

## 90-Day Mortality in Hypercarbic Patients Reduced With Early NIV at Extubation

*Non-Invasive Ventilation After Extubation in Hypercapnic Patients With Chronic Respiratory Disorders: Randomised Controlled Trial.*

Ferrer M, Sellares J, et al:

*Lancet*; 2009; August 12 (pub ahead of print):

For patients ready for extubation but hypercarbic, 24 hours of prophylactic NIV decreased 90-day mortality, but not reintubation rate.

**Background:** Non-invasive ventilation (NIV) has shown mixed results when used to prevent reintubation. Small studies of early prophylactic use have been positive, but one study for rescue after signs of respiratory failure appeared found increased mortality with NIV from delay of necessary reintubation (Esteban et al, 2004).

**Objective:** To compare NIV to conventional oxygen therapy after extubation with rates of reintubation and survival in patients with chronic respiratory disease.

**Design:** Randomized controlled trial.

**Participants:** 106 patients, largely medical ICU admissions, with planned extubation after a successful spontaneous breathing trial with PaCO<sub>2</sub> >45 mm Hg. Patients with decreased consciousness, poor cough, copious secretions, GI bleeding, or poor NIV facial interface were excluded.

**Methods:** NIV patients (n=54) received NIV via face mask from Respironics set with IPAP 12 to 20 cm and EPAP 5 to 6 cm for up to 24 hours. NIV was set to respiratory rate <25, with O<sub>2</sub> added to keep SpO<sub>2</sub> >92%. Control patients received supplemental oxygen. All patients received routine respiratory care as needed. Respiratory failure was defined as respiratory acidosis, P/F<120, respiratory rate >35, or clinical signs of agitation or respiratory failure. Reasons for reintubation were also pre-defined. Rescue trial use of NIV for up to 4 hours was allowed in both groups prior to reintubation. Primary end point was rate of respiratory failure and secondary end point was 90-day survival.

**Results:** Respiratory failure rates were 15% (NIV) versus 48% (control) [OR, 5.32; 95% CI, 2.11 to 13.46; *P* <0.001]. Overall, 11% in the NIV compared to 19% of controls met reintubation criteria (nonsignificant). There were no differences in ICU or hospital lengths of stay, ICU mortality (6% vs 8%), or hospital mortality (11% vs 22%; *P* =0.26). Mortality at 90 days was reduced in the NIV group (11% vs 31%; OR, 3.56; 95% CI, 1.27 to 10.0; *P* =0.024).

**Conclusions:** Early use of NIV decreased the rate of respiratory failure after extubation as well as 90-day mortality in patients with hypercarbia.

**Reviewer's Comments:** This well-done study was powered to a minor end point--signs of respiratory distress. Since work of breathing is reduced by NIV, it is unsurprising that respiratory failure as defined here was less common in NIV patients. Among the more clinically meaningful end points, there is a discrepancy between the significant effects on 90-day mortality and lack of benefit of NIV on events during hospitalization. There is not an apparent mechanism whereby 24 hours of NIV would alter late mortality without affecting reintubation rates, length of stay, or other earlier markers of mortality risk. This suggests that the groups may have differed in their prognosis in ways not captured by the APACHE score at study entry. Prophylactic use of NIV remains sensible for patients at high risk of reintubation. However, I cannot fully accept the authors' conclusions that the control group deaths, largely after ICU discharge, were attributable to their having missed 24 hours of NIV. (Reviewer-Henry E. Fessler, MD).

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## Statins: New Therapeutics for ARDS?

*Simvastatin Decreases Lipopolysaccharide-Induced Pulmonary Inflammation in Healthy Volunteers.*

Shyamsundar M, McKeown ST, et al:

*Am J Respir Crit Care Med*; 2009; 179 (June 15): 1107-1114

Simvastatin reduces lung and systemic inflammation in human volunteers in a lipopolysaccharide inhalation model of ARDS.

**Background:** Hydroxymethylglutaryl (HMG) CoA reductase inhibitors (statins) have pleiotropic anti-inflammatory and antimicrobial effects, leading some to speculate on their therapeutic potential in the ICU. Reports in several animal models of acute respiratory distress syndrome (ARDS) have indicated that statins reduce lung injury, while several retrospective studies in humans have shown that statins are associated with improved outcomes in pneumonia, sepsis, and bacteremia. To date, a single retrospective study of statins in ARDS patients was unable to find any effect of statins on outcomes, but prospective trials are underway.

**Objective:** To investigate in vivo if simvastatin modulates ARDS mechanisms in a model of lung inflammation induced by inhalation of lipopolysaccharide (LPS) in healthy human volunteers.

**Design:** Prospective double-blind placebo-controlled study.

**Participants:** 30 healthy adult subjects.

**Intervention:** Subjects were randomized to receive placebo, 40 mg/day simvastatin, or 80 mg/day simvastatin for 4 days before LPS inhalation.

**Methods:** Measurements of inflammation were made in bronchoalveolar lavage fluid (BALF) 6 hours post-inhalation and in plasma 24 hours post-inhalation.

**Results:** Simvastatin pretreatment reduced LPS-induced BALF neutrophilia, myeloperoxidase, tumor necrosis factor- $\alpha$ , matrix metalloproteinases 7, 8, and 9, and C-reactive protein (CRP), as well as plasma CRP (all  $P < 0.05$  vs placebo). There was no significant difference between the 40- and 80-mg doses. BALF from simvastatin-treated subjects was less inflammatory as assessed by its reduced activation of the inflammatory transcription factor NF-kappa B in cultured macrophages.

**Conclusions:** Simvastatin has anti-inflammatory effects in the airspace and serum in humans exposed to inhaled LPS, a model of ARDS.

**Reviewer's Comments:** Statins, originally developed for serum cholesterol reduction, have long been known also to attenuate pro-inflammatory cellular functions (eg, cytokine production, oxidant release, chemotaxis), leading to their progressive exploration in a variety of inflammatory conditions ranging from organ transplantation to Alzheimer's disease. Multiple studies in animals have demonstrated that statins are therapeutic in acute lung injury (ALI), liver injury, and sepsis, and retrospective studies in human sepsis and pneumonia have mostly found improved outcomes in statin-treated patients. Statins will next have to undergo prospective testing in critically ill patients. As there are presently at least 2 ongoing phase II clinical trials investigating the prevention and treatment of ALI with simvastatin, answers will be forthcoming. This paper is a landmark study, as it provides critical mechanistic evidence that simvastatin modulates several hallmark events in human ALI (neutrophil recruitment, cytokine induction) after only 4 days of pretreatment--a window that is pertinent to prevention/treatment of early ALI in patients. A recent report (Kruger et al, *Intensive Care Med* 2009) that septic patients are prone to suprathreshold plasma levels of atorvastatin likely due to altered metabolism suggests that caution is, however, warranted as we explore statins in the ICU. (Reviewer-Michael B. Fessler, MD).

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## CT Findings Predict Complicated *C difficile* Infection

Prediction of Complicated *Clostridium difficile* Infection by Pleural Effusion and Increased Wall Thickness on Computed Tomography.

Valiquette L, Pepin J, et al:

*Clin Infect Dis*; 2009; 49 (August 15): 554-560

A retrospective analysis reveals pleural effusion and increased colonic wall thickness to be independent CT radiographic predictors of complicated *C difficile* infection.

**Background:** Abdominal CT findings have been evaluated as predictors of complicated *Clostridium difficile* infection (CDI) and have been incorporated recently into a proposed CDI severity score (Belmares et al, *J Infect* 2007), but no such findings have been confirmed to have independent value for predicting complicated CDI. Whether abdominal CT findings add to clinical/laboratory assessment is uncertain.

**Objective:** To correlate abdominal CT findings with complicated CDI, and to compare CT findings before and after emergence of the hypervirulent epidemic BI/NAP1/027 *C difficile* strain.

**Design:** Retrospective cohort study.

**Methods:** Review was performed of all patients aged  $\geq 18$  years hospitalized in a single Canadian secondary/tertiary hospital who had an abdominal CT performed within 72 hours of toxin-confirmed CDI between January, 1998 and December 2006. Complicated CDI was defined as death within 30 days of diagnosis or development of megacolon, perforation, colectomy, or shock. Based on institutional data, BI/NAP1/027 emergence was in 2002. Scans were graded using a standardized form by 2 blinded radiologists for: colonic wall thickening ( $\geq 4$  mm), pancolitis, target sign, pericolonic fat stranding, accordion sign, pleural effusion, ascites, and subcutaneous edema. CT findings and laboratory values were correlated to complicated CDI using multivariate logistic regression.

**Results:** Of 1189 patients with newly diagnosed CDI, 165 satisfied inclusion criteria. Patients who underwent CT were younger, had higher peak white blood cell (WBC) counts and serum creatinine levels, and were more likely to experience fever than those who did not undergo CT. No difference in CT findings was noted before/after emergence of BI/NAP1/027. Pleural effusion (adjusted odds ratio [AOR], 2.6; 95% confidence interval [CI], 1.1 to 6.6), colonic wall thickness  $>15$  mm (AOR, 6.0; 95% CI, 1.1 to 33.9), peak WBC count  $\geq 30 \times 10^9/L$  (AOR, 4.8; 95% CI, 1.4 to 16.4), albumin level  $<20$  g/L (AOR, 6.9; 95% CI, 2.4 to 20.1), and immunosuppression (AOR, 4.7; 95% CI, 1.5 to 15.3) were independently associated with complicated CDI.

**Conclusions:** In a selected sample of CDI patients, CT provided prognostic information additional to that derived from clinical/laboratory parameters. No change in CT characteristics was noted after the emergence of BI/NAP1/027.

**Reviewer's Comments:** This is the largest study to review CT abnormalities in a cohort of patients with confirmed CDI, and the first to include radiographic variables in a predictive multivariate model of complicated CDI. Two specific CT findings, pleural effusion and increased wall thickness, were identified that have independent prognostic value; the former, unlike radiographic ascites, was found to persist as a predictor after model adjustment for hypoalbuminemia. As this was a retrospective study of a select subset of CDI patients, no conclusions can be drawn regarding sensitivity of CT for diagnosing CDI. Indications for obtaining CTs in CDI patients and whether CTs can positively impact management of complicated CDI are additional unresolved questions. (Reviewer-Michael B. Fessler, MD).

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## Improving Catheter Care Has Major Impact on CRBSI Prevention

*Impact of a Prevention Strategy Targeting Hand Hygiene and Catheter Care on the Incidence of Catheter-Related Bloodstream Infections.*

Zingg W, Imhof A, et al:

*Crit Care Med*; 2009; 37 (July): 2167-2173

The employment of a hand hygiene training program along with education on catheter care decreases the incidence of CRBSIs in ICU settings.

**Background:** Catheter-related bloodstream infections (CRBSIs) contribute to intensive care unit (ICU) morbidity and mortality. The process involved in insertion of the central venous catheter (CVC), ie, use of maximal barrier precautions, skin disinfection with chlorhexidine, and use of CVCs coated with antimicrobials, has been shown to impact CRBSIs. However, the role of catheter care in development of CRBSI is less defined.

**Objective:** To determine if an educational program targeting hand hygiene and catheter care would improve CRBSIs in an adult ICU setting.

**Design:** Prospective interventional cohort study involving surgical and medical ICUs at a single center. The study was divided into a baseline and intervention period.

**Participants/Methods:** All adult patients hospitalized in any of the ICUs with  $\geq 1$  CVC were eligible for the study. There were no exclusion criteria. CRBSI was considered ICU acquired if diagnosed  $\geq 48$  hours after admission or within 48 hours after discharge from the ICU. Uni- and multivariate logistic regression was used to identify independent risk factors for CRBSI.

**Interventions:** The intervention consisted of a 4-phase educational program focusing on hand hygiene and catheter care.

**Results:** 499 patients representing 974 CVCs (6200 catheter-days) and 500 patients representing 1015 CVCs (7279 catheter-days) were included in the baseline and intervention periods, respectively. Incidence densities of CRBSI were 3.9 per 1000 catheter-days and 1.0 per 1000 catheter-days in the baseline and intervention periods, respectively ( $P < 0.001$ ). Baseline period, male gender, and stay in the medical ICU were found to be independent risk factors for the development of CRBSI. There was no difference in mortality between the baseline and intervention period. Compliance with hand hygiene increased minimally from 59.1% at baseline to 65.0% ( $P = 0.466$ ) during the intervention period. However, proper performance of hand disinfection procedures improved significantly from 22.5% during the baseline period to 42.6% during the intervention period ( $P < 0.003$ ).

**Conclusions:** The authors conclude that the employment of a hand hygiene training program along with education on catheter care decreases the incidence of CRBSIs in ICU settings.

**Reviewer's Comments:** This is a nice study emphasizing the importance of hand hygiene in preventing nosocomial CRBSIs. This study also demonstrates that a relatively cost-effective intervention can be successful and effective. Furthermore, this study highlights patient populations at particular risk for developing CRBSIs, ie, male patients and patients in the medical ICU. Although there was significant improvement in the proper performance of hand disinfection procedures after educational intervention, the rate remained below 50%. This suggests that we need to consider different mechanisms to ensure proper hand hygiene, and more importantly, proper aseptic catheter care, in addition to continuing educational programs. (Reviewer-Mahendra Damarla, MD).

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## Is Ketamine a Safer Alternative to Etomidate for Emergency Intubation?

*Etomidate Versus Ketamine for Rapid Sequence Intubation in Acutely Ill Patients: A Multicentre Randomised Controlled Trial.*

Jabre P, Combes X, et al:  
*Lancet*; 2009; 374 (July 25): 293-300

Ketamine is safe for use during emergency intubation and does not suppress the adrenal axis when compared to etomidate.

**Background:** Critically ill patients often require intubation. Etomidate has been a staple drug of choice in rapid sequence intubation. However, etomidate has been implicated in the development of adrenal insufficiency, thereby possibly worsening morbidity and mortality in a susceptible patient population.

**Objective:** To determine if a single dose of etomidate compared to ketamine for emergency intubation would alter morbidity of critically ill patients.

**Design:** Randomized controlled single-blind trial conducted in France.

**Participants/Methods:** Adult patients who needed sedation for emergency intubation and did not meet exclusion criteria were prospectively enrolled and randomized to receive 0.3 mg/kg of etomidate or 2 mg/kg of ketamine for intubation. The primary end point was the maximum sequential organ failure assessment (SOFA) score during the first 3 days in the intensive care unit (ICU) on the modified intention-to-treat population (469 patients; n=234 in etomidate group and n=235 in ketamine group).

**Results:** The maximum SOFA score did not differ significantly between the 2 groups (10.3 and 9.6 for patients treated with etomidate and ketamine, respectively;  $P = 0.056$ ). There was no difference in 28-day mortality between the 2 groups. The basal cortisol level was lower in patients treated with etomidate than ketamine. The percentage of non-responders to the adrenocorticotropic hormone stimulation test was higher in the etomidate group compared to the ketamine group (81% vs 42%). There were a higher percentage of patients diagnosed with adrenal insufficiency in the group treated with etomidate than ketamine (86% and 48%, respectively). There were no adverse side effects associated with usage of either drug.

**Conclusions:** The authors conclude that ketamine is a safe alternative to etomidate for emergency intubation in critically ill patients. The use of ketamine could be considered in patients that are susceptible to worse outcomes as a result of adrenal axis suppression, ie, patients with sepsis.

**Reviewer's Comments:** This study confirms the adrenal effects of etomidate in critically ill patients and finds that ketamine may be a safer alternative. The incidence of adrenal insufficiency in this study emphasizes the detrimental role of critical illness on adrenal function. The relatively low representation of septic patients (16%) leaves the role of etomidate mediated-adrenal suppression on mortality in septic patients undefined. Although the SOFA scores were not significantly different, the  $P$  value was very close to the arbitrary threshold for significance. This suggests that a slightly larger study would have shown a difference in this variable, although the values are quantitatively close. I liked this study because it calls into question the routine practice of using etomidate in critically ill patients for its stable hemodynamic profile. (Reviewer-Mahendra Damarla, MD).

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## CRBSI Decreased With Simulation-Based Education for CVC Insertion

*Use of Simulation-Based Education to Reduce Catheter-Related Bloodstream Infections.*

Barsuk JH, Cohen ER, et al:

*Arch Intern Med*; 2009; 169 (August 10): 1420-1423

In this study, training of internal medicine residents using simulation-based education decreased the risk of catheter-related bloodstream infection by 85%.

**Objective:** To determine the effect of simulation-based education for central venous catheter (CVC) insertion on the incidence of catheter-related blood stream infections (CRBSIs).

**Methods:** The study period was a 32-month period in the medical and surgical intensive care units (ICUs) of a single university hospital. For the initial 16 months, traditional educational methods were used for teaching placement of CVCs. After the initial 16 months, the medical ICU instituted a simulation-based training program in CVC insertion, while the surgical ICU continued with a traditional training method. Simulation-based education consisted of a 1-hour lecture followed by 3 hours of hands-on training via a simulator. The primary outcome measure was CRBSI. CRBSI was determined independently by the hospital's infection control committee, which was blinded to the nature of the study and the timing of the intervention.

**Results:** During the initial 16-month period of comparison, the rate of CRBSI in the medical ICU was 3.20 per 1000 catheter-days compared to 4.86 per 1000 catheter-days in the surgical ICU. After introduction of the simulation-based education, there was a significant drop in CRBSI's in the medical ICU to 0.5 per 1000 catheter days ( $P = 0.001$ ). This represented only 4 CRBSIs in >8000 catheter-days, and an overall reduction in CRBSI by 84.5%. Compared to the surgical ICU during this same period, there were also fewer CRBSIs in the medical ICU (0.5 vs 5.26 per 1000 catheter-days;  $P = 0.001$ ).

**Conclusions:** Use of simulation-based education in CVC insertion is associated with fewer CRBSIs.

**Reviewer's Comments:** This article demonstrates that use of simulation-based education for placement of CVC may significantly reduce the incidence of CRBSI. Simulation-based education is becoming increasingly prevalent in both the training of resident physicians and continuing medical education. It makes logical sense that practical experience with a simulator can lead to improved comfort with a procedure that in turn may lead to greater ability to perform the procedure without breaching sterile precautions. However, the results of this trial need to be interpreted with caution, as the overall rates of CRBSI were low in both units. Furthermore, there is some difficulty comparing the surgical ICU to the medical ICU, as the patient populations are quite different. The most useful comparison is to look at the rates of CRBSI in the medical ICU before and after the simulator-based education, where a remarkable drop was seen. The reason why the simulator-based education decreased CRBSI cannot be determined from the data presented; the authors do not report any data about how practices changed following simulator-based training or technical details about the procedures. (Reviewer-Cynthia D. Brown, MD).

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## Less Fluids Equals More Ventilator-Free Days in ALI Patients

*Less Is More: Improved Outcomes in Surgical Patients With Conservative Fluid Administration and Central Venous Catheter Monitoring.*

Stewart RM, Park PK, et al:

*J Am Coll Surg*; 2009; 208 (May): 725-735

A conservative fluid management strategy is safe and effective in surgical patients with acute lung injury to decrease duration of mechanical ventilation.

**Objective:** To analyze the effect of fluid management and central monitoring in surgical patients with acute lung injury (ALI).

**Design:** Post-hoc subgroup analysis of a randomized controlled trial.

**Methods:** The Fluid and Catheter Treatment Trial (FACTT) trial enrolled individuals with ALI in a randomized trial to assess the effects of fluid management and central monitoring on outcomes in ALI. For the current analysis, individuals were classified as surgical if they had an APACHE III surgical diagnosis, trauma, or were admitted to a surgical, cardiac surgical, or burn intensive care unit. Individuals were randomized in a 2 x 2 factorial design to a liberal versus conservative fluid management strategy and a pulmonary artery catheter (PAC) versus central venous catheter (CVC). The primary outcome was 60-day mortality.

**Results:** Of the 1000 patients enrolled in the FACTT trial, 244 individuals were deemed to be surgical patients. Consistent with the parent FACTT trial, the surgical patients had no difference in mortality based upon on catheter or fluid management assignment. Those individuals randomized to liberal fluid management protocol received more fluids over 7 days than those in the conservative fluid management protocol (+4.7 +/- 0.9 L vs -4.1 +/- 0.8 L;  $P < 0.001$ ). In addition, individuals randomized to the conservative fluid management strategy had more ventilator-free days at 28 days (13 +/- 1 vs 15 +/- 1;  $P = 0.04$ ). In contrast to the parent trial, those with CVCs also had more ventilator-free days when compared to those with PACs (16 +/- 1 vs 13 +/- 1;  $P = 0.03$ ).

**Conclusions:** Surgical patients with ALI had more ventilator-free days when managed with a conservative fluid management strategy. In addition, use of CVCs may also lead to fewer days on the ventilator.

**Reviewer's Comments:** This subgroup analysis for fluid and catheter management in the surgical subgroup of the FACTT trial is important because the results were largely congruent with that of the parent trial, showing that a conservative fluid management strategy did not lead to adverse outcomes in surgical patients. As with any subgroup analysis, it is important to recognize the caveats in the interpretation of these results, particularly those results that differ from that of the parent trial. In the surgical subgroup, those with a CVC had more ventilator-free and ICU-free days than those managed with a PAC. This is likely explained by the fact that those with in the PAC group received significantly more fluids, a finding not present in the parent trial. Whether these findings would be borne out in a larger prospective trial specific to surgical patients is unknown. Another concern when interpreting this trial is that the surgical population was not defined prospectively upon enrollment. Thus, the population studied does not account for individuals with medical diagnoses admitted to surgical ICUs, which could bias the results toward the findings in the parent trial. (Reviewer-Cynthia D. Brown, MD).

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## Outcome in Septic ALI Patients Depends on Early, Late Fluid Management Strategies

*The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock.*

Murphy CV, Schramm GE, et al:

*Chest*; 2009; 136 (July): 102-109

Septic patients with ALI who achieved both goal-directed early fluid resuscitation and a late even- to negative-fluid balance had optimal survival in this retrospective cohort.

**Background:** Aggressive, goal-directed fluid resuscitation is vital to the treatment of sepsis. Sepsis, however, can cause acute lung injury (ALI), for which conservative fluid management is beneficial. The consequences of different approaches to fluid management in septic patients with ALI are unclear.

**Objective:** To compare outcomes in septic ALI patients treated with aggressive early fluid resuscitation, conservative late fluid management, both, or neither.

**Design:** Retrospective cohort of patients with septic shock requiring >24 hours of mechanical ventilation at 2 academic hospitals.

**Participants:** 212 patients who developed ALI within 72 hours of beginning vasopressor therapy for septic shock were included. Exclusion criteria were: length of stay <7 days after vasopressor initiation, cardiogenic shock, treatment with vasopressors at an outside facility prior to transfer, ECMO, or mechanical ventricular assistance.

**Methods:** Primary outcome was hospital mortality. Secondary outcomes included length of stay indices and duration of mechanical ventilation. Successful early aggressive fluid resuscitation was defined as an initial fluid bolus of  $\geq 20$  mL/kg and achievement of a central venous pressure  $\geq 8$  mm Hg within 6 hours of vasopressor initiation. Delayed conservative fluid management was defined as  $\geq 2$  consecutive days (of the 7 days following vasopressor initiation) marked by even-to-negative fluid balance.

**Results:** Patient survival was 59%. There was no significant difference in the volume of initial fluid resuscitation received between non-survivors and survivors, and cumulative fluid balance over the first 3 days was identical between groups. However, non-survivors were less likely to have a documented central venous pressure  $\geq 8$  mm Hg. Therefore, patients who satisfied both criteria for early aggressive fluid resuscitation had a dramatically improved mortality than did those who failed to achieve this early goal (32% vs 60.6%). During days 3 to 7, fluid balance was negative in survivors, a significant difference from the positive balance in non-survivors. Patients who met the authors' definition of late conservative fluid management had 24.8% mortality in contrast to 62.6% of those who failed to reach that goal. Patients who met both early and late fluid management criteria had 18.3% mortality; patients who met neither had 77.1% mortality.

**Conclusions:** Both early and late fluid management of septic shock complicated by ALI can influence patient outcomes.

**Reviewer's Comments:** This study demonstrates that it is both possible and desirable to achieve both early aggressive fluid resuscitation and a later, more conservative fluid balance in the care of patients with sepsis and ALI. Interestingly, survivors and non-survivors had similar early fluid resuscitation; however, survivors were more apt to achieve a central venous "goal" with resuscitation. It is unclear, however, if the value of late even- or negative-fluid balance reflects the good outcomes associated with intact renal function or other elements of care by physicians who practice evidence-based medicine, irrespective of any active effort to maintain a conservative fluid strategy. (Reviewer-Eric P. Schmidt, MD).

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## Higher Rates of CPR, Lower Rates of Survival Linked to Elderly Black Patients

*Epidemiologic Study of In-Hospital Cardiopulmonary Resuscitation in the Elderly.*

Ehlenbach WJ, Barnato AE, et al:

*N Engl J Med*; 2009; 361 (July 2): 22-31

In-hospital CPR of elderly patients, while resulting in an 18.3% rate of survival to hospital discharge, has been associated with decreasing rates of discharge to home.

**Background:** Discussions regarding advanced directives and goals of care are common in the intensive care unit. One factor that weighs heavily upon these discussions is the expected outcome following cardiopulmonary resuscitation (CPR). Little, however, is known about CPR outcomes in the elderly, a population in which such information is particularly relevant.

**Objective:** To determine trends in the use of CPR and factors that contribute to CPR outcome in patients aged  $\geq 65$  years.

**Design:** Review of Medicare hospital claims from 1992 to 2005, with identification of patients at least 65 years of age who underwent CPR during their hospital stay.

**Participants:** 433,985 patients were identified who underwent in-hospital CPR. Patients were excluded if hospital billing occurred via Social Security Disability or via HMO co-enrollment.

**Methods:** Primary outcome was survival to hospital discharge. Additionally, discharge destination (home, other hospital, nursing home, hospice) was recorded as an estimate of functional status. Patient characteristics (age, sex, race, mean income of residence ZIP code, burden of chronic illness, admission diagnosis, admission from nursing home) and hospital factors (size, teaching affiliation, urban environment) were used to perform a multivariate logistic regression. Overall, 12.8% of patients were excluded from the regression for missing data (primarily ZIP code income data).

**Results:** CPR occurred 2.73 times per 1000 admissions, with an 18.3% rate of survival to discharge. Both rates were essentially stable over time. In 1992, 60% of survivors were discharged to home; in 2005, this dropped to  $<40\%$ , with discharges to nursing homes or other hospitals becoming more common. In-hospital deaths were increasingly more likely to be preceded by CPR attempts (3.8% in 1992; 5.2% in 2005). Survival was negatively correlated with male gender, increasing age, black race, comorbidities, admission from a skilled nursing facility, increasing hospital size, and urban hospital setting.

**Conclusions:** Survival after in-hospital CPR did not improve from 1992 through 2005. The proportion of in-hospital deaths preceded by CPR increased, whereas the proportion of survivors discharged home after undergoing CPR decreased. Black race was associated with higher rates of CPR, but lower rates of survival after CPR.

**Reviewer's Comments:** Several findings of this study are surprising. The 18.3% survival in elderly patients exceeds the 17.0% survival noted in a previous study of patients of all ages (Peberdy et al, *Resuscitation* 2003). Furthermore, survival to discharge did not increase over time, suggesting that the benefits of efforts to improve CPR delivery may be limited to out-of-hospital arrests. The stable incidence of CPR and increasing likelihood of a CPR attempt before in-hospital death suggests a rising proportion of unsuccessful CPR in the elderly. Fewer CPR survivors are returning home immediately after discharge. It is not clear, however, if this represents diminished functional status or reflects evolving trends in patient disposition--for example, earlier discharge to a rehabilitation facility as opposed to a longer stay at the acute care hospital. (Reviewer-Eric P. Schmidt, MD).

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## ICU CXRs Provide Route for Nosocomial Infection Transmission

*Contamination of Portable Radiograph Equipment With Resistant Bacteria in the ICU.*

Levin PD, Shatz O, et al:

*Chest*; 2009; 136 (August): 426-432

Interventions to improve infection control practices should include radiologic equipment and technicians.

**Background:** Nosocomial infections are common, yet preventable sequelae of critical illness. Much attention has been focused on strategies to prevent the transmission of resistant bacteria between patients, although most interventions focus on primary care providers, including nurses and physicians.

**Objective:** To assess infection control (IC) practices of radiology technicians during routine chest x-rays in the ICU.

**Design:** Prospective trial.

**Participants:** Radiology technicians performing routine chest x-ray (CXR) in a single 20-bed ICU in Israel.

**Methods:** A 4-phase study was performed including: (1) covert observation of infection control techniques of technicians; (2) microbiological testing of CXR equipment for resistant bacteria; (3) education of technicians regarding infection control policies (intervention); and (4) follow-up of adherence to policies for 5 months. Data were collected and compared on technician adherence to 14 pre-defined IC practices during the observation (1, 2), intervention (3), and follow-up (4) phases. Outcomes included changes in IC policy adherence and isolation of resistant bacteria from CXR equipment and ICU patients.

**Results:** Observation (173), intervention (113), and follow-up (120) assessments were made over the 13-month study. Adequate adherence to IC policies increased from 1% in the observation period to 42% in the intervention period ( $P < 0.001$ ), but again decreased to 10% during the follow-up phase ( $P < 0.001$  vs intervention period). Bacteria were cultured from CXR equipment after patient contact in 63% during the observation period versus 33% in the intervention phase ( $P = 0.002$ ). During the observation phase ( $n=30$ ), 26 resistant organisms were cultured compared to 0 ( $n=29$ ) during the intervention phase ( $P < 0.01$ ), but increased again during follow-up. In 83% of patients, at least 1 patient in the ICU had cultures positive for similar resistant organisms.

**Conclusions:** Radiology technicians and equipment are a source of transmission of resistant bacteria in the ICU. Moreover, although intervention improved compliance with IC policies, the benefit was not sustained after education stopped.

**Reviewer's Comments:** In the face of increasing awareness of nosocomial infections and infection control practices, this study provides compelling information regarding the need to target ancillary services. The investigators convincingly demonstrate that poor compliance with infection control practices is associated with culture results of equipment used for routine CXRs, and that educational intervention improves these findings. Unfortunately, they also demonstrate regression to pre-intervention rates of adherence if the educational component is not ongoing. Focus for improvement on IC needs to include all people and equipment that have patient contact. Several studies have shown no benefit to routine daily chest x-rays. One approach combining infection control with cost control is to simply get out of the habit of ordering them. (Reviewer-Jeffrey B. Hoag, MD, MS).

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## High CRP Predicts Improved ARDS Survival

*Plasma C-Reactive Protein Levels Are Associated With Improved Outcome in ARDS.*

Bajwa EK, Khan UA, et al:

*Chest*; 2009; 136 (August): 471-480

Elevated C-reactive protein levels are associated with decreased mortality, less organ failure, and fewer days of mechanical ventilation in patients with ARDS.

**Background:** Biomarkers have been studied extensively as prognosticators in a variety of inflammatory disease processes. Acute respiratory distress syndrome (ARDS) is one such syndrome where biomarkers may be helpful. C-reactive protein (CRP) is a biomarker that has been evaluated in several diseases where levels have been shown to correlate with changes in inflammation.

**Objective:** To characterize the relationship between outcomes and CRP levels in patients with ARDS.

**Design:** Prospective observational study from a single tertiary care medical center ICU.

**Participants/Methods:** The study was performed from 1999 to 2005. Patients at risk for ARDS (sepsis, trauma, multiple transfusions, aspiration) were screened, and excluded if they had age <18 years, non-sepsis-related neutropenia, immuno-enhancing agents (GM-CSF), HIV, bone marrow transplant, or DNI status. Demographic data and outcomes were collected on patients. CRP levels were measured within 48 hours of fulfilling criteria for ARDS. Primary outcome was 60-day mortality. Secondary outcomes were multiple organ dysfunction syndrome (MODS) and mechanical ventilation (MV)-free days.

**Results:** Of 418 patients with ARDS, 177 were enrolled. Excluded patients were similar in demographics, and the most common reason cited for non-inclusion was delay in surrogate consent. Survivors (60%) were younger and had lower APACHE scores. ARDS survivors also had significantly higher CRP levels (176.5 vs 133.5 mg/dL;  $P = 0.02$ ). There was also a significant trend in decreasing CRP level with increasing mortality ( $P = 0.02$ ). Corticosteroid therapy was associated with significantly lower CRP levels and higher mortality; however, severity of illness substantially influenced this relationship. Higher CRP levels were associated with lower MODS ( $P = 0.001$ ) and increased MV-free days ( $P = 0.02$ ).

**Conclusions:** In early ARDS, higher CRP levels were associated with improved mortality, MODS scores, and MV needs.

**Reviewer's Comments:** Biomarkers with prognostic significance are appealing in diseases with high mortality, such as ARDS. In this observational study, CRP levels measured within 48 hours of diagnosis of ARDS had an unexpected inverse relationship with outcomes. Contrary to many studies that demonstrate higher levels of CRP with increased inflammation, the relationship appears to reverse in ARDS. The authors postulate several mechanisms whereby CRP may itself decrease neutrophil influx and inflammation; however, this remains largely speculation. Although this study presents interesting information, it suffers from lack of data regarding the time course of CRP trends, as this was measured once in each patient. They authors also lost many patients due to difficulty with surrogate consent, although groups enrolled were similar to non-participants. Despite limitations, further investigation into mechanisms and prognostic trends is warranted. (Reviewer-Jeffrey B. Hoag, MD, MS).

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