Acute cytomegalovirus infection occurs frequently in immunocompetent mechanically ventilated patients, and clinical signs of infection are often absent.

**Background:** Critically ill patients can develop relative immunosuppression associated with their acute medical illnesses. Acute cytomegalovirus (CMV) infection is likely to occur in this setting, although the actual incidence has been poorly characterized.

**Objective:** To assess the incidence, risk factors, and outcome of acute CMV infection in non-immunosuppressed intensive care unit (ICU) patients.

**Design:** Prospective observational study.

**Participants/Methods:** Over a 2-year period, all non-immunosuppressed patients admitted to a single-center medical ICU who received mechanical ventilation for >1 day \( (n=242) \) were followed prospectively for development of active CMV infection. CMV serology and antigenemia was performed at admission and weekly until ICU discharge or death. Bronchoalveolar lavage with viral culture was performed on all suspected cases of pneumonia.

**Results:** Of the 242 eligible patients, 39 (16.1%) developed active CMV infection after 48 hours of mechanical ventilation. The median time from ICU admission to development of CMV antigenemia was 16 days (interquartile range, 6 to 25 days). Individuals with CMV infection were older (68 vs 62 years; \( P =0.018 \)), more likely to have been admitted for pneumonia (59% vs 32%; \( P =0.002 \)), and more likely to have used corticosteroids in the last month (26% vs 10%; \( P =0.018 \)). Patients diagnosed with CMV infection did not have more frequent fever at the time of diagnosis. Both ICU and in-hospital mortality were worse in those infected with CMV; these differences did not achieve statistical significance.

**Conclusions:** The authors conclude that, while active CMV infection occurs commonly in non-immunocompromised ICU patients undergoing mechanical ventilation, this infection did not appear to impact mortality.

**Reviewer’s Comments:** Acute infection with CMV in the immunocompromised host is associated with increased morbidity and mortality. This study explores the risk of CMV infection in an immunocompetent ICU population, and is the second such study which found a high incidence of new infection using surveillance screening. These findings highlight the need for physicians caring for the ICU patient to consider CMV as a new pathogen, especially in those with prolonged length of stay. What remains unclear is whether CMV is merely a marker of prolonged critical illness, or contributes to worse outcomes. (Reviewer-M. Bradley Drummond, MD).

© 2009, Oakstone Medical Publishing

Keywords: Cytomegalovirus, ICU, Mechanical Ventilation, Epidemiology, Incidence

Print Tag: Refer to original journal article
Limited Bedside TTE Can Estimate LV Function in ICU Patients

Assessment of Left Ventricular Function by Intensivists Using Hand-Held Echocardiography.

Melamed R, Sprenkle MD, et al:

Chest 2009; 135 (June): 1416-1420

In this study, intensivists with minimal formal training correctly differentiated normal and abnormal cardiac function in 86% of cases.

**Background:** In the critically ill patient, rapid assessment of cardiac function can allow for tailored therapies. Formal transthoracic echocardiograms (TTE) may have a delay in performance and interpretation. Little data exist on the ability of intensivists with minimal training to successfully perform and interpret limited bedside TTE.

**Objective:** To examine the ability of minimally trained intensivists to assess (LV) ventricular systolic function using a hand-held unit when compared to near-simultaneous comprehensive TTE performed by an experienced echocardiographer.

**Design:** Prospective single-center observational study.

**Participants:** 44 medical ICU patients who had a formal TTE ordered by their primary physician during routine clinical care.

**Methods:** Prior to the study, intensivists underwent 2 hours of didactic training and 4 hours of hands-on training in image acquisition and visual estimate of LV function. Within 2 hours of the formal TTE, patients underwent a limited bedside TTE by an intensivist blinded to patient diagnosis and formal TTE results. Intensivists categorized LV function as normal, mild-to-moderate decrease in contractility, or severe decrease in contractility. The formal TTE was used as a "gold standard" to compare with intensivist results.

**Results:** Intensivists correctly differentiated normal and abnormal LV function in 38 of 44 cases (86%). The positive predictive value for the intensivist identifying any abnormal function was 89%, while the negative predictive value was 85%. The κ statistic for agreement between intensivist and echocardiographer for any abnormality was 0.72 (95% confidence interval [CI], 0.52 to 0.93; \( P < 0.001 \)). When assessing the ability of the intensivist to accurately determine the degree of ventricular dysfunction, intensivists correctly placed LV dysfunction in the appropriate category in 82% of cases. The erroneous classification was associated with an overestimation of function in 6 of 8 cases. The κ statistic for agreement between intensivist and echocardiographer for correct dysfunction category was 0.68 (95% CI, 0.48 to 0.88; \( P < 0.001 \)).

**Conclusions:** The authors conclude that intensivists with minimal training were able to estimate LV function with reasonable accuracy using a hand-held unit in the ICU. When mistakes were made in function assessment, intensivists most often overestimated LV function.

**Reviewer’s Comments:** Ultrasound is becoming standard of practice for vascular access and thoracentesis. In Europe, basic echocardiography is frequently performed by intensivists. This report demonstrates that intensivists can assess LV function with reasonable accuracy after just minimal training. Although limited by the varied pre-study experience of some intensivists in echocardiography and the small sample size, the present study contributes to the growing data on the benefit of intensivist-performed diagnostic imaging. In the future, limited TTE may be used as frequently as ultrasound-guided vascular access and thoracentesis. (Reviewer-M. Bradley Drummond, MD).

© 2009, Oakstone Medical Publishing

Keywords: Echocardiography, Intensivist, Left Ventricular Function

Print Tag: Refer to original journal article
CMV virus isolation in immunocompetent critically ill patients is associated with increased mortality.

**Background:** Cytomegalovirus (CMV) is nearly universally acquired early in life and remains latent, unless the host immune function is altered, especially T-cell function, such as in HIV or transplantation. Active CMV disease has also been associated with the development of transient immunosuppression such as that seen during a prolonged ICU stay, sepsis, and septic shock.  

**Objective:** To evaluate the prevalence and mortality associated with active CMV in immunocompetent ICU patients.  

**Design:** Systematic literature review.  

**Methods:** Studies were of adults without preexisting immunosuppression on ICU admission or those who were not on immunosuppressive medications. Multiple databases were queried for studies that evaluated the rate of CMV infection in immunocompetent patients. Studies that included only immunocompromised patients were rejected. Findings and study design were extracted. Cases were defined by the presence of active CMV infection where CMV was detected by ≥1 of the following methods: viral culture, polymerase chain reaction (PCR), or CMV antigen. Patients were considered non-immunosuppressed or immunocompetent if they were neither receiving immunosuppressive medications nor were diagnosed with an immunosuppressive disease at ICU admission.  

**Results:** 13 studies were identified, with a total of 1258 patients; 9 were prospective and 4 retrospective. Using CMV diagnosis by viral culture, the rate of infection was 12%; if PCR or antigen were analyzed, the rate of active infection was 20% to 31%. If studies were further narrowed by inclusion of data on CMV IgG serology, the positivity rate rose significantly in the PCR, culture, and antigen groups up to 36%. The CMV positivity rate was 1% in the studies evaluating CMV infection in the first 5 days of ICU care, but in late screening, the rate was 21%. CMV was more frequent in septic patients, and mortality rate associated with CMV infection was 1.93 times as high as that for patients without infection.  

**Conclusions:** Active CMV infection occurs frequently in immunocompetent ICU patients, especially in the setting of sepsis, prior CMV exposure, and high disease severity. A causal relationship could not be established.  

**Reviewer’s Comments:** This study does not answer the important question of whether CMV disease in immunocompetent patients is just a marker of severity of illness or an actual pathogen that contributes significantly to mortality. Because most studies used viral isolation by culture, PCR, or antigen detection and not tissue changes consistent with actual viral infection, no causal conclusions can be drawn from these data. Moreover, the authors do not comment on the success of attempts to treat CMV disease in these studies. It remains unknown if antivirals aimed at CMV in immunocompetent hosts will alter mortality or simply add another potentially toxic drug to already very sick patients.  

© 2009, Oakstone Medical Publishing  

Keywords: Cytomegalovirus, Immunocompetence, ICU, Mortality  

Print Tag: Refer to original journal article
Higher Mortality in MALA Linked to Depressed PT Activity

Metformin-Associated Lactic Acidosis: A Prognostic and Therapeutic Study.
Seidowsky A, Nseir S, et al:

Crit Care Med 2009; 37 (July): 2191-2196

Prolonged hemodialysis is associated with improved survival in metformin-associated lactic acidosis.

Background: Lactic acidosis is one of the most important adverse effects associated with metformin use, occurring in approximately 3 per 100,000 metformin-treated patients per year.

Objective: To document the characteristics and prognostic factors of patients admitted to the ICU for life-threatening metformin-associated lactic acidosis (MALA), and to determine the optimal duration of hemodialysis in MALA.

Design: Retrospective cohort study.

Participants: Adults admitted with MALA to the ICU.

Methods: Definite metformin-associated lactic acidosis was defined by the diagnosis charted by the treating physician plus hyperlactatemia and metformin accumulation with a plasma level >2.0 mg/L (normal, 0.5 to 2.0 mg/L, measured by high-performance liquid chromatography). Clinical characteristics, laboratory values, characteristics of extrarenal support, and hemodialysis treatment were all extracted from the medical records.

Results: 42 patients were included in the study. In all cases, the patients were chronically treated with metformin for type 2 diabetes mellitus. At admission, 50% were in shock, 45% required mechanical ventilation, and 74% were in acute renal failure. Thirteen patients had intentionally overdosed, while the remainder were inadvertent. Patients with inadvertent overdose had a higher mortality at 48% versus 0% of patients with intentional overdose. Survivors were more likely to be older, have a lower pH, higher lactate level, lower prothrombin activity, and less need for mechanical or circulatory support. Mean metformin levels were not different in the 2 groups. In a multivariate model, the only variable significantly associated with mortality was the level of prothrombin (PT) activity at admission, with a relative risk of nearly 60. Thirty-one patients were treated with hemodialysis within the first 12 hours of ICU admission. Cumulative duration of hemodialysis was longer in survivors at 17 hours versus 10 hours in non-survivors.

Conclusions: The outcome of metformin-associated lactic acidosis is favorable in intentional overdose, and prognosis is best assessed by PT activity. Prolonged hemodialysis was necessary to correct the overdose.

Reviewer's Comments: This study was interesting in that it presents a large collection of patients with a rare, but serious complication of a commonly used drug. The finding that decreased PT activity predicted mortality, even in the absence of underlying liver disease, suggests that metformin itself might be hepatotoxic, which is supported by recent basic science data. This paper also supports use of hemodialysis to manage this complication, including a prolonged course both to remove the biguanide and to correct the acid-base disorder. This paper might be a useful reference for clinicians caring for patients with metformin-associated lactic acidosis. (Reviewer-Anna R. Hemnes, MD).

© 2009, Oakstone Medical Publishing

Keywords: Metformin, Lactic Acidosis, Hemodialysis

Print Tag: Refer to original journal article
Candidal bloodstream infections are now caused by *C. albicans* in <50% of cases. This should be kept in mind when prescribing empiric antifungal therapy.

**Background:** Candidemia is a major cause of bloodstream infections, but its epidemiology is changing.

**Objective:** To determine contemporary epidemiology and outcomes of candidemia in major North American medical centers.

**Design:** Observational study.

**Participants:** Data were extracted from the Prospective Antifungal Therapy (PATH) Alliance database. The PATH Alliance is a multicenter observational registry that collects data on patients with invasive fungal infections.

**Methods:** Pediatric and adult patients enrolled in the registry from July 2004 to March 2008 at 28 centers with a diagnosis of candidemia were included. Only the first episode of candidemia was reported. Patients with >1 species of *Candida* were excluded. Patient characteristics, fungal species, antifungal therapy, and survival were analyzed.

**Results:** 2019 patients were included in the analysis. *C. albicans* was the most common cause of candidemia (45.6%), but collectively, the non-*C. albicans* *Candida* species caused the majority of infections (54.4%). Other species included *C. glabrata* (26.0%), *C. parapsilosis* (15.7%), *C. tropicalis* (8.1%), and *C. krusei* (2.5%). In total, 43% of patients received prophylaxis or empiric antifungal therapy in the prior 30-day period. *C. glabrata* was more common in older patients, patients with solid organ transplants, and those who received prior antifungal therapy. *C. krusei* was more common in patients who received prior antifungal therapy and patients with hematologic malignancy. Fluconazole was the most frequently prescribed antifungal (67.7%), while use of amphotericin products was rare. Overall 12-week mortality was 35.2%. *C. krusei* was associated with the highest mortality rate (52.9%). Older patients also had high mortality (52.7% in patients aged >65 years).

**Conclusion:** This study provides information on predicted candidemia epidemiology, along with current prescribing practices. Differences in patient outcomes based on causative species may be due in part to activity of antifungal therapy. Additional research is needed to determine the best therapy for these infections.

**Reviewer's Comments:** These results are timely given the recent publication of the Infectious Diseases Society of America's clinical practice guidelines for the management of candidiasis (*Clin Infect Dis* 2009; 48:503-535). Fluconazole is no longer a safe bet for unstable patients, as infection with *C. albicans* is not assured, particularly in patients with prior azole exposure. Early empiric use of fluconazole may have contributed to the higher mortality in patients with *C. krusei* because it is not active against this species. IDSA guidelines recommend empiric use of an echinocandin (caspofungin, micafungin, anidulafungin) in unstable patients or those with prior azole exposure. This is the best bet early on, while awaiting speciation and sensitivity if it is available. Keep in mind that echinocandins are not active against cryptococcus, so patients at risk should have cryptococcal antigen testing when unspeciated yeast is reported and you elect to empirically treat with an echinocandin. (Reviewer-Annette M. Rowden, PharmD).

© 2009, Oakstone Medical Publishing

Keywords: Candidemia, Epidemiology, Outcomes

Print Tag: Refer to original journal article
Limit IV Colistin Tx to 2 Weeks to Avoid Renal Toxicity

Nephrotoxicity Associated With Intravenous Colistin (Colistimethate Sodium) Treatment at a Tertiary Care Medical Center.

Hartzell JD, Neff R, et al:

Clin Infect Dis 2009; 48 (June 15): 1724-1728

IV colistin can cause significant renal impairment in patients with normal baseline renal function, particularly when treatment duration exceeds 2 weeks.

**Background:** The use of IV polymyxin B and polymyxin E (colistimethate sodium [CMS]) was largely abandoned in the 1970s due to the availability of less toxic alternatives (eg, aminoglycosides). The emergence of multidrug-resistant gram-negative bacteria brought these agents out of retirement. Reported rates of nephrotoxicity are highly variable, and are frequently confounded by the lack of control for additional risk factors for nephrotoxicity.

**Objective:** To determine the rate of CMS-associated nephrotoxicity in young, previously healthy patients without underlying risks for kidney dysfunction.

**Design:** Retrospective review.

**Participants:** Patients treated at Walter Reed Army Medical Center who received CMS for >72 hours were evaluated. Patients on renal replacement therapy (RRT) prior to initiation of CMS were excluded.

**Methods:** Data on clinical characteristics, CMS exposure, and exposure to other nephrotoxins were collected. Renal dysfunction was classified by the RIFLE criteria, which ranks degrees of renal dysfunction from mild to requiring chronic dialysis.

**Results:** 66 patients were assessed over a 5-year period. Acinetobacter baumannii was the primary infecting organism. Patients were virtually all male, young (mean age, 27 years), with low APACHE II scores (mean, 8.3), and normal renal function at baseline. Overall, 45% of patients met criteria for renal toxicity (creatinine increased to at least 1.5 x baseline); 21% had CMS therapy stopped due to nephrotoxicity. No patient required RRT. Renal injury was completely reversed at 3 months in almost all patients. Patients receiving >14 days of therapy were 3.7 times more likely to develop toxicity than during shorter courses. Other variables were not associated with renal toxicity.

**Conclusions:** In a homogenous population without comorbidities, the direct nephrotoxic effects of CMS can be analyzed. To allow consistent comparisons of toxicity across studies, the RIFLE criteria should be uniformly utilized. Toxicity with CMS is related to total cumulative dose. Creatinine needs to be regularly monitored in patients receiving prolonged treatment.

**Reviewer’s Comments:** This study is valuable because it highlights the high rate of inherent renal toxicity from CMS. In patients with good renal function at baseline, toxicity that develops is not overly concerning. Although common, it does not lead to an RRT requirement and is largely reversible. In sicker patients with more comorbidities and impaired renal function at baseline, development of a dialysis requirement is not uncommon. Concerns for toxicity appropriately relegate CMS to a treatment of last resort. This has an upside in that less use of CMS will result in a slower emergence of CMS resistance, given few other therapeutic options. Since duration of treatment predicts development of toxicity, we are reminded to not treat to eradicate colonization and not treat for longer than necessary. For most infections, 2 weeks should be an adequate treatment course. (Reviewer-Annette M. Rowden, PharmD).

© 2009, Oakstone Medical Publishing

Keywords: Colistin (colistimethate sodium), Renal Dysfunction, Nephrotoxicity

Print Tag: Refer to original journal article
Patients with catastrophic lung failure may be salvaged with extracorporeal membrane oxygenation.

**Objective:** To evaluate the survival rate of extracorporeal membrane oxygenation (ECMO) in patients with acute respiratory failure.

**Design:** Retrospective evaluation from a single tertiary care medical center. **Patients:** 81 patients aged >2 months who had failed maximal mechanical ventilator support between 1990 and 2008.

**Methods:** Charts were reviewed, and patients were placed into 6 groups based on diagnosis: sepsis (8), bacterial or fungal pneumonia (15), viral pneumonia (9), trauma or thermal injury (10), immunocompromise (11), or other (24). ECMO was used only after all foci of infection were adequately drained. Patients with coagulopathy, ongoing bleeding, or irreversible lung injury were excluded. Ventilator management while on ECMO was set to maintain a positive inspiratory pressure (PIP) of <30 cm H$_2$O. Patients were systemically anticoagulated with heparin.

**Results:** Average age was 23 years (range, 2 months to 61 years). Overall hospital survival was 53%. ECMO was used for an average of 274 hours. There was a trend toward lower survival with increasing time on ECMO. Patients with the highest survival rates were those treated for viral pneumonia, followed by bacterial or fungal pneumonia. Survival between veno-venous ECMO was similar to that of ECMO using veno-arterial perfusion. Patients who survived to hospital discharge were younger (mean, 19 vs 27 years). Patients who were on mechanical ventilation for <10 days prior to initiation of ECMO also had a higher survival rate. Non-survivors also had a higher pre-ECMO Fio$_2$, PEEP requirement, and exposure to higher PIPs.

**Conclusions:** In some self-limiting lung diseases, ECMO provides a bridge in patients with acute lung failure. Immunocompromised patients or those with sepsis or pre-hospital injury have a lower survival than do patients with viral, bacterial, or fungal pneumonia.

**Reviewer's Comments:** ECMO and extracorporeal CO$_2$ removal have both failed to improve outcome in randomized trials compared to conventional mechanical ventilation. In the era of lung-protective ventilation strategies, their role diminishes even further. It is difficult to know what message to take from this mixed bag of diagnoses, ages, and therapies collected over almost 2 decades. ECMO will always continue to have its advocates, simulated by the occasional spectacular success story. It has no role in routine therapy of severe acute respiratory distress syndrome and no role in inexperienced centers, and its role in even the rare case at centers with experience remains undefined. (Reviewer-I. Michael Leitman, MD).

© 2009, Oakstone Medical Publishing

Keywords: Acute Respiratory Failure, Extracorporeal Circulation

Print Tag: Refer to original journal article
Preop Statin Offers Better Postop Benefits in Noncardiac Surgery

Bisoprolol and Fluvastatin for the Reduction of Perioperative Cardiac Mortality and Myocardial Infarction in Intermediate-Risk Patients Undergoing Noncardiovascular Surgery: A Randomized Controlled Trial (DECREASE-IV).

Dunkelgrun M, Boersma E, et al:

Ann Surg 2009; 249 (June): 921-926

Patients undergoing noncardiovascular surgery who are at intermediate risk for death or cardiovascular complications appear to benefit from preoperative treatment with bisoprolol.

**Background:** Beta-Blockers and statins have been shown to reduce death and cardiac complications in high-risk patients undergoing vascular surgery.

**Objective:** To evaluate the safety and efficacy of beta-blockade and anticholesterol agents in the prevention of perioperative death and cardiovascular complications following non-cardiac surgery.

**Design:** Prospective randomized, placebo-controlled open-label trial.

**Participants/Methods:** 1066 patients of intermediate cardiovascular risk were assigned to receive bisoprolol and fluvastatin before operation. Patients were considered to be at "intermediate risk" if they had a 1% to 6% risk of death and myocardial infarction based on clinical criteria and type of operation. Patients who were on preoperative statin therapy or beta-blockers were excluded from the study. Patients were assigned to 1 of 4 groups: fluvastatin, bisoprolol, both drugs, or no preoperative treatment (control). Bisoprolol was given to achieve a preoperative heart rate of 50 to 70 bpm. Fluvastatin (80 mg) was given daily. Thirty-day survival and myocardial event rates were the primary end points.

**Results:** Patients treated with bisoprolol before surgery had a lower preoperative heart rate. The 533 patients randomized to the bisoprolol arm had a lower rate of cardiac death or nonfatal myocardial infarction (2.1% vs 6.0% for bisoprolol-control). Patients assigned to receive fluvastatin had a non-statistically significant trend toward a lower cardiac morbidity or mortality. The addition of fluvastatin to bisoprolol did not appreciably decrease the death or complication rate. The rate of ischemic stroke was not affected by preoperative therapy.

**Conclusions:** Patients undergoing noncardiovascular surgery who are at intermediate risk for death or cardiovascular complications appear to benefit from preoperative treatment with bisoprolol. Unlike prior studies that have shown statistically significant benefits from preoperative statin therapy, preoperative fluvastatin showed only a trend toward improving outcome.

**Reviewer's Comments:** This trial was well designed, although unblinded. Its major weakness was premature closure at only about 18% of planned size. Excluding the large number of patients already on beta-blockers or statin therapy slowed accrual of the 6000 patients needed according to the authors' power analysis. This likely resulted in the study's failure to reach a statistically significant conclusion regarding the benefit of preoperative fluvastatin therapy. Nearly 80% of subjects were already on beta-blockers or statins. This is a much higher rate than most studies in the U.S. and may reflect the health care system in the Netherlands. (Reviewer-I. Michael Leitman, MD).

© 2009, Oakstone Medical Publishing

Keywords: Non-Cardiovascular Surgery, Beta-Blockers, Statins, Myocardial Infarction

Print Tag: Refer to original journal article
Guillain-Barré syndrome patients with high baseline cortisol may benefit from increased monitoring for respiratory failure and dysautonomia.

**Background:** Predicting respiratory failure in Guillain-Barré syndrome (GBS) is challenging but important. 

**Objective:** To determine the relationship between baseline plasma cortisol and development of respiratory failure, dysautonomia, sepsis, and hyponatremia. 

**Design:** Prospective study. 

**Participants:** 93 patients with GBS at admission; those with non-idiopathic GBS and Miller Fisher syndrome were excluded. 

**Methods:** Plasma cortisol was measured immediately on admission to the ICU (T0) and 60 minutes (T60) after administration of 250 μg of adrenocorticotropic hormone. Definitions for adrenal insufficiency (AI) were as follows: ICU definition - T0 <15 μg/dL or T0 between 15 and 34 μg/dL and cortisol increment <9 μg/dL at T60; endocrine definition - T0 and T60 <22 μg/dL. 

**Results:** 3 groups were identified: (1) 16 patients mechanically ventilated within 24 hours of admission; (2) 17 patients ventilated after 24 hours; and (3) 60 patients never ventilated. Mean plasma cortisol levels were 22.9 ng/mL (T0) and 45.4 ng/mL (T60). Criteria for AI were met in 32% (ICU definition) and 6% (endocrine definition) of patients. T0 cortisol level was not correlated with age, simplified acute physiology score, or delay between clinical onset and inclusion in study. Mean plasma cortisol was significantly higher in group 2 (28.5 ng/mL vs 20.4 ng/mL in group 3). Baseline cortisol was not correlated with heart rate or blood pressure but was significantly higher in 11 patients who later developed dysautonomia (33 ng/mL), compared with 21 ng/mL in those who did not. Baseline plasma cortisol was an independent risk factor for respiratory failure after adjusting for inability to lift the head, delay between onset and admission <7 days, and vital capacity <60%; it remained an independent predictor after adjustment by a validated electrophysiological model. 

**Conclusions:** Baseline plasma cortisol is significantly higher in patients who progress to respiratory failure after 24 hours and in those who develop cardiovascular dysautonomia. 

**Reviewer's Comments:** The findings of this study still require confirmation in a larger cohort. The authors propose that baseline plasma cortisol reflects the clinical severity of GBS and intensity of the immune attack rather than directly contributing to clinical deterioration. There was no association between cortisol levels and either plasma interleukin-6 or transforming growth factor-beta1. This study did not, however, measure cytokine levels or other components of the adrenal axis, which may have better addressed the question of mechanism. These findings may explain why corticosteroids are ineffective in GBS. With regard to the high incidence of AI in this study with clear relevance to other clinical data, the adrenals of patients with GBS might already be maximally stimulated at baseline, and diagnostic criteria based on a minimum rise in cortisol after adrenocorticotropic hormone are probably invalid in such patients. (Reviewer-Wendy C. Ziai, MD).
Predict Cardiac Arrest Prognosis Using Q-EEG Markers

Hypothermia-Treated Cardiac Arrest Patients With Good Neurological Outcome Differ Early in Quantitative Variables of EEG Suppression and Epileptiform Activity.

Wennervirta JE, Ermes MJ, et al:

Crit Care Med 2009; 37 (August): 2427-2435

The recovery of cortical electrical function by quantitative EEG can be monitored during and immediately after induced hypothermia and provides prognostic information.

Background: Mild, induced hypothermia improves outcomes after out-of-hospital ventricular fibrillation (VF) cardiac arrest. The ability of quantitative EEG (Q-EEG) to predict early neurologic prognosis is not clear.

Objective: To evaluate the ability of Q-EEG characteristics to differentiate patients with good and poor neurologic outcomes after out-of-hospital VF.

Design: Prospective study.

Participants: 30 consecutive patients resuscitated from out-of-hospital VF in <35 minutes to restoration of spontaneous circulation and treated with therapeutic hypothermia for 24 hours.

Methods: EEG was recorded continuously from arrival until extubation, transfer, or 5 days after cardiac arrest. EEG recordings were analyzed offline by a neurophysiologist blinded to clinical outcome. Q-EEG variables evaluated were as follows: burst suppression ratio (BSR), 2 entropy-based variables (response entropy [RE] and state entropy [SE]), and wavelet subband entropy (WSE) to detect epileptiform activity.

Results: An average of 22 hours/patient EEG monitoring was analyzed during the first 24 hours and 18 hours/patient between 24 and 48 hours. Within the 6-month follow-up period, 21 patients had a best-achieved Glasgow-Pittsburgh Cerebral Performance Category (CPC) of 1 or 2 (good outcome; out of 5); 4 achieved CPC 3, and 5 achieved CPC 4. No patient remained in a persistent vegetative state (CPC 4). At 6 months, 21 patients remained alive. The EEG initially showed slow burst suppression in all patients, which was gradually followed by a low-amplitude rhythmic activity. The occurrence of continuous EEG was not different by outcome group during hypothermia but occurred in more patients (95% vs 33%) during normothermia. BSR was significantly lower in patients with good outcomes during the first and second 24-hour periods after cardiac arrest. RE and SE were both significantly higher in the good outcome group in the first 24 hours but not at 24 to 48 hours. WSE was slightly higher in the good outcome group in the second 24-hour period and was significantly lower in status epilepticus patients, all of whom died.

Conclusions: Q-EEG variables are associated with neurologic outcomes after cardiac arrest in hypothermia-treated patients during the first 24 hours and at 24 to 48 hours.

Reviewer's Comments: The BSR during both the first and second day after cardiac arrest predicted poor outcome, and it appeared to be the most useful quantitative EEG variable. Also, decreasing WSE predicted status epilepticus. Although status is not difficult to diagnose on EEG, WSE might be useful to practitioners who lack rapid access to EEG interpretation. Monitoring EEG during hypothermia is feasible because, at body temperatures of 33°C, EEG is not significantly suppressed. Predictive values of these data require validation in a larger independent patient group and comparison to usual clinical predictors before implementation in clinical practice. (Reviewer-Wendy C. Ziai, MD).

© 2009, Oakstone Medical Publishing

Keywords: Pre-Hospital Cardiac Arrest, Quantitative EEG, Recovery, Induced Hypothermia

Print Tag: Refer to original journal article
Plaque characteristics on CT angiography in stable coronary artery disease subjects can identify vulnerable plaques that place subjects at risk for development of acute coronary syndrome.

**Background:** Autopsy studies show that the pathobiology underlying acute coronary syndrome (ACS) is a lipid plaque with a necrotic core and overlying thin fibrous cap that has ruptured and resulted in thrombosis. This plaque rarely causes antecedent angina because of positive vessel remodeling or the outward expansion of the vessel wall underlying this plaque. CT angiography (CTA) is a noninvasive test that not only accurately detects coronary stenoses but also plaque characteristics.

**Objective:** To determine whether CTA detects vulnerable plaques in stable patients and predicts future development of ACS.

**Participants:** 1059 stable subjects with known or suspected coronary artery disease (CAD) who underwent CTA.

**Methods:** Vulnerable plaque was prospectively assessed by 2 features on CTA: (1) low-attenuation plaque that was <30 HU and (2) positive arterial remodeling at the site of the plaque with vessel diameter ≥10% larger than the reference segment. Subjects were followed a mean of 27 months for development of ACS.

**Results:** A total of 10,037 coronary artery segments were evaluated for vulnerable plaque. Of patients, 34% had a ≥75% stenotic lesion in at least 1 coronary vessel. During follow-up, ACS developed in 15 patients (1.5%). However, in 45 patients with both features of vulnerable plaque on CTA, 22% developed ACS. Of 27 patients with only 1 vulnerable plaque feature, 3.7% developed ACS. Importantly, only 4 of 820 patients (0.5%) with no vulnerable plaque characteristics developed ACS. On multivariate Cox regression analysis, presence of vulnerable plaque on CTA was a significant predictor for future ACS. There were no clinical characteristics distinguishing patients with vulnerable plaques who did or did not develop ACS in follow-up. Patients with vulnerable plaque who developed ACS had greater vessel remodeling and greater low-attenuation plaque volume compared to those with vulnerable plaque who remained clinically stable.

**Conclusions:** Plaque characteristics on CTA in stable CAD subjects can identify vulnerable plaques that place subjects at risk for development of ACS.

**Reviewer's Comments:** This important study shows for the first time that we can noninvasively diagnose vulnerable plaques in stable patients that increase the risk of subsequent ACS. The population studied was quite low risk, with only 1.5% developing ACS in follow-up. It is uncertain whether the results of the CTA affected treatment of these patients. It is also uncertain how the results of a CTA would affect our current treatment of CAD patients, ie, aspirin and statin therapy. CTA is associated with too much cost and radiation to be a useful clinical tool to predict ACS development in a low-risk population. Nevertheless, the importance of this study cannot be understated. It is likely we have a new research tool for assessment of new therapies that might result in plaque stabilization. (Reviewer-Steven P. Schulman, MD).
Background: Percutaneous coronary intervention (PCI) is superior to fibrinolytics for ST-segment elevation myocardial infarction (STEMI) patients at high-volume catheterization centers. Nevertheless, fibrinolytic therapy is used in many community hospitals for treatment of STEMI. Patients who do not clinically reperfuse are typically transferred for emergent or rescue PCI. In patients who do reperfuse, it is unclear whether they should be transferred for PCI of the infarct-related artery (IRA).

Objective: To assess whether early routine transfer for PCI is preferable for STEMI patients treated with fibrinolytic therapy in community hospitals.

Participants/Methods: 1059 STEMI patients admitted to community hospitals without onsite PCI were treated with the fibrinolytic agent tenecteplase and standard medical therapy. Patients were then randomized to early PCI, which was urgent transfer to a PCI center with the goal of performing PCI of the IRA within 6 hours of receiving fibrinolytic therapy. The standard treatment group remained at the presenting hospital for at least 24 hours unless rescue PCI was required. It was recommended that otherwise-stable patients in this group undergo catheterization within 2 weeks. The primary end point was 30-day death, reinfarction, recurrent ischemia, heart failure, or cardiogenic shock.

Results: In the standard therapy group, 35% of patients underwent rescue PCI, and 89% eventually underwent catheterization at a median of 32.5 hours following fibrinolytics. In the early PCI group, 98.5% of patients underwent catheterization at a median of 2.8 hours after fibrinolytics. Most subjects had PCI with stent of the IRA. The primary end point occurred in 11.0% of the early PCI group compared to 17.2% of the standard treatment group. This benefit was driven by a reduction in recurrent ischemia, heart failure, and reinfarction. Major bleeding was not different between groups.

Conclusions: Early transfer and PCI following fibrinolytic therapy at community hospitals reduce the risk for recurrent ischemic events and should be part of the overall strategy in the treatment of STEMI.

Reviewer's Comments: Reperfusion therapy has evolved a great deal over the last 2 decades. Early studies of routine PCI following fibrinolytic therapy involved balloon angioplasty with poorly steerable catheters and no antiplatelet therapies except aspirin. With the advent of stents, steerable catheters, and antiplatelet therapies, the outcome of PCI in high-risk patients is much improved. Immediate PCI should not be considered in the fibrinolytic-treated patient (due to excess risk) unless there is clinical evidence that the patient has not reperfused, ie, failure for ST-segment elevation to improve on the ECG. This important study shows that, in the current PCI era, the STEMI patient treated in the community with fibrinolytic therapy should be transferred over the next several hours to a tertiary facility to perform semi-urgent PCI. (Reviewer-Steven P. Schulman, MD).

© 2009, Oakstone Medical Publishing

Keywords: Percutaneous Coronary Intervention, Fibrinolytic Therapy, ST-Segment Elevation

Print Tag: Refer to original journal article