-2R, lysozyme, KL-6, and number of BAL lymphocytes. On multivariate analysis, KL-6 was the only parameter significantly associated with increased parenchymal infiltration. At presentation, chest radiographic staging did not correlate with increased parenchymal infiltration.

**Conclusions:** In patients with pulmonary sarcoidosis, the most useful markers for assessing lymphocytic alveolitis appear to be initial levels of sIL-2R, lysozyme, and KL-6. However, initial levels of KL-6 appear to be the most useful marker for predicting increased parenchymal infiltration in pulmonary sarcoidosis.

**Reviewer's Comments:** Sarcoidosis is a difficult disease to make decisions about regarding treatment. Activity was usually measured by scanning or ACE levels. These data suggest that KL-6 might be a useful marker for gauging the intensity of parenchymal infiltration. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Predicting Progression, Serum Marker Comparison, sIL-2R, Lysozyme, KL-6

Print Tag: Refer to original journal article
Although brain natriuretic-32 peptide cannot be recommended for diagnosing pleural effusions secondary to congestive heart failure, 5-N-terminal pro-brain natriuretic peptide appears to be useful for differentiating cardiac versus noncardiac causes of pleural effusions.

**Background:** The causes of pleural effusions must be differentiated so that the correct diagnosis is made. In patients with congestive heart failure (CHF), pleural fluid concentrations of 5-N-terminal pro-brain natriuretic peptide (NT-proBNP) are elevated. Unfortunately, measuring NT-proBNP can be expensive and difficult in the lab, but measuring brain natriuretic-32 peptide (BNP) peptide concentrations is performed more commonly and may not be as expensive.

**Objective:** To determine if levels of BNP in pleural effusions are diagnostically useful for differentiating between CHF versus other disease as the cause of the effusions.

**Methods:** 80 pleural fluid samples were selected, with 20 samples coming from CHF cases, 20 from post-coronary artery bypass grafting (post-CABG) cases, 20 from pneumonia cases, and 20 from malignancy cases. Levels of BNP and NT-proBNP were measured using 2 different enzyme immunoassay kits.

**Results:** NT-proBNP was a good marker for differentiating CHF from the other entities. The median level of NT-proBNP was significantly higher in pleural effusions secondary to CHF than in post-CABG effusions, malignant effusions, and parapneumonic effusions. However, BNP was not as effective at differentiating CHF-related effusions when compared with NT-proBNP. The median level of BNP in pleural effusions secondary to CHF was significantly higher than in parapneumonic effusions, was only marginally higher than in malignant effusions, and was not significantly higher than in post-CABG effusions.

**Conclusions:** NT-proBNP is superior to BNP for differentiating pleural effusions secondary to CHF from post-CABG effusions, malignant effusions, and parapneumonic effusions. While BNP cannot be recommended for diagnosing pleural effusions secondary to CHF, NT-proBNP appears to be useful for differentiating cardiac versus noncardiac causes of pleural effusions.

**Reviewer's Comments:** Pleural effusions from heart failure are not always easy to identify, especially if they are long standing. It appears from these data that NT-proBNP is superior to BNP in identifying an effusion as being the result of heart failure. This might offset the downside of the added expense of this measurement. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Pleural Effusions, Congestive Heart Failure, Brain Natriuretic Peptides

Print Tag: Refer to original journal article
In selected patients with severe chronic obstructive pulmonary disease and hypoxemia, creation of an iliofemoral arteriovenous fistula will improve exercise capacity, which may be predicted by baseline response to oxygen supplementation as measured by a 6-minute walk distance.

**Background:** In patients with chronic obstructive pulmonary disease (COPD), ambulatory oxygen improves acute exercise performance. However, other patients with COPD may not respond to oxygen therapy. Arteriovenous fistulae (AVF) are known to increase mixed venous oxygen content and cardiac output, resulting in increased oxygen delivery.

**Objective:** To determine if the creation of an iliofemoral AVF increases functional exercise capacity in patients with COPD.

**Design:** Small feasibility study.

**Participants:** 12 patients with severe end-stage COPD (FEV$_1$ <50% predicted; mean PaO$_2$, 57.5 mm Hg) on long-term 24-hour oxygen therapy for ≥6 months.

**Methods:** An iliofemoral AVF was created in each patient. The 6-minute walk distance (6MWD) was measured in each patient while breathing room air and then again while breathing supplemental oxygen. Measurements were made at baseline (before AVF creation) and then again at 6 and 12 weeks after AVF creation.

**Results:** The study group (10 men, 2 women) had a mean age of 66 years and a mean post-bronchodilator FEV$_1$ of 19%. Overall, the baseline 6MWD was 217 m with room air and 279 m with supplemental oxygen. At 12 weeks after AVF creation, the 6MWD was 276 m with room air and 308 m with supplemental oxygen. In oxygen responders, the baseline and 12-week 6MWDs were 99 m and 222 m on room air, respectively, and were 232 m and 254 m on supplemental oxygen, respectively. In oxygen nonresponders, the baseline and 12-week 6MWDs were 301 and 314 m on room air, respectively, and were 312 m and 347 m on supplemental oxygen, respectively. Therefore, patients who increased their baseline 6MWD with the addition of supplemental oxygen demonstrated the greatest increase in 6MWD at 12 weeks after creation of the AVF. Patients who did not significantly increase their baseline 6MWD with the addition of supplemental oxygen (nonresponders) also did not significantly increase their 6MWD after creation of an AVF. Lung function did not change after creation of the AVF. Cardiac output increased by approximately 1 L/minute after creation of the AVF, although mean pulmonary arterial pressure was unchanged.

**Conclusions:** An iliofemoral AVF may improve exercise capacity in selected patients with severe COPD and hypoxemia. Baseline response to oxygen supplementation during a 6MWD may predict a similar response to AVF creation. Because this study only showed the short-term benefits of an AVF in these patients, further studies are needed to evaluate the long-term benefits of an AVF in this population.

**Reviewer’s Comments:** This is a very interesting study. Creating a bypass to peripheral circulation, ie, a left-to-right shunt increases the PO$_2$ of the blood entering the lung for reoxygenation and increases CO. Both would be helpful to improve exercise in patients with COPD. The question arises as to whether this might lead to long-term high output failure. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Exercise Capacity, Supplemental Oxygen, Effect of Arteriovenous Fistula

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In patients with severe chronic obstructive pulmonary disease, a low workload (50% maximum) on an arm cycloergometer is associated with lower levels of dynamic hyperinflation and appears to be more feasible than workloads of 65% and 80% for training.

**Background:** Rehabilitation programs use upper extremity training to help enhance the quality of activities of daily living for patients. However, in patients with chronic obstructive pulmonary disease (COPD), upper limb exercises may result in dynamic pulmonary hyperinflation (DH) and reduced inspiratory capacity (IC).

**Objective:** To determine if DH is proportional to the workload in patients with severe COPD who are undergoing an exercise program using an arm cycloergometer.

**Design:** Prospective randomized study.

**Participants:** 24 patients from Brazil with severe COPD (FEV₁ <50% predicted), no exacerbations in the 30 days before the test, and no previous participation in a pulmonary rehabilitation program.

**Methods:** A baseline IC was determined. Patients then performed a symptom-limited endurance exercise (maximum of 20 minutes) on the arm cycloergometer at 1 of 3 workloads: 50%, 65%, and 80% of the peak workload. After a 24-hour rest, the patient returned for another round of endurance arm exercise testing at one of the other workloads. The patient completed a total of 3 exercise sessions and the IC before and after each of the 3 workloads was measured.

**Results:** DH was observed in 41% of patients during exercise at a constant workload at 50% maximum, in 67% of patients at a workload of 65% maximum, and in 79% of patients at a workload of 80% maximum. The endurance time was 12.5 minutes at a workload of 50%, 10.1 minutes with a workload of 65%, and 7.6 minutes with a workload of 80%. When a minute ventilation of 39 L/minute was achieved, exercise usually was interrupted, regardless of the workload. The progressive shortening of expiratory time and the increase in respiratory frequency was associated with the increasing workloads, thus accounting for the increase in DH as workload increased. In patients with severe COPD, a low workload (50% of maximum) appears to be most feasible when undergoing upper extremity training with an arm cycloergometer.

**Conclusions:** Pulmonary hyperinflation during upper arm exercises is associated with the workload on the arm cycloergometer. As workloads increase, the IC decreases, resulting in DH. DH is directly related to decreased performance efficiency and endurance times in patients with severe COPD.

**Reviewer’s Comments:** It is now pretty well established that dynamic hyperinflation is a main culprit in decreasing exercise tolerance in patients with COPD. These data also suggest that it does not matter how one performs the exercise in which DH can occur. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Pulmonary Hyperinflation, Upper Extremity Training, Workload Effects

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