Routine Addition of Corticosteroids for CAP Not Helpful

Efficacy of Corticosteroids in Community-Acquired Pneumonia: A Randomized Double-Blinded Clinical Trial.
Snijders D, Daniels JMA, et al:
Am J Respir Crit Care Med 2010; 181 (May 1): 975-982

Routine use of corticosteroids in the treatment of community-acquired pneumonia is not indicated.

**Objective:** To evaluate the effect of routine use of corticosteroids in the treatment of community-acquired pneumonia (CAP).

**Design:** Clinical, randomized, double-blind placebo-controlled study.

**Methods:** Patients were selected prospectively and received 40 mg of prednisolone or placebo for 7 days. The prednisolone or placebo was administered either orally or IV, depending on the route of antibiotic administration. Eligibility was based on (1) written consent, (2) clinical symptoms suggestive of CAP, (3) new consolidation on x-ray, and (4) age ≥18 years. Exclusions were (1) prior immunosuppression, (2) malignancy, (3) pregnancy or breast feeding, (4) use of macrolides for >24 hours, (5) use of ≥15 mg of prednisolone for >24 hours, (6) chronic use of steroids, (7) infection likely not CAP, (8) obstructive pneumonia, (9) pneumonia developing within 8 days of recent hospital discharge, and (10) inability to cooperate. Amoxicillin was the antibiotic of choice unless allergy existed. Moxifloxacin was used in patients who were allergic to amoxicillin or if atypical pathogens were suspected. Choice of antibiotic and change of antibiotic decisions were left to the care team. Appropriate cultures and lab studies were obtained and are described. The primary end point was clinical outcome on day 7. Secondary end points were outcome on day 30, length of stay, time to clinical stability, 30-day mortality, and serum C-reactive protein (CRP) levels. Outcome was defined as cure, failure, or indeterminate. The definition of each of these is provided in the article. Methods of statistical analysis are also provided.

**Results:** 213 patients were studied. Average age was 63 ± 18 years; 58% of patients were male. CRP levels and chronic heart disease incidence differed between groups. When looking at primary and secondary end points, no advantage relative to morbidity or mortality was seen in the treatment group. In fact, some parameters actually seemed worse in the treatment group. Streptococcus pneumoniae was the most common organism. Hyperglycemia, confusion, and superinfection were seen in both groups.

**Conclusions:** Routine use of corticosteroids in addition to antibiotics in the treatment of CAP does not improve morbidity or mortality, and it should not be advocated.

**Reviewer's Comments:** I am not surprised by the findings in this study. However, physicians should be reminded about what does not routinely work. That being said, there are patients with CAP and multiple comorbidities who might benefit from corticosteroids. That is a clinical decision that should be made by the patient's treating physician. (Reviewer-Allan R. Goldstein, MD).

© 2010, Oakstone Medical Publishing

Keywords: Community-Acquired Pneumonia, Steroids

Print Tag: Refer to original journal article
In adult asthmatics, reduced vitamin D levels are associated with impaired lung function and increased airway hyperresponsiveness.

**Background:** There have been data published in the pediatric literature suggesting an association between lower vitamin D levels and the need for increased doses of inhaled corticosteroids to control asthma in children. The same study suggested that as vitamin D levels increased, there was a decreased need for inhaled corticosteroids.

**Objective:** To evaluate the effects of varying vitamin D levels on manifestations of asthma.

**Design:** Prospective study.

**Participants:** 54 nonsmoking adult patients with persistent asthma.

**Methods:** The clinical history of asthma was confirmed by either bronchodilator responsiveness or airway hyperreactivity. Of 54 patients, 24 were using inhaled corticosteroids at time of enrollment.

**Results:** Investigators found that as the serum vitamin D level increased, so did the FEV\textsubscript{1} level. They performed least squares regression of the relationship between lung function as measured by FEV\textsubscript{1} and serum vitamin D. This indicated there was a 22.7 ± 9.3 mL increase in FEV\textsubscript{1} for each nanogram per milliliter increase in vitamin D. In those subjects with airway hyperresponsiveness to methacholine, reduced serum vitamin D concentrations were associated with greater degrees of airway hyperresponsiveness. Investigators also found that increasing levels of vitamin D were associated with enhanced glucocorticoid response in vitro.

**Conclusions:** These investigators believe they have shown a strong correlation between vitamin D levels and lung function in adult asthmatics.

**Reviewer's Comments:** The authors suggest that it may be worthwhile to check vitamin D levels that are poorly controlled in asthmatic patients on inhaled corticosteroids. They suggest that, if the vitamin D level is low, administration of vitamin D may help improve asthma control. I suspect that not many pulmonary physicians have been measuring vitamin D levels in their asthmatic patients. This may change in the near future. I hope that we will see randomized double-blind trials involving vitamin D supplementation in asthmatics. (Reviewer-Richard A. Nusser, MD).

© 2010, Oakstone Medical Publishing

Keywords: Vitamin D Levels, Lung Function, Steroid Response

Print Tag: Refer to original journal article
Measuring cough reflex may improve the incidence of achieving a successful extubation.

**Objective:** To determine if involuntary cough peak flow (CPFi) measurement improves the chances of achieving a successful extubation.

**Participants/Methods:** 150 patients who had been intubated for at least 3 days, had passed a 2-hour spontaneous breathing test (SBT), and were judged to be ready for extubation by their physician were studied. Weaning protocols were used and were the same in the Medical and Surgical ICUs. Nursing, respiratory, and medical staff members were involved in extubation procedures. Informed consent was obtained. Weaning parameters were measured daily and are clearly noted. All patients meeting criteria underwent an SBT via a T-piece for 0.5 to 2.0 hours. Once meeting criteria for extubation, cough assessment was instituted. The CPFi was induced by removing the T-piece and dripping 2 cc of normal saline into the endotracheal tube (ETT) at end inspiration and measuring cough strength by a flow sensor attached to the T-piece, which had been reattached to the ETT. Criteria for termination of the trial are recorded in the original article. Respiratory strength was graded 0 to 3, with 3 being the strongest flow. Demographics, Acute Physiology, and Chronic Health Evaluation (APACHE) scores, ETT diameter, and laboratory data were recorded. ICU and hospital length of stay following extubation and time to reintubation were also recorded. Statistical analysis methods are described.

**Results:** 118 patients were successfully extubated. The 32 who failed extubation had lower CPFi scores and higher APACHE scores. The stronger the cough, the more likely was successful extubation. Abnormal mentation and increased sputum volume reduced the likelihood of adequate cough and successful extubation. Time in the ICU and in the hospital was greater for those who initially failed extubation.

**Conclusions:** The addition of CPFi increases the likelihood of successful extubation and identifies those patients who will require more attention and treatment before extubation can be accomplished.

**Reviewer's Comments:** This is a very neat physiologic study. I doubt most hospitals will be able to provide CPFi monitoring. However, it does identify patients at highest risk for extubation failure. Careful attention to each patient considered for extubation is still the best "test." Protocols make the process easier and more successful. Attention to detail and moving along methodically will lead to success. (Reviewer-Allan R. Goldstein, MD).

© 2010, Oakstone Medical Publishing

Keywords: ICU, Involuntary Cough Peak Flow, Extubation

Print Tag: Refer to original journal article
In patients with chronic obstructive pulmonary disease, vitamin D deficiency is seen frequently and correlates with disease severity.

**Background:** Recent evidence has suggested an association between vitamin D deficiency and a number of chronic diseases including cancer, autoimmune disease, infections, and cardiovascular disorders. Janssens and colleagues investigated possible vitamin D deficiency in patients with chronic obstructive pulmonary disease (COPD). Some studies show that variations in the vitamin D binding gene are associated with the risk of COPD. In particular, the variants rs7041 and rs4588 were believed to play a significant role in determining the 25-hydroxyvitamin D (25-OHD) levels seen in healthy women.

**Objective:** (1) To measure 25-OHD levels in smokers and ex-smokers and to correlate these findings with pulmonary function; and (2) to evaluate the presence of genetic variants of vitamin binding gene and its relationship to serum vitamin D levels.

**Design:** Prospective evaluation.

**Methods:** The principle circulating vitamin D metabolite in 25-OHD was evaluated. Investigators measured serum levels of 262 patients with COPD who were not taking any vitamin D supplementation. These patients were compared to a healthy control group of 152 subjects who were matched for age, sex, and smoking history. Investigators used the GOLD classification system to characterize COPD patients. Investigators genotyped all study participants for rs7041 and rs4588.

**Results/Conclusions:** "Vitamin D deficiency occurs frequently in COPD and correlates with the severity of COPD."

**Reviewer's Comments:** This interesting paper provides some practical information for pulmonologists. Bone disease is extremely common in COPD patients. Presence of vitamin deficiency will accelerate development of osteopenia and osteoporosis. Vitamin D deficiency, as this study found, is common in COPD and is more prevalent as the severity of COPD increases. Pulmonologists need to look for vitamin deficiency and provide necessary supplementation. Whether vitamin D will be helpful in slowing progression of COPD awaits further studies. (Reviewer-Richard A. Nusser, MD).

© 2010, Oakstone Medical Publishing

Keywords: Vitamin D Deficiency

Print Tag: Refer to original journal article
Objective: To examine the relationship between increases in disability and depressive symptoms among individuals with chronic obstructive pulmonary disease (COPD).

Participants/Methods: 3 waves of a population-based longitudinal cohort study were used. All patients resided in the United States and were aged 55 to 75 years. Telephone interviews were used to gather information. Diagnoses of COPD or chronic bronchitis were established, and asthma as a lone diagnosis was excluded. Follow-up phone calls were made over several years. Disability was measured by the valued life activities scale. Disability was rated on a scale of 0 to 3. Depression was measured by the Geriatric Depression Scale Short Form (this tool was described and validated). Total scores ranged from 0 to 15. Age, sex, race, education, and smoking history were obtained. Chronic comorbid conditions were identified. The COPD Severity Score was described and was used as a composite measure of disease severity. Statistical methods were described in the article.

Results: Most patients were aged ≥66 years, female, and current or former smokers. At initiation of the study, one third of patients met criteria for depression. These individuals had less education, were current smokers, had more comorbidities, and had a higher COPD Severity Score. As time passed, those who became more disabled were noted to have more depression symptoms associated with their overall disability. Adjusting for all factors, depression did not differ between COPD and chronic bronchitis.

Conclusions: In patients with COPD, disability from the disease leads to a significant incidence of depression, which, in turn, adds to the disability.

Reviewer's Comments: Identifying and treating depression in patients with COPD is part of overall care in these patients. Treatment of depression may improve quality of life and reduce health care costs. (Reviewer-Allan R. Goldstein, MD).

© 2010, Oakstone Medical Publishing

Keywords: Depression, Disability

Print Tag: Refer to original journal article
Imatinib -- Not the Drug for Treating IPF

*Imatinib Treatment for Idiopathic Pulmonary Fibrosis: Randomized Placebo-Controlled Trial Results.*

Daniels CE, Lasky JA, et al:

Am J Respir Crit Care Med 2010; 181 (March 15): 604-610

---

Imatinib does not improve survival or lung function in patients with idiopathic pulmonary fibrosis.

**Background:** Idiopathic pulmonary fibrosis/usual interstitial pneumonia (IPF/UIP) is the most common of the idiopathic interstitial pneumonias. The American Thoracic Society/European Respiratory Society recommends treating IPF/UIP with a combination of corticosteroids and immunosuppressive therapy. However, there are no good data to suggest that this therapy is actually beneficial. There has been considerable interest in finding an effective pharmacologic agent that would halt progression of this disease and improve survival. Imatinib mesylate is a tyrosine kinase inhibitor. This drug has activity against platelet-derived growth factor receptors, which are felt to be involved with development of lung fibrosis.

**Objective:** To assess the efficacy and safety of imatinib for treatment of IPF.

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

**Participants/Methods:** Patients aged 20 to 79 years were eligible for study if their diagnosis was established within the previous 3 to 36 months. Diagnosis was established by high-resolution CT scan or surgical lung biopsy. To be eligible for study, patients needed to demonstrate clinical worsening in the past year, defined as either a >10% decline in percent predicted FVC, worsening chest x-ray, or worsening dyspnea. Investigators wished to study patients with mild to moderate disease, so patients whose FVC was <55% of predicted value at screening, diffusing capacity of carbon monoxide (DL\textsubscript{CO}) <35% of predicted value at screening, and Pa\textsubscript{O2} <60 mm Hg were excluded. A total of 119 patients were enrolled in 13 centers in the United States and Mexico. Patients were randomized in a 1:1 fashion to receive Gleevec 600 mg by mouth daily or placebo; treatment was for 96 weeks. The primary outcome was a combined measure of disease progression, defined as >10% decline from baseline FVC, or death.

**Results:** This was a negative study. There was no difference between groups in the primary end point, which was time to disease progression or time to death. There was no difference in secondary end points at 48, 72, or 96 weeks for changes in FVC or DL\textsubscript{CO}. Eight patients in the imatinib group died, as well as 10 in the placebo group. The overall incidence of acute exacerbation in this study was 5%.

**Conclusions:** Imatinib did not improve survival or lung function in patients with IPF.

**Reviewer's Comments:** The search for an effective drug to treat IPF/UIP continues. The most important message from this study for the pulmonologist is, if possible, to enroll their patients in clinical trials that are now underway. The Panther-IPF trial will compare N-acetylcysteine versus the combination of N-acetylcysteine, prednisone, and azathioprine versus placebo. The Anticoagulant Effectiveness in Idiopathic Pulmonary Fibrosis study will compare warfarin to placebo in patients with IPF. (Reviewer-Richard A. Nusser, MD).

© 2010, Oakstone Medical Publishing

Keywords: Idiopathic Pulmonary Fibrosis, Imatinib

Print Tag: Refer to original journal article
Lactate Levels Can Guide Early Resuscitation Goals in Severe Sepsis

Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy: A Randomized Clinical Trial.

Jones AE, Shapiro NI, et al:

JAMA 2010; 303 (February 24): 739-746

Using a 10% reduction in lactate as a goal of adequate oxygen delivery in early goal-directed therapy in patients with severe sepsis results in similar outcomes as using continuous central venous oxygen saturation.

Background: The Surviving Sepsis Campaign international consensus guidelines recommend early resuscitation to optimize oxygen delivery. Although the best measure of oxygen delivery is debated, the published protocol utilized central venous oxygen saturation (ScvO2) of >70%. Serum lactate has been shown to prognosticate outcome, with higher levels being associated with worse morbidity and mortality.

Objective: To demonstrate that lactate falling by 10% results in similar outcomes as achieving 70% ScvO2 in early goal-directed therapy for patients with severe sepsis.

Design: Multicentered randomized open-label non-inferiority study.

Participants: 300 patients with severe sepsis and hypoperfusion or shock being treated in emergency departments of 3 urban U.S. hospitals.

Methods: All patients had baseline lactate drawn and central catheter capable of continuously measuring venous oxygen saturation placed. IV fluid resuscitation targeted central venous pressure of 8 to 12 and vasopressors were added to maintain mean arterial pressure of 65 mm Hg. Once these were achieved, a surrogate of adequate oxygen delivery was measured. If the lactate had not fallen by at least 10% from baseline (in the lactate clearance group) or ScvO2 was <70% (ScvO2 group), patients were transfused blood to hematocrit of 30 and then started on dobutamine. The early goal-directed therapy was discontinued at 6 hours and patients were admitted to the ICU where care was directed by non-study physicians.

Results: 80% had shock and 40% had lactate levels >4 at enrollment. Both groups received about 4.5 liters of crystalloid in the first 6 hours with three fourths requiring vasopressors. Only 5% of patients required blood transfusions and 4% dobutamine during the first 6 hours. Over the first 72 hours, there was no difference in need for mechanical ventilation (50% of patients) between groups. Hospital mortality was similar in both groups (23% targeting ScvO2 vs 17% with lactate). Both ICU (5.6 vs 5.9 days) and hospital (12.1 vs 11.4 days) lengths of stay were similar between groups.

Conclusions: Using lactate clearance resulted in similar clinical outcomes as ScvO2 in an algorithm of early goal-directed therapy in patients with severe sepsis.

Reviewer's Comments: Since the publication of Rivers' New England Journal of Medicine article describing the benefits of early goal-directed therapy, many have wondered if continuous venous oxygen saturation monitoring was required. The catheters designed to continuously monitor ScvO2 are expensive and require training to use. This article demonstrates that serial lactate measurements targeting a clearance of at least 10% produce similar clinical outcomes as targeting ScvO2 > 70%. I plan on incorporating lactate clearance in my practice in place of the expensive catheter as the goal for adequate resuscitation of patients with severe sepsis or septic shock. (Reviewer-Todd W. Rice, MD, MSc).

© 2010, Oakstone Medical Publishing

Keywords: Lactate, Severe Sepsis, Central Venous Oxygen Saturation

Print Tag: Refer to original journal article
Higher PEEP Reduces ARDS but Not ALI Mortality in Meta-Analysis

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome: Systematic Review and Meta-Analysis.

Briel M, Meade M, et al:

JAMA 2010; 303 (March 3): 865-873

In this meta-analysis, lung protective ventilation strategies using higher levels of PEEP resulted in significantly lower mortality in a subgroup of patients with ARDS (ie, P/F<200).

**Background:** Lung protective ventilation strategies theorize that low tidal volumes prevent overdistention of alveoli while positive end-expiratory pressure (PEEP) prevents repetitive collapse and reopening of injured alveoli. The ARDS Network demonstrated that volume and pressure-limited ventilation decreased mortality and increased the number of days alive and off the ventilator. However, studies evaluating higher levels of PEEP have been less conclusive. Higher PEEP may both prevent collapse and exacerbate overdistention of more normal alveoli.

**Objective:** To determine the association of higher versus lower PEEP on outcomes in adults with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) being ventilated with low tidal volume strategies.

**Design:** Individual patient data meta-analysis; pre-specified subgroup analysis of patients with ALI versus ARDS.

**Participants:** 2299 patients with ALI or ARDS combined from 3 large randomized trials.

**Methods:** PEEP levels were set according to tables in 2 trials and titrated to plateau pressure in the third. The meta-analysis used individual patient, not aggregate data.

**Results:** Over 80% of patients had ARDS rather than ALI and most had medical etiologies for their lung injury (50% pneumonia, 50% sepsis, 20% aspiration). The mean PEEP was 15 in the higher PEEP group and 9 in the lower PEEP group. Overall, higher and lower PEEP had similar hospital mortality (32.9% vs 35.2%, respectively; \( P = 0.25 \)). Complication rates such as pneumothorax and need for vasopressors were similar in the 2 groups. In the subgroup of patients who had P/F ratio <200 (ie, ARDS) at enrollment, higher PEEP resulted in marginally significantly lower mortality (34.1% vs. 39.1%; \( P = 0.049 \)) and more days alive with unassisted breathing (12 vs 7; \( P = 0.004 \)). However, in the smaller subgroup of patients with P/F ratios 200 to 300 at enrollment, higher PEEP resulted in a trend toward higher mortality (27.2% vs 19.4%; \( P = 0.07 \)).

**Conclusions:** Higher PEEP did not result in improved mortality or clinical outcomes in all patients with ALI but did in the subgroup of patients with the more severe ARDS at enrollment.

**Reviewer's Comments:** This meta-analysis is methodologically interesting in that it used data from individual patients, rather than treating each study as a data point. While this improves the ability to detect relationships, it does not overcome the limitation of all meta-analyses that the studies only share some features in common. Higher PEEP did demonstrate a mortality benefit in the most severely hypoxic subgroup. Conversely, in patients with P/F ratios between 200 and 300, higher PEEP trended toward increasing mortality. Overall, these results are hard to incorporate into clinical practice due to the relatively arbitrary cutoff of P/F=200. If higher PEEP (lower oxygen) is going to be used, these data suggest it should be restricted to patients with P/F <200, while less ill patients should be managed with lower PEEP (higher oxygen). (Reviewer-Todd W. Rice, MD, MSc).

© 2010, Oakstone Medical Publishing

Keywords: Positive End-Expiratory Pressure, Acute Lung Injury

Print Tag: Refer to original journal article
Pleural Ultrasonography Detects Pneumothorax After Chest Tube Removal

Pleural Ultrasound Compared to Chest Radiographic Detection of Pneumothorax Resolution After Drainage.

Galbois A, Ait-Oufella H, et al:

Chest 2010; April 9 (): epub ahead of print

Background: The portability and overall ease of use of ultrasonography allows rapid assessment of unstable, critically ill patients. However, does this value of ultrasonography assist the management of more stable patients—such as in the removal of chest tubes in patients with pneumothoraces?

Objective: To compare the value of pleural ultrasonography to portable chest radiography in the management and removal of chest tubes placed for pneumothorax.

Design: Observational study at a single academic medical center in France.

Participants: 44 inpatients with pneumothorax treated with 8 French tube thoracostomy were evaluated. Exclusion criteria included mechanical ventilation and subcutaneous emphysema.

Methods: Patients underwent serial pleural ultrasonography and portable chest radiography at 3 intervals: 24 hours after the cessation of any pleural air leak, 6 hours after tube clamping, and 6 hours after tube removal. Ultrasonography was conducted by a single investigator and was repeated by an ICU fellow (who had undergone 2 hours of training). Each intercostal space was examined along the midclavicular and midaxillary lines, as well as along the scapula edge. Ultrasonographic diagnosis of pneumothorax required 2 findings: the loss of lung sliding during respiration and the "A-line sign"—horizontal linear artifacts (indicating air) in the absence of vertical artifacts (indicating lung). Discrepancies between radiography and ultrasonography were resolved by aspiration of air from the chest tube or CT scanning. The attending physician was unblinded and decided any therapeutic intervention.

Results: 33 of 44 pneumothoraces recurred during the chest tube removal process. Pleural ultrasonography detected all 33 recurrences (with 1 false positive); chest radiography detected only 20 of 33 recurrences. The attending physician elected to change management in each pneumothorax missed by chest radiography—usually by continuing chest tube suction. Pleural ultrasonography results were available within 35 minutes (SD, 34 minutes); chest radiography results were available within 71 minutes (SD, 56 minutes). There was good agreement between fellows and the lead investigator (kappa 0.78), with a rapid learning curve.

Conclusions: Pleural ultrasonography reliably detects residual pneumothorax during chest tube removal.

Reviewer's Comments: While this study supports the sensitivity of pleural ultrasonography for residual pneumothorax, the value of this finding is unclear. The clinical significance of pneumothoraces missed by chest radiography is unknown. While each "missed" pneumothorax led to an intervention in this trial, the decision to intervene was made for unstated reasons by an unblinded (and potentially biased) observer. The question of clinical significance is particularly important, given that adoption of ultrasonography could require more physician effort than chest radiography. While ultrasonography results were available within 35 minutes, it is unclear how much of that time required physician presence at the bedside (and away from other patients). Until these questions are answered, the value of pleural ultrasonography during chest tube removal remains uncertain. (Reviewer-Eric P. Schmidt, MD).

© 2010, Oakstone Medical Publishing

Keywords: Ultrasonography, Chest Radiography, Pneumothorax, Tube Thoracostomy

Print Tag: Refer to original journal article
Lung Recruitability Influences the Benefit or Harm of PEEP in ARDS

Lung Opening and Closing During Ventilation of Acute Respiratory Distress Syndrome.

Caironi P, Cressoni M, et al:

Am J Respir Crit Care Med 2010; 181 (March 15): 578-586

Background: Positive end-expiratory pressure (PEEP) is essential to the management of acute respiratory distress syndrome (ARDS). PEEP maintains alveolar recruitment, reducing the damaging effects of cyclic airspace opening and closing during ventilation. However, trials have failed to show a survival benefit of high levels of PEEP, suggesting that the benefits of PEEP may be limited to certain patient subgroups.

Objective: To characterize the beneficial (decreased alveolar opening/closing) and harmful (increased alveolar strain) effects of high PEEP as a function of lung "recruitability" in ARDS patients.

Design: Review of a published observational study of ARDS patients.

Participants: 68 patients with ARDS enrolled at 4 international academic hospitals were evaluated. Exclusion criteria included age <16 years, pregnancy, and chronic obstructive pulmonary disease.

Methods: All patients underwent CT scanning during a 45-cm H₂O recruitment maneuver and during mechanical ventilation at 5 cm H₂O and 15 cm H₂O PEEP. A patient's "potentially recruitable lung" was defined by the increase in aerated lung after a recruitment maneuver. Patients in the upper 50th percentile of recruitable lung (>9.4% total lung weight) were defined as highly recruitable; patients in the lower 50th percentile were defined as less recruitable. Alveolar opening and closing was quantified by tidal changes in aerated lung volume; alveolar strain was defined by lung volume at peak inspiration normalized to resting lung volume (FRC). These variables were compared to mortality via multivariate analysis.

Results: Highly recruitable patients had homogenously distributed lung consolidation; less recruitable patients had more basal, focal disease. Less recruitable patients had little (2%) alveolar opening/closing at baseline; this did not change with an increase in PEEP. In contrast, highly recruitable patients had 8.1% of lung tissue undergoing cyclic opening/closing at 5 cm H₂O PEEP; an increase to 15 cm H₂O decreased this "at risk" lung to 3.6%. Surprisingly, both groups suffered similar increases in alveolar strain with the increase in PEEP. Highly recruitable patients had higher mortality in multivariate analysis, suggesting an injurious effect of cyclic opening/closing. High PEEP treatment was associated with improved survival in patients in the highest quartile of recruitability.

Conclusions: In ARDS patients with highly recruitable lungs, the harmful effect of PEEP on alveolar strain is countered by a beneficial effect of decreasing alveolar opening/closing. In less recruitable patients, there is no beneficial effect of PEEP to counter this increased strain.

Reviewer's Comments: A key beneficial effect of PEEP is the prevention of alveolar opening/closing. This study demonstrates that only patients with high lung "recruitability" experience this benefit. In these patients, decreased lung opening/closing may outweigh the negative effects of PEEP on alveolar strain. Therefore, a key step in ARDS management may be the clinical diagnosis of lung recruitability. This study suggests one mechanism of diagnosis: patients with homogenous consolidation on CT are more likely to have high recruitability. More studies are needed to guide this therapeutic decision. (Reviewer-Eric P. Schmidt, MD).

© 2010, Oakstone Medical Publishing

Keywords: Lung Injury, PEEP, Ventilator-Induced Lung Injury

Print Tag: Refer to original journal article
The data from this study support using standard dosing of oseltamivir in severely ill patients with H1N1. No dosing adjustment is needed in obesity, while reduced dosing is indicated in renal failure.

**Background:** The most appropriate dosing of oseltamivir for treatment of critically ill patients with the H1N1 pandemic flu is unknown. World Health Organization guidelines for managing severe infection suggest consideration of higher than normal dosing (>75 mg orally twice daily). A concern with patients who are severely ill is that gastrointestinal absorption of medications will be inadequate and could lead to therapeutic failure.

**Objective:** To determine pharmacokinetic parameters of oseltamivir given orally or by nasogastric tube in patients admitted to the ICU with severe respiratory failure due to suspected or confirmed pandemic (H1N1) influenza.

**Design:** Prospective non-comparative observational study.

**Participants:** Patients aged >18 years admitted to 9 ICUs in Canada and Spain.

**Methods:** Multiple blood samples were obtained after receipt of the fourth or later oseltamivir dose. Results were normalized to 75 mg twice daily for patients receiving larger doses. Pharmacokinetic modeling was performed and kinetic parameters were determined. The impact of renal dysfunction on kinetic parameters was also evaluated.

**Results:** 43 pharmacokinetic analyses from 41 patients were performed. Mean patient age was 41 years and weight was 99 kg. Half of the patients had some degree of renal impairment and 17% required renal replacement therapy. At the time blood samples for oseltamivir were obtained, 73% of patients were receiving continuous enteral feeding and 32% were on vasopressors. Median steady state trough concentrations of the active carboxylate metabolite of oseltamivir were as high as or higher than levels seen in normal volunteers given the same dosage. There was a delay in peak serum concentrations in study patients, but the extent of drug absorption was comparable to that seen in ambulatory patients. There was no association between body weight and serum concentrations. Drug exposure was much higher in patients with renal impairment.

**Conclusions:** The data support using standard dosing of oseltamivir in severely ill patients with H1N1. No dosing adjustment is needed in obesity, while reduced dosing is indicated in renal failure.

**Reviewer’s Comments:** During the outbreak of H1N1 pandemic flu over the last year, we faced severely ill patients without much information about how to care for them. During times of critical illness, there are frequently concerns about absorption of drugs administered through feeding tubes. This study is valuable because it demonstrates that this fear is unfounded for oseltamivir. In these large, critically ill individuals, standard dosing resulted in serum concentrations that were as high as or higher than that seen in normal volunteers. We still don’t know if supra-normal dosing is more efficacious, but we now know that we need not increase dosing in obese patients or overcome impaired gastrointestinal absorption during critical illness. (Reviewer-Annette M. Rowden, PharmD).

© 2010, Oakstone Medical Publishing

Keywords: Oseltamivir, Dosing, H1N1, Obesity, Severe Respiratory Failure

Print Tag: Refer to original journal article
Insights of Surrogates, Docs Helpful for Prognostication


Boyd EA, Lo B, et al:

Crit Care Med 2010; 38 (May): 1270-1275

For critically ill ICU patients, prognostication should be a 2-way discussion between physicians and surrogate decision-makers to share information regarding the patient’s condition and characteristics relevant to survival.

Background: For many critically ill ICU patients, surrogates must make decisions on their behalf. Even after timely, honest discussions with the physician about the patient's prognosis, a gap sometimes remains between the physician's and surrogate's estimates of patient prognosis.

Objective: To determine how surrogate decision-makers formulate their prognostic estimates for critically ill patients in the ICU.


Participants: 179 adult surrogate decision-makers for 142 adult ICU patients on mechanical ventilation with an APACHE II score >25.

Methods: Between days 3 and 5 of the patient being on mechanical ventilation, each surrogate was asked to privately estimate the patient's chances of survival. Then, a semi-structured interview was conducted with each surrogate, asking them to explain what factors influenced their prognostic estimates.

Results: For surrogates, the mean prognostic estimate for patient survival was 69%. Only 2% of surrogates based their prognostic estimates solely on physician estimates, while 47% used physician estimates to partly inform their estimates of survival. A surrogate's prognostic estimates were also influenced by the patient's will to live and other unique intrinsic qualities, such as stubbornness or determination (27%), the patient's previous physical fitness and age (37%), and the patient's physical status/appearance in the ICU (64%), which included facial expressions, skin hue, apparent comfort level, degree of synchrony with the ventilator, day-to-day progress, and activity level. The surrogate's knowledge of the patient's history of illness and/or survival of severe illness influenced 28% of prognostic estimates. Surrogates believed that the prognosis was improved by rallying the support of family/friends, support groups, and church groups (5%) and by their own level of optimism about patient survival (36%). The prognostic estimate also was influenced by the surrogate's intuition (19%), faith in God (20%), belief in the power of reciprocity (2%; patient's life works and/or kind behaviors being paid back by the universe), and hope for a miracle (4%).

Conclusions: A physician's estimate of survival for critically ill ICU patients is mainly influenced by experience with previous patients in similar circumstances. However, a surrogate decision-maker's estimate of survival for an ICU patient is only partially shaped by discussions with the attending physician. Both physicians and surrogates provide important insights into the patient. Therefore, prognostication should be a two-way communication between physician and surrogates to share their understanding of the patient's condition and unique characteristics that may be relevant to predicting survival.

Reviewer's Comments: This study suggests that there may be other factors to consider when prognosticating. The question is how much to rely on a patient's previous will to live to make decisions about prognostication. A future study may be useful. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Medical Directives, Surrogate Decision-Makers, Perceived Prognosis

Print Tag: Refer to original journal article
Assuming that the end-expiratory lung volume is unaffected by different levels of PEEP leads to a significant underestimation of alveolar recruitment in patients with acute respiratory distress syndrome.

**Background:** In patients with acute respiratory distress syndrome (ARDS), use of positive end-expiratory pressure (PEEP) prevents alveolar collapse and promotes alveolar recruitment, which protects the lung from ventilator-induced injury. Because the effect of PEEP on lung recruitment is highly variable in ARDS patients, alveolar recruitment must be quantified at bedside. Some researchers assume that PEEP does not affect the end-expiratory lung volume (EELV), but this assumption is not supported by clinical or experimental data.

**Objective:** To determine the effect of different PEEP levels on EELV and to determine the effect of neglecting EELV (considering it a constant) in measuring alveolar recruitment.

**Design:** Intervential human study.

**Participants:** 10 patients with ARDS who were sedated and mechanically ventilated.

**Methods:** A pressure-volume curve was obtained for each of 3 different levels of PEEP (5, 10, and 15 cm H\(_2\)O). In addition, the volume expired from PEEP to zero pressure was calculated to determine PEEP-related lung volume. Finally, the functional residual capacity (FRC) was determined for each of the 3 levels of PEEP.

**Results:** The absolute lung volume at end of expiration (EELV0) was affected by the level of PEEP: EELV0 increased with increasing PEEP levels. This increase accounted for a relevant amount of the measured recruited lung volume. The authors speculated that, after PEEP-induced alveolar recruitment, newly open alveoli behave differently, with some re-closing rapidly and others remaining open after PEEP's removal. The authors believe that it is unlikely that all newly opened alveoli will collapse when PEEP is removed.

**Conclusions:** When estimating alveolar recruitment in patients with ARDS, EELV0 cannot be ignored. Using newer technologies on today's ventilators, EELV0 and EELV PEEP can and should be measured so that recruitment can be determined as a relative rather than absolute change of lung volume. Ignoring PEEP-induced changes in EELV0 will result in an underestimation of alveolar recruitment.

**Reviewer's Comments:** Alveolar recruitment is an important lung protective strategy. This study sheds light on the mechanism and possible confounding influences of the effect of PEEP on EELV. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Assessing Alveolar Recruitment, Absolute Lung Volume

Print Tag: Refer to original journal article
Hyperventilation is the most effective means for acutely lowering intracranial pressure, so brief use of hypocapnia can be useful in patients with acute brain injury. However, prolonged hypocapnia is frequently harmful.

**Background:** In patients with acute brain injury, prophylactic hyperventilation has been widely used to induce hypocapnia and acutely reduce intracranial pressure (ICP). Extremes of hypocapnia for prolonged periods have been advocated for the treatment of acute brain injury.

**Objective:** To determine the prevalence of hypocapnia in the management of acute brain injury and to determine the outcomes associated with this treatment strategy.

**Design:** Review of the literature published between 1966 and 2009. **Prevalence:** Prophylactic hyperventilation to induce hypocapnia is widely used in adults and children with acute brain injury. For example, 36% of board-certified neurosurgeons in the United States routinely use prophylactic hyperventilation in patients with severe traumatic brain injury. **Deleterious Effects:** A serious concern associated with hypocapnia is that it may cause adverse neuronal oxygen supply and demand through various mechanisms, resulting in brain ischemia. During prolonged hypocapnia, the pH of the cerebrospinal fluid (CSF) is buffered toward normal and cerebral blood flow normalizes by 6 hours. This CSF buffering ablates the effectiveness of ongoing hypocapnia. Also during prolonged hypocapnia, further reductions in carbon dioxide are difficult to achieve, making it difficult to acutely reduce ICP any further without causing lung damage. Finally, when normocapnia eventually is restored, a rebound elevation in ICP may occur, potentially resulting in brain stem herniation or intracranial hemorrhage (premature infants). Some other adverse outcomes associated with hypocapnia include decreased perfusion to the heart and other organs, and acute lung injury or acute respiratory distress syndrome due to the high tidal volumes used to achieve hypocapnia. **Benefits:** Hyperventilation is the most effective means for acutely lowering ICP, so brief use of hypocapnia can be useful while definitive measures to manage ICP are being instituted. Normocapnia should be restored as soon as feasible because hypocapnia becomes ineffective within hours.

**Conclusions:** Prophylactic hyperventilation in brain injury is increasingly recognized as being frequently harmful and rarely, if ever, beneficial. Prolonged hypocapnia does not improve neurologic outcomes in patients with brain injury, and its use is associated with worsening cerebral ischemia, worse outcomes, and injury to other organs. Therefore, use of hypocapnia should be brief and limited to emergency management of life-threatening ICP or to acutely reduce brain bulk in the operating room while definitive measures to manage ICP are being instituted. Further prospective trials of prophylactic hyperventilation in brain injury are difficult to justify.

**Reviewer's Comments:** This paper dispels almost 3 decades of thought about hyperventilation in brain injury patients. As it turns out, the reduced cerebral blood flow is more detrimental than the change in ICP at least after 6 hours of therapy. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

**Keywords:** Acute Brain Injury, Therapeutic Hypocapnia, Outcomes

**Print Tag:** Refer to original journal article
Excess HCAP Mortality Related to Limiting of Support

Why Mortality Is Increased in Health-Care-Associated Pneumonia: Lessons From Pneumococcal Bacteremic Pneumonia.

Rello J, Luján M, et al:

Chest 2010; 137 (May): 1138-1144

Patients with health-care-associated pneumonia tend to be significantly older, have more comorbidities, higher PSI scores, and higher mortality rates than do patients with community-acquired pneumonia.

Background: Information on the etiology and management of health-care–associated pneumonia (HCAP) is limited. Patients with HCAP tend to be older and have more comorbidities, thus giving them a higher pneumonia severity index (PSI) score.

Objective: To compare differences in epidemiology and management of patients with HCAP versus patients with community-acquired pneumonia (CAP), and to determine some of the factors associated with HCAP outcome.

Design: Prospective cohort study.

Participants: Adult patients hospitalized with bacteremic Streptococcus pneumoniae pneumonia.

Methods: CAP and HCAP cohorts were compared for demographics and clinical data.

Results: 184 patients had CAP and 44 had HCAP. Compared with the CAP cohort, the HCAP cohort presented more frequently with baseline comorbidities, more severe illness, and higher PSI scores. Significantly fewer HCAP patients were admitted to the ICU than were CAP patients. Resistance to macrolides was more common in the HCAP cohort (36%) than in the CAP cohort (13%). More complications were seen in the HCAP cohort than in the CAP cohort. While the HCAP cohort was more severely ill than the CAP cohort, but use of advanced care modalities was lower in the HCAP cohort than in the CAP cohort. The mortality rate was significantly higher in the HCAP cohort (29.5%) than in the CAP cohort (7.6%). The 30-day mortality rate also was significantly higher in the HCAP cohort (OR, 4.58; 95% CI, 1.91 to 10.94) than in the CAP cohort. On multivariate logistic regression analysis, an increased 30-day mortality rate was associated with HCAP (OR, 5.56), a PaO_2/Fio_2 ratio <250 (OR, 3.90), and need for vasopressor therapy (OR, 4.22).

Conclusions: Presenting demographics, severity of illness, and complications are significantly different for patients with pneumococcal HCAP than for patients with pneumococcal CAP. For example, patients with HCAP tend to be significantly older and have more comorbidities and higher PSI scores than do CAP patients. In addition, HCAP is associated with a significantly higher mortality rate than is CAP. The results of this study suggest that the excess mortality rate for HCAP patients is due, in part, to the decision to limit the support given to patients of advanced age with comorbidities.

Reviewer's Comments: This is a nice descriptive study about differences between HCAP and CAP. The differences warrant a distinction since outcomes are different, the population is different, and the pattern of ab resistance is different. (Reviewer—Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Health-Care-Associated Pneumonia, Mortality

Print Tag: Refer to original journal article
Dynamic hyperinflation (DH) occurs frequently in daily life in patients with moderate to severe COPD. This suggests that DH is one of the factors involved in limiting daily activity in COPD patients.

**Background:** Patients with chronic obstructive pulmonary disease (COPD) have decreased everyday physical activity. Although several factors contribute to these exercise limitations, one important contributor is dynamic hyperinflation (DH), which occurs when ventilatory demand increases, leaving less time for expiration. This results in an increase in end-expiratory lung volume (EELV) and a decrease in inspiratory reserve volume (IRV), causing dyspnea. Whether the stage of COPD, according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), affects the severity of DH is unknown.

**Objective:** To determine if DH contributes to limitations in the activities of daily living (ADLs) in patients with COPD, and to determine if the GOLD stage of COPD affects DH.

**Participants:** Clinically stable patients with COPD GOLD II (n=10), GOLD III (n=12), and GOLD IV (n=10) disease.

**Methods:** Each patient selected an ADL at home that typically caused the most dyspnea. As the task was performed, respiratory physiology was measured using Oxycon® Mobile, a telemetric breath-by-breath system. Inspiratory capacity (IC), total lung capacity (TLC), end-expiratory lung volume (EELV), and tidal volume were measured.

**Results:** Patients in the various GOLD classifications had comparable distribution of age, gender, body mass index, and smoking history. At the end of ADLs, an increase in EELV was seen in all patients without significant differences being noted between the various GOLD classes. However, GOLD III patients tended to have more DH than did GOLD IV patients. Dyspnea was reported by all patients at the end of their ADL, and GOLD IV patients had the highest levels of dyspnea.

**Conclusions:** In patients with COPD, DH occurs during real-life ADLs, regardless of GOLD stage of disease severity. This finding suggests that, in COPD patients, DH plays a role in daily activity limitation, which may contribute to decreased physical activity and health-related quality of life.

**Reviewer's Comments:** This paper presents some data that are counterintuitive. It appears that dynamic hyperinflation can occur independently of the severity of GOLD class for COPD. This DH, however, significantly interferes with the patient’s quality of life. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

**Keywords:** Dynamic Hyperinflation, COPD Global Initiative, COPD Stage

**Print Tag:** Refer to original journal article
MI Risk Doubled After COPD Exacerbation

Increased Risk of Myocardial Infarction and Stroke Following Exacerbation of COPD.

Donaldson GC, Hurst JR, et al:

Chest 2010; 137 (May): 1091-1097

The risks of myocardial infarction and stroke are increased following an exacerbation of chronic obstructive pulmonary disease (COPD). Treating COPD exacerbations may reduce the risk of cardiovascular events.

Background: Some studies have shown that respiratory infections in the general population increase the risk of myocardial infarction (MI). In patients with chronic obstructive pulmonary disease (COPD), exacerbations are due to lower respiratory tract infections, which are associated with an increase in systemic inflammatory markers. The increased systemic inflammation associated with these acute exacerbations could be a risk factor for cardiovascular events.

Objective: To determine the risk of MI and stroke following an exacerbation of COPD.

Design: Self-controlled case series.

Participants: 25,857 patients with a physician diagnosis of COPD.

Methods: The incidence of MI or stroke was compared during the "high-risk" periods immediately after a COPD exacerbation (extending through the first 7 weeks after an exacerbation) versus the "low-risk" periods when the patient was stable. Patients were observed for 2 years, from February 25, 2003, to February 24, 2005. COPD exacerbations were defined in 3 different ways: (1) a prescription for oral steroids (except fludrocortisones), (2) a prescription of preselected oral antibiotics commonly used in treating exacerbations, and (3) a prescription of oral steroids and a preselected oral antibiotic.

Results: In COPD patients, the incidence rate was 1.1 per 100 patient-years for MI and was 1.4 per 100 patient-years for stroke. Exacerbation rates were significantly higher in patients experiencing MI than in those who did not experience MI. The risk of MI was significantly higher during the 1-day to 5-day period after a COPD exacerbation when exacerbations were defined by the prescription of both steroids and antibiotics. The risk of MI was increased 2.27 times during the 1-day to 5-day period after a COPD exacerbation. Compared with patients who did not have a stroke, those who had a stroke also had a significantly higher rate of exacerbations (risk increased 1.26 times) during the first 49 days after an exacerbation as defined by courses of steroids, but not when defined by antibiotic prescription only or when defined by prescriptions for both antibiotics and oral steroids.

Conclusions: COPD exacerbations are associated with a 2.27-fold increased risk of MI during the first 5 days after an exacerbation. In addition, COPD exacerbations are associated with an increased risk of stroke during the first 49 days after an exacerbation. Treating stable COPD and exacerbations of COPD may help reduce the risk of cardiovascular events in patients with COPD.

Reviewer's Comments: I am not surprised that COPD exacerbations would be a risk factor for MI. Many patients with COPD have coronary artery disease as well, and the hypoxia and increased pulmonary artery pressures could help precipitate an MI. The paper, however, warns us to carefully follow patients having an exacerbation for early signs of cardiac ischemia. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Exacerbation, Myocardial Infarction Risk

Print Tag: Refer to original journal article
The usefulness of chest radiographs in the early detection of active tuberculosis (TB) has been questioned. In this study, high-resolution CT identified active TB in 9 participants with normal chest radiographs.

**Background:** Tuberculosis (TB) outbreaks typically have been investigated with tuberculin skin test (TST), chest radiographs (CXR), and acid-fast smears of sputa. However, high-resolution CT (HRCT) scanning has been found to detect lesions suggestive of active pulmonary TB in patients who have normal CXR findings.

**Objective:** To determine if HRCT scanning can differentiate active and latent TB infections in a cohort of 92 soldiers in the South Korean army in which a TB outbreak was reported.

**Methods:** 4 cases of TB were identified between April and November 2007 among a cohort of 92 soldiers who shared 9 barracks, 1 bathroom, and 1 dining room. During the outbreak investigation, the following tests were performed for each soldier: CXR, TST, QuantiFERON®-TB Gold In-Tube assay (QFT), and acid-fast smear and mycobacterial culture of sputum. Soldiers with any positive finding underwent HRCT. Soldiers with active TB were treated for 6 months with isoniazid, rifampicin, pyrazinamide, and ethambutol.

**Results:** Of 87 soldiers who completed all studies, all were HIV-negative and none had a self-reported history of TB. Median duration of contact with the index TB patient was 251 days. On CXR, abnormal lesions were seen in 11 soldiers. HRCT was performed in 50 soldiers, and lesions suggesting active TB were seen in 18 (no lesions on CXR, n=9; negative TST, n=3; negative QFT, n=2), while lesions suggesting bacterial pneumonia were seen in 5. After a 1-week course of broad-spectrum antibiotics, radiographic lesions did not change for 18 soldiers with lesions suggestive of active TB, but lesions disappeared for 5 soldiers with lesions suggestive of bacterial pneumonia. Among 39 patients with negative results on both TST and QFT, none developed active TB (follow-up range, 85 to 613 days). Seventeen soldiers were diagnosed with latent TB (positive TST; positive QFT; negative HRCT). Of 13 patients with discordant results (negative HRCT; positive for either TST or QFT but not both), 9 underwent repeat testing at 3 months, and 8 were diagnosed with latent TB.

**Conclusions:** Differentiating between active TB and latent TB is important in TB outbreak investigations. Use of high-resolution CT more reliably differentiates active versus latent TB than does use of CXRs. Risks and costs of using HRCT in TB outbreak investigations must be considered carefully.

**Reviewer's Comments:** HRCT appears to offer a lot in determining if a patient has active or latent disease. The expense has to be considered as well as radiation dosage in considering this part of the routine evaluation for TB exposure. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Tuberculosis, Active Cases, Detection, Chest CT

Print Tag: Refer to original journal article
Unweanable NMD Patients Can Be Safely Extubated

Extubation of Patients With Neuromuscular Weakness: A New Management Paradigm.

Bach JR, Gonçalves MR, et al:

Chest 2010; 137 (May): 1033-1039

The paradigm of “weaning then extubation” can be changed to “extubation to permit self-weaning” for patients with neuromuscular disease.

Background: Intubated patients with neuromuscular disease (NMD) cannot successfully pass "spontaneous breathing trials" and are considered to be unweanable. No guidelines exist for extubating unweanable patients with NMD. Some of these patients depended on noninvasive mechanical ventilation (NIV) for years before intubation, and some have ineffective cough peak flows (CPF) and cannot be extubated due to accumulation of airway secretions.

Objective: To report success rates of extubating unweanable patients with NMD using weaning criteria similar to those used for patients with traumatic tetraplegia and others.

Design: Uncontrolled study of only 1 extubation approach.

Participants: 157 NIV-dependent patients aged ≥4 years with NMD for whom intubation could not be avoided.

Methods: All intubated patients were treated conventionally to maintain normocapnia and normal respiratory rates. Mechanically assisted coughing (MAC) was performed to rapidly achieve full chest expansion and then complete emptying of lungs. Patients were extubated directly to NIV on assist/control of 800 to 1500 mL at a rate of 10 to 14 minutes in ambient air. A combination of nasal, oronasal, and mouthpiece interfaces was used to provide NIV. Patients kept 15-mm angled mouthpieces accessible and weaned themselves, when possible, by taking fewer and fewer intermittent positive pressure ventilations (IPPVs) as tolerated. Patients were taught to maximally expand their lungs by air stacking ventilator-delivered volumes to the lungs, and then an abdominal thrust was provided to manually assist the cough.

Results: 20 patients had been continuously NIV dependent for 12.2 years before intubation, while 41 used NIV part-time and 96 used no NIV before intubation. Experience with NIV and MAC was significant in predicting extubation success. There were 172 extubations on 157 patients. For patients with assisted CPF ≥160 L/minute, all 98 extubations were successful. For patients with CPF <160 L/minute, 59 of 74 extubations were successful. Upon extubation, most patients with a vital capacity of ≥200 mL were weaned from continuous to part-time NIV, which required 3 to 21 days and was usually accomplished at home. Extubation of unweanable patients was associated with no mortality, fewer days intubated, no tracheostomies, and return home.

Conclusions: Unweanable intubated patients with NMD who satisfy specific criteria can be successfully extubated to full NIV and MAC. The paradigm of "weaning then extubation" can be changed to "extubation to permit self-weaning" for patients with NMD. NMD patients with measurable assisted cough flows should no longer be advised to refuse intubation.

Reviewer's Comments: This rather important paper points out that 1 protocol for weaning cannot be applied to all patients. This special group of patients requires a lot of clinical judgment and less reliance on established procedures. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Extubation, Unweanable Patients, Neuromuscular Weakness

Print Tag: Refer to original journal article
Silver-Coated ETTs Linked to Reduced Mortality in VAP

Association Between a Silver-Coated Endotracheal Tube and Reduced Mortality in Patients With Ventilator-Associated Pneumonia.

Afessa B, Shorr AF, et al:

Chest 2010; 137 (May): 1015-1021

In patients with ventilator-associated pneumonia, the rate of ventilator-associated pneumonia due to potentially multidrug-resistant bacteria was 50% lower when silver-coated endotracheal tubes were used.

**Background:** Preventive strategies have been shown to reduce the incidence of or delay the onset of ventilator-associated pneumonia (VAP), but they do not necessarily reduce VAP-related mortality.

**Objective:** To determine if use of silver-coated endotracheal tubes (ETT) reduces VAP-related mortality.

**Design/Participants:** Retrospective cohort analysis of a subset of 93 patients who developed VAP in the North American Silver-Coated Endotracheal Tube (NASCENT) study conducted in 54 centers in North America between 2002 and 2006.

**Methods:** In the NASCENT study, adults requiring mechanical ventilation with an ETT for ≥24 hours were randomly assigned to intubation with either a silver-coated ETT or a control tube (no silver coating). In the current cohort analysis, the microbiology associated with VAP was assessed. The cause of VAP-associated death during hospitalization was defined as pneumonia or sepsis. Multivariate analysis was performed to determine the influence of silver-coated ETTs on patient mortality.

**Results:** Of 93 patients in whom VAP developed, 37 were in the silver-coated ETT group and 56 were controls. Five of 37 patients in the silver group died (14%), while 20 of 56 patients in the control group died (36%). Therefore, the mortality rate was approximately 60% lower in the silver group than in the control group. In the subgroup in which initial antibiotic therapy was considered appropriate, 2 of 31 patients in the silver-coated group died (6%), while 16 of 47 patients in the control group died (34%). Sepsis or pneumonia was considered the cause of death for 1 of 5 patients who died in the silver-coated group and for 9 of 20 patients who died in the control group. In these cases, multidrug-resistant bacteria were identified in 1 of 1 patient in the silver group and in 6 of 9 patients in the control group. On multivariate analysis, 2 major unexpected findings were revealed. First, in patients without VAP, the mortality rate was 17% higher in the silver group than in the control group. Second, delayed-onset VAP was associated with a reduced risk of death.

**Conclusions:** Silver-coated ETTs may be associated with reduced mortality in patients with microbiologically confirmed VAP. In addition, the rate of VAP due to potentially multidrug-resistant bacteria was 50% lower in the silver group than in the control group. More studies are needed to confirm these findings.

**Reviewer’s Comments:** The major problem with this study is that the number of patient studies with VAP was very low. In addition, they have to be able to explain why the overall mortality rate of patients without VAP was higher in the silver-coated group. There are many more patients who do not get VAP than those who do, and this could be a big problem. (Reviewer-Eric Howard Gluck, MD, JD).

© 2010, Oakstone Medical Publishing

Keywords: Ventilator-Associated Pneumonia, Mortality, Silver-Coated Endotracheal Tubes

Print Tag: Refer to original journal article