

Outcomes in Patients with Vasodilatory Shock and Renal Replacement Therapy Treated with Intravenous Angiotensin II

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Objective: Acute kidney injury requiring renal replacement therapy in severe vasodilatory shock is associated with an unfavorable prognosis. Angiotensin II treatment may help these patients by potentially restoring renal function without decreasing intrarenal oxygenation. We analyzed the impact of angiotensin II on the outcomes of acute kidney injury requiring renal replacement therapy.

Design: Post hoc analysis of the Angiotensin II for the Treatment of High-Output Shock 3 trial.

Setting: ICUs.

Patients: Patients with acute kidney injury treated with renal replacement therapy at initiation of angiotensin II or placebo (n = 45 and n = 60, respectively).

Interventions: IV angiotensin II or placebo.

Measurements and Main Results: Primary end point: survival through day 28; secondary outcomes included renal recovery through day 7 and increase in mean arterial pressure from baseline of ≥ 10 mm Hg or increase to ≥ 75 mm Hg at hour 3. Survival rates through day 28 were 53% (95% CI, 38%–67%) and 30% (95% CI, 19%–41%) in patients treated with angiotensin II and placebo ($p = 0.012$), respectively. By day 7, 38% (95% CI, 25%–54%) of angiotensin II patients discontinued RRT versus 15% (95% CI, 8%–27%) placebo ($p = 0.007$). Mean arterial pressure response was achieved in 53% (95% CI, 38%–68%) and 22% (95% CI, 12%–34%) of patients treated with angiotensin II and placebo ($p = 0.001$), respectively.

Conclusions: In patients with acute kidney injury requiring renal replacement therapy at study drug initiation, 28-day survival and mean arterial pressure response were higher, and rate of renal replacement therapy liberation was greater in the angiotensin II group versus the placebo group. These findings suggest that patients with vasodilatory shock and acute kidney injury requiring renal replacement therapy may preferentially benefit from angiotensin II.

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Comparison of Antivenom Dosing Strategies for Rattlesnake Envenomation.

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Author information

OBJECTIVES: This study compares maintenance with clinical- and laboratory-triggered (as-needed [PRN]) antivenom dosing strategies with regard to patient-centered outcomes after rattlesnake envenomation.

DESIGN: This is a retrospective cohort study of adult rattlesnake envenomations treated at a regional toxicology center. Data on demographics, envenomation details, antivenom administration, length of stay, and laboratory and clinical outcomes were compared between the PRN and maintenance groups. Primary outcomes were hospital length of stay and total antivenom used, with a hypothesis of no difference between the two dosing strategies.

SETTING: A single regional toxicology center

PATIENTS: Three-hundred ten adult patients envenomated by rattlesnakes between 2007 and 2014 were included. Patients were excluded if no antivenom was administered or for receiving an antivenom other than Crofab (BTG International, West Conshohocken, PA).

INTERVENTIONS: This is a retrospective study of rattlesnake envenomations treated with and without maintenance antivenom dosing.

MAIN RESULTS: One-hundred forty-eight in the maintenance group and 162 in the PRN group were included. There was no difference in demographics or baseline envenomation severity or hemotoxicity (32.7% vs 40.5%; respectively; $p = 0.158$) between the two groups. Comparing the PRN with the maintenance group, less antivenom was used (8 [interquartile range, 6-12] vs 16 [interquartile range, 12-18] vials, respectively; $p < 0.001$), and hospital length of stay was shorter (27 hr [interquartile range, 20-44 hr] vs 34 hr [interquartile range, 24-43 hr], respectively; $p = 0.014$). There were no differences in follow-up outcomes of readmission, retreatment, or bleeding and surgical complications.

CONCLUSIONS: Hospital length of stay was shorter, and less antivenom was used in patients receiving a PRN antivenom dosing strategy after rattlesnake envenomation.

Crit Care Med. 2018 Jun;46(6):958-964. doi: 10.1097/CCM.0000000000003122.

Intra-Abdominal Hypertension Is More Common Than Previously Thought: A Prospective Study in a Mixed Medical-Surgical ICU.

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OBJECTIVES:

To determine the prevalence of intra-abdominal hypertension in mixed medical-surgical critically ill patients using modern definitions and measurement techniques. Secondly to determine variables associated with intra-abdominal hypertension and ICU mortality.

DESIGN:

A prospective observational study.

formally defines IAH as “sustained or repeated pathologic elevation in IAP greater than or equal to 12mm Hg.”

Diagnosis of ACS was made using WSACS definitions, clinical judgement, and the general surgery team was always consulted.

The IAP is approximately 5-7 mmHg in critically ill adults

ACS is defined as a sustained IAP>20mmHg (with or without an APP < 60mmHg) that is associated with new organ dysfunction/failure

SETTING:

Single institution trauma, medical and surgical ICU in Canada.

PATIENTS:

Consecutive adult patients admitted to the ICU (n = 285).

INTERVENTION:

Intra-abdominal pressure measurements twice a day during admission to the ICU.

MEASUREMENTS AND MAIN RESULTS:

In 285 patients who met inclusion criteria, 30% were diagnosed with intra-abdominal hypertension at admission and a further 15% developed intra-abdominal hypertension during admission. The prevalence of abdominal

compartment syndrome was 3%. Obesity, sepsis, mechanical ventilation, and 24-hour fluid balance (> 3 L) were all independent predictors for intra-abdominal hypertension. Intra-abdominal hypertension occurred in 28% of nonventilated patients. Admission type (medical vs surgical vs trauma) was not a significant predictor of intra-abdominal hypertension. Overall ICU mortality was 20% and was significantly higher for patients with intra-abdominal hypertension (30%) compared with patients without intra-abdominal hypertension (11%). Intra-abdominal hypertension of any grade was an independent predictor of mortality (odds ratio, 3.33; 95% CI, 1.46-7.57).

CONCLUSIONS:

Intra-abdominal hypertension is common in both surgical and nonsurgical patients in the intensive care setting and was found to be independently associated with mortality. Despite prior reports to the contrary, intra-abdominal hypertension develops in nonventilated patients and in patients who do not have intra-abdominal hypertension at admission. Intra-abdominal pressure monitoring is inexpensive, provides valuable clinical information, and there may be a role for its routine measurement in the ICU. Future work should evaluate the impact of early interventions for patients with intra-abdominal hypertension.

Renal Blood Flow, Glomerular Filtration Rate, and Renal Oxygenation in Early Clinical Septic Shock*

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Online Clinical Investigations

OBJECTIVE:

Data on renal hemodynamics, function, and oxygenation in early clinical septic shock are lacking. We therefore measured renal blood flow, glomerular filtration rate, renal oxygen consumption, and oxygenation in patients with early septic shock.

DESIGN:

Prospective comparative study.

SETTING:

General and cardiothoracic ICUs.

PATIENTS:

Patients with norepinephrine-dependent early septic shock (n = 8) were studied within 24 hours after arrival in the ICU and compared with postcardiac surgery patients without acute kidney injury (comparator group, n = 58).

INTERVENTIONS:

None.

MEASUREMENTS AND MAIN RESULTS:

Data on systemic hemodynamics and renal variables were obtained during two 30-minute periods. Renal blood flow was measured by the infusion clearance of para-aminohippuric acid, corrected for renal extraction of para-aminohippuric acid. Renal filtration fraction was measured by renal extraction of chromium-51 labeled EDTA. Renal oxygenation was estimated from renal oxygen extraction. Renal oxygen delivery (-24%; p = 0.037) and the renal blood flow-to-cardiac index ratio (-21%; p = 0.018) were lower, renal vascular resistance was higher (26%; p = 0.027), whereas renal blood flow tended to be lower (-19%; p = 0.068) in the septic group. Glomerular filtration rate (-32%; p = 0.006) and renal sodium reabsorption (-29%; p = 0.014) were both lower in the septic group. Neither renal filtration fraction nor renal oxygen consumption differed significantly between groups. Renal oxygen

extraction was significantly higher in the septic group (28%; $p = 0.022$). In the septic group, markers of tubular injury were elevated.

CONCLUSIONS:

In early clinical septic shock, renal function was lower, which was accompanied by renal vasoconstriction, a lower renal oxygen delivery, impaired renal oxygenation, and tubular sodium reabsorption at a high oxygen cost compared with controls.

Early Enteral Nutrition Provided Within 24 Hours of ICU Admission: A Meta-Analysis of Randomized Controlled Trials*

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Feature Articles

OBJECTIVES:

To identify, appraise, and synthesize the most current evidence to determine whether early enteral nutrition alters patient outcomes from critical illness.

DATA SOURCES:

Medline and Embase were searched. The close out date was November 20, 2017.

STUDY SELECTION:

Early enteral nutrition was defined as a standard formula commenced within 24 hours of ICU admission. Comparators included any form of nutrition support "except" early enteral nutrition. Only randomized controlled trials conducted in adult patients requiring treatment in an ICU were eligible for inclusion.

DATA EXTRACTION:

The primary outcome was mortality. Secondary outcomes included pneumonia, duration of mechanical ventilation, and ICU and hospital stay.

DATA SYNTHESIS:

Six-hundred ninety-nine full-text articles were retrieved and screened. Sixteen randomized controlled trials enrolling 3,225 critically ill participants were included. Compared with all other types of nutrition support, commencing enteral nutrition within 24 hours of ICU admission did not result in a reduction in mortality (odds ratio, 1.01; 95% CI, 0.86-1.18; $p = 0.91$; $I = 32\%$). However, there was a differential treatment effect between a priori identified subgroups ($p = 0.032$): early enteral nutrition reduced mortality compared with delayed enteral intake (odds ratio, 0.45; 95% CI, 0.21-0.95; $p = 0.038$; $I = 0\%$), whereas a mortality difference was not detected between early enteral nutrition and parenteral nutrition (odds ratio, 1.04; 95% CI, 0.89-1.22; $p = 0.58$; $I = 30\%$). Overall, patients who were randomized to receive early enteral nutrition were less likely to develop pneumonia (odds ratio, 0.75; 95% CI, 0.60-0.94; $p = 0.012$; $I = 48\%$).

CONCLUSIONS:

Overall, there was no difference between early enteral nutrition and all other forms of nutrition support. A priori planned subgroup analysis revealed early enteral nutrition reduced mortality and pneumonia compared with delayed enteral intake; however, there were no clear clinical advantages of early enteral nutrition over parenteral nutrition.

Ventilator Bundle and Its Effects on Mortality Among ICU Patients: A Meta-Analysis*

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Review Articles

The Ventilator Bundle contains four components, elevation of the head of the bed to 30-45 degrees, daily 'sedation vacation' and daily assessment of readiness to extubate, peptic ulcer disease prophylaxis, and deep venous thrombosis prophylaxis, aimed to improve outcome in mechanically ventilated patients, but not all are associated with VAP prevention.

OBJECTIVES:

To assess the effectiveness of the ventilator bundle in the reduction of mortality in ICU patients.

DATA SOURCES:

PubMed, Scopus, Web of Science, Cochrane Library for studies published until June 2017.

STUDY SELECTION:

Included studies: randomized controlled trials or any kind of nonrandomized intervention studies, made reference to a ventilator bundle approach, assessed mortality in ICU-ventilated adult patients.

DATA EXTRACTION:

Items extracted: study characteristics, description of the bundle approach, number of patients in the comparison groups, hospital/ICU mortality, ventilator-associated pneumonia-related mortality, assessment of compliance to ventilator bundle and its score.

DATA SYNTHESIS:

Thirteen articles were included. The implementation of a ventilator bundle significantly reduced mortality (odds ratio, 0.90; 95% CI, 0.84-0.97), with a stronger effect with a restriction to studies that reported mortality in ventilator-associated pneumonia patients (odds ratio, 0.71; 95% CI, 0.52-0.97), to studies that provided active educational activities was analyzed (odds ratio, 0.88; 95% CI, 0.78-0.99), and when the role of care procedures within the bundle (odds ratio, 0.87; 95% CI, 0.77-0.99). No survival benefit was associated with compliance to ventilator bundles. However, these results may have been confounded by the differential implementation of evidence-based procedures at baseline, which showed improved survival in the study subgroup that did not report implementation of these procedures at baseline (odds ratio, 0.82; 95% CI, 0.70-0.96).

CONCLUSIONS:

Simple interventions in common clinical practice applied in a coordinated way as a part of a bundle care are effective in reducing mortality in ventilated ICU patients. More prospective controlled studies are needed to define the effect of ventilator bundles on survival outcomes.

Feasibility and Safety of Intravascular Temperature Management for Severe Heat Stroke: A Prospective Multicenter Pilot Study

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Online Clinical Investigations

OBJECTIVES:

Heat stroke is a life-threatening condition with high mortality and morbidity. Although several cooling methods have been reported, the feasibility and safety of treating heat stroke using intravascular temperature management are unclear. This study evaluated the efficacies of conventional treatment with or without intravascular temperature management for severe heat stroke.

The principle of intravascular temperature management during therapeutic hypothermia involves use of a catheter with a closed circuit for circulating cold saline through the catheter to cool the blood.

DESIGN:

Prospective multicenter study.

SETTING:

Critical care and emergency medical centers at 10 tertiary hospitals.

PATIENTS:

Patients with severe heat stroke hospitalized during two summers.

INTERVENTIONS:

Conventional cooling with or without intravascular temperature management.

MEASUREMENTS AND MAIN RESULTS:

Cooling efficacy, Sequential Organ Failure Assessment score, occurrence rate of serious adverse events, and prognosis based on the modified Rankin Scale and Cerebral Performance Category. Patient outcomes were compared between five centers that were prospectively assigned to perform conventional cooling (control group: eight patients) and five centers that were assigned to perform conventional cooling plus intravascular temperature management (intravascular temperature management group: 13 patients), based on equipment availability. Despite their higher initial temperatures, all patients in the intravascular temperature management group reached the target temperature of 37°C within 24 hours, although only 50% of the patients in the control group reached 37°C ($p < 0.01$). The intravascular temperature management group also had a significant decrease in the Sequential Organ Failure Assessment score during the first 24 hours after admission (4.0 vs 1.5; $p = 0.04$). Furthermore, the intravascular temperature management group experienced fewer serious adverse events during their hospitalization, compared with the control group. The percentages of favorable outcomes at discharge and 30 days after admission were not statistically significant.

CONCLUSIONS:

The combination of intravascular temperature management and conventional cooling was safe and feasible for treating severe heat stroke. The results indicate that better temperature management may help prevent organ failure. A large randomized controlled trial is needed to validate our findings.

Diagnostic Accuracy of Chest Radiograph, and When Concomitantly Studied Lung Ultrasound, in Critically Ill Patients With Respiratory Symptoms: A Systematic Review and Meta-Analysis

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Online Review Article

OBJECTIVES:

Chest radiograph is considered the first-line diagnostic imaging modality for patients presenting with pulmonary symptoms in the ICU. In this meta-analysis, we aim to evaluate the diagnostic accuracy of chest radiograph, and when concomitantly studied lung ultrasound, in comparison with the gold-standard CT for adult critically ill patients with respiratory symptoms.

DATA SOURCES:

PubMed, EMBASE, and Gray literature.

STUDY SELECTION:

Studies comparing chest radiograph, and if performed lung ultrasound, with CT for adult ICU patients with respiratory symptoms.

DATA EXTRACTION:

Quality was scored with Quality Assessment of Diagnostic Accuracy Studies-2, and study setting, test characteristics, and study design were extracted.

DATA SYNTHESIS:

In the meta-analysis, we included 10 full-text studies, including 543 patients, and found that chest radiograph has an overall sensitivity of 49% (95% CI, 40-58%) and specificity of 92% (86-95%). In seven studies, where also lung ultrasound was studied, lung ultrasound had an overall sensitivity of 95% (92-96%) and specificity of 94% (90-97%). Substantial heterogeneity was found. A planned subgroup analysis for individual pathologies was performed. The results of four abstract-only studies, included in the systematic review, were considered unlikely to significantly influence results of our meta-analysis. Study limitations were that most studies were of low power combined with methodological limitations.

CONCLUSIONS:

This meta-analysis demonstrates that chest radiograph has a low sensitivity and reasonable specificity compared with CT for detecting lung pathology in critically ill patients. The studies also investigating lung ultrasound, showed lung ultrasound to be clearly superior to chest radiograph in terms of sensitivity with similar specificity, thereby opting to be the first-line diagnostic tool in these patients.

Insidious Harm of Medication Diluents as a Contributor to Cumulative Volume and Hyperchloremia

A Prospective, Open-Label, Sequential Period Pilot Study*

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Critical Care Medicine: August 2018 - Volume 46 - Issue 8 - p 1217-1223

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Feature Articles

OBJECTIVES:

Although the potential dangers of hyperchloremia from resuscitation fluids continue to emerge, no study to date has considered the contribution of medication diluents to cumulative volume and hyperchloremia. This study compares saline versus dextrose 5% in water as the primary medication diluent and the occurrence of hyperchloremia in critically ill patients.

DESIGN:

Prospective, open-label, sequential period pilot study.

SETTING:

Medical ICU of a large academic medical center.

PATIENTS:

Adult patients admitted to the medical ICU were eligible for inclusion. Patients who were admitted for less than 48 hours, less than 18 years old, pregnant, incarcerated, or who had brain injury were excluded.

INTERVENTIONS:

Saline as the primary medication diluent for 2 months followed by dextrose 5% in water as the primary medication diluent for 2 months.

MEASUREMENTS AND MAIN RESULTS:

A total of 426 patients were included, 216 in the saline group and 210 in the dextrose 5% in water group. Medication diluents accounted for 63% of the total IV volume over the observation period. In the saline group, 17.9% developed hyperchloremia compared with 10.5% in the dextrose 5% in water group (p = 0.037), which was statistically significant in multivariable analysis (odds ratio, 0.50; 95% CI, 0.26-0.94; p = 0.031). In the saline group, 34.2% developed acute kidney injury versus 24.5% in the dextrose 5% in water group (p = 0.035); however, this was not statistically significant when adjusting for baseline covariates. No other significant differences in dysnatremias, insulin requirements, glucose control, ICU length of stay, or ICU mortality were observed.

CONCLUSIONS:

This study identified that medication diluents contribute substantially to the total IV volume received by critically ill patients. Saline as the primary medication diluent compared with dextrose 5% in water is associated with hyperchloremia, a possible risk factor for acute kidney injury.

Blue Light Enhances Bacterial Clearance and Reduces Organ Injury During Sepsis*

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Online Laboratory Investigations

OBJECTIVES:

The physiology of nearly all mammalian organisms are entrained by light and exhibit circadian rhythm. The data derived from animal studies show that light influences immunity, and these neurophysiologic pathways are maximally entrained by the blue spectrum. Here, we hypothesize that bright blue light reduces acute kidney injury by comparison with either bright red or standard, white fluorescent light in mice subjected to sepsis. To further translational relevance, we performed a pilot clinical trial of blue light therapy in human subjects with appendicitis.

High-illuminance, blue spectrum light can attenuate neutrophilic inflammation and organ injury in two murine models of warm ischemia/reperfusion. Others have shown that fish exposed to green or blue light-emitting diodes (LEDs) during starvation exhibited less oxidative stress in comparison with those exposed to red LEDs (26). These data suggest that the blue spectrum of light is a critical determinant of its biological effects.

DESIGN:

Laboratory animal research, pilot human feasibility trial.

SETTING:

University basic science laboratory and tertiary care hospital.

SUBJECTS:

Male C57BL/6J mice, adult (> 17 yr) patients with acute appendicitis.

INTERVENTIONS:

Mice underwent cecal ligation and puncture and were randomly assigned to a 24-hour photoperiod of bright blue, bright red, or ambient white fluorescent light. Subjects with appendicitis were randomized to receive postoperatively standard care or standard care plus high-illuminance blue light.

MEASUREMENTS AND MAIN RESULTS:

Exposure to bright blue light enhanced bacterial clearance from the peritoneum, reduced bacteremia and systemic inflammation, and attenuated the degree of acute kidney injury. The mechanism involved an elevation in cholinergic tone that augmented tissue expression of the nuclear orphan receptor REV-ERB α and occurred independent of alterations in melatonin or corticosterone concentrations. Clinically, exposure to blue light after appendectomy was feasible and reduced serum interleukin-6 and interleukin-10 concentrations.

CONCLUSIONS:

Modifying the spectrum of light may offer therapeutic utility in sepsis.

Corticosteroids in Sepsis: An Updated Systematic Review and Meta-Analysis

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Critical Care Medicine: September 2018 - Volume 46 - Issue 9 - p 1411–1420

doi: 10.1097/CCM.00000000000003262

Feature Articles

OBJECTIVE:

This systematic review and meta-analysis addresses the efficacy and safety of corticosteroids in critically ill patients with sepsis.

DATA SOURCES:

We updated a comprehensive search of MEDLINE, EMBASE, CENTRAL, and LILACS, and unpublished sources for randomized controlled trials that compared any corticosteroid to placebo or no corticosteroid in critically ill children and adults with sepsis.

STUDY SELECTION:

Reviewers conducted duplicate screening of citations, data abstraction, and, using a modified Cochrane risk of bias tool, individual study risk of bias assessment.

DATA EXTRACTION:

A parallel guideline committee provided input on the design and interpretation of the systematic review, including the selection of outcomes important to patients. We assessed overall certainty in evidence using Grading of Recommendations Assessment, Development and Evaluation methodology and performed all analyses using random-effect models. For subgroup analyses, we performed metaregression and considered p value less than 0.05 as significant.

DATA SYNTHESIS:

Forty-two randomized controlled trials including 10,194 patients proved eligible. Based on low certainty, corticosteroids may achieve a small reduction or no reduction in the relative risk of dying in the short-term (28-31 d) (relative risk, 0.93; 95% CI, 0.84-1.03; 1.8% absolute risk reduction; 95% CI, 4.1% reduction to 0.8% increase), and possibly achieve a small effect on long-term mortality (60 d to 1 yr) based on moderate certainty (relative risk, 0.94; 95% CI, 0.89-1.00; 2.2% absolute risk reduction; 95% CI, 4.1% reduction to no effect). Corticosteroids probably result in small reductions in length of stay in ICU (mean difference, -0.73 d; 95% CI, -1.78 to 0.31) and hospital (mean difference, -0.73 d; 95% CI, -2.06 to 0.60) (moderate certainty). Corticosteroids result in higher rates of shock reversal at day 7 (relative risk, 1.26; 95% CI, 1.12-1.42) and lower Sequential Organ Failure Assessment scores at day 7 (mean difference, -1.39; 95% CI, -1.88 to -0.89) (high certainty). Corticosteroids likely increase the risk of hyponatremia (relative risk, 1.64; 95% CI, 1.32-2.03) and hyperglycemia (relative risk, 1.16; 95% CI, 1.08-1.24) (moderate certainty), may increase the risk of neuromuscular weakness (relative risk, 1.21; 95% CI, 1.01-1.52) (low certainty), and appear to have no other adverse effects (low or very low certainty). Subgroup analysis did not demonstrate a credible subgroup effect on any of the outcomes of interest ($p > 0.05$ for all).

CONCLUSIONS:

In critically ill patients with sepsis, corticosteroids possibly result in a small reduction in mortality while also possibly increasing the risk of neuromuscular weakness.

Economic Evaluation of a Patient-Directed Music Intervention for ICU Patients Receiving Mechanical Ventilatory Support*

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Critical Care Medicine: September 2018 - Volume 46 - Issue 9 - p 1430–1435
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Clinical Investigations

OBJECTIVES:

Music intervention has been shown to reduce anxiety and sedative exposure among mechanically ventilated patients. Whether music intervention reduces ICU costs is not known. The aim of this study was to examine ICU costs for patients receiving a patient-directed music intervention compared with patients who received usual ICU care.

DESIGN:

A cost-effectiveness analysis from the hospital perspective was conducted to determine if patient-directed music intervention was cost-effective in improving patient-reported anxiety. Cost savings were also evaluated. One-way and probabilistic sensitivity analyses determined the influence of input variation on the cost-effectiveness.

SETTING:

Midwestern ICUs.

PATIENTS:

Adult ICU patients from a parent clinical trial receiving mechanical ventilatory support.

INTERVENTIONS:

Patients receiving the experimental patient-directed music intervention received a MP3 player, noise-canceling headphones, and music tailored to individual preferences by a music therapist.

MEASUREMENTS AND MAIN RESULTS:

The base case cost-effectiveness analysis estimated patient-directed music intervention reduced anxiety by 19 points on the Visual Analogue Scale-Anxiety with a reduction in cost of \$2,322/patient compared with usual ICU care, resulting in patient-directed music dominance. The probabilistic cost-effectiveness analysis found that average patient-directed music intervention costs were \$2,155 less than usual ICU care and projected that cost saving is achieved in 70% of 1,000 iterations. Based on break-even analyses, cost saving is achieved if the per-patient cost of patient-directed music intervention remains below \$2,651, a value eight times the base case of \$329.

CONCLUSIONS:

Patient-directed music intervention is cost-effective for reducing anxiety in mechanically ventilated ICU patients.

Prophylactic Seizure Medication and Health-Related Quality of Life After Intracerebral Hemorrhage

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Critical Care Medicine: September 2018 - Volume 46 - Issue 9 - p 1480–1485
doi: 10.1097/CCM.0000000000003272
Neurologic Critical Care

OBJECTIVES:

Prophylactic levetiracetam is currently used in ~40% of patients with intracerebral hemorrhage, and the potential impact of levetiracetam on health-related quality of life is unknown. We tested the hypothesis that prophylactic levetiracetam is independently associated with differences in cognitive function health-related quality of life.

DESIGN:

Patients with intracerebral hemorrhage were enrolled in a prospective cohort study. We performed mixed models for T-scores of health-related quality of life, referenced to the U.S. population at 50 ± 10, accounting for severity of injury and time to follow-up.

SETTING:

Academic medical center.

PATIENTS:

One-hundred forty-two survivors of intracerebral hemorrhage.

INTERVENTIONS:

None.

MEASUREMENTS AND MAIN RESULTS:

T-scores of Neuro-Quality of Life Cognitive Function v2.0 was the primary outcome, whereas Neuro-Quality of Life Mobility v1.0 and modified Rankin Scale (a global functional scale) were secondary measures. We prospectively documented if prophylactic levetiracetam was administered and retrieved administration data from the electronic health record. Patients who received prophylactic levetiracetam had worse cognitive function health-related quality of life (T-score 5.1 points lower; $p = 0.01$) after adjustment for age ($p = 0.3$), National Institutes of Health Stroke Scale ($p < 0.000001$), lobar hematoma ($p = 0.9$), and time of assessment; statistical models controlling for prophylactic levetiracetam and the Intracerebral Hemorrhage Score, a global measure of intracerebral hemorrhage severity, yielded similar results. Lower T-scores of cognitive function health-related quality of life at 3 months were correlated with more total levetiracetam dosage ($p = 0.01$) and more administered doses of levetiracetam in the hospital ($p = 0.03$). Patients who received prophylactic levetiracetam were more likely to have a lobar hematoma (27/38 vs 19/104; $p < 0.001$), undergo electroencephalography monitoring (15/38 vs 21/104; $p = 0.02$), but not more likely to have clinical seizures (4/38 vs 7/104; $p = 0.5$). Levetiracetam was not independently associated with the modified Rankin Scale scores or mobility health-related quality of life ($p > 0.1$).

CONCLUSIONS:

Prophylactic levetiracetam was independently associated with lower cognitive function health-related quality of life at follow-up after intracerebral hemorrhage.

Executive Summary: Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

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Special Article

Presenting Symptoms Independently Predict Mortality in Septic Shock: Importance of a Previously Unmeasured Confounder*

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Clinical Investigations

OBJECTIVES:

Presenting symptoms in patients with sepsis may influence rapidity of diagnosis, time-to-antibiotics, and outcome. We tested the hypothesis that vague presenting symptoms are associated with delayed antibiotics and increased mortality. We further characterized individual presenting symptoms and their association with mortality.

DESIGN:

Retrospective cohort study.

SETTING:

Emergency department of large, urban, academic U.S. hospital.

PATIENTS:

All adult patients with septic shock treated in the emergency department between April 2014 and March 2016.

INTERVENTIONS:

None.

MEASUREMENTS AND MAIN RESULTS:

Of 654 septic shock cases, 245 (37%) presented with vague symptoms. Time-to-antibiotics from first hypotension or elevated lactate was significantly longer for those with vague symptoms versus those with explicit symptoms of infection (1.6 vs 0.8 hr; $p < 0.01$), and in-hospital mortality was also substantially higher (34% vs 16%; $p < 0.01$). Patients with vague symptoms were older and sicker as evidenced by triage hypotension, Sequential Organ Failure Assessment score, initial serum lactate, and need for intubation. In multivariate analysis, vague symptoms were independently associated with mortality (adjusted odds ratio, 2.12; 95% CI, 1.32-3.40; $p < 0.01$), whereas time-to-antibiotics was not associated with mortality (adjusted odds ratio, 1.01; 95% CI, 0.94-1.08; $p = 0.78$). Of individual symptoms, only the absence of fever, chills, or rigors (odds ratio, 2.70; 95% CI, 1.63-4.47; $p < 0.01$) and presence of shortness of breath (odds ratio, 1.97; 95% CI, 1.23-3.15; $p < 0.01$) were independently associated with mortality.

CONCLUSIONS:

More than one third of patients with septic shock presented to the emergency department with vague symptoms that were not specific to infection. These patients had delayed antibiotic administration and higher risk of mortality even after controlling for demographics, illness acuity, and time-to-antibiotics in multivariate analysis. These findings suggest that the nature of presenting symptoms is an important component of sepsis clinical phenotyping and may be an important confounder in sepsis epidemiologic studies.

Deresuscitation of Patients With Iatrogenic Fluid Overload Is Associated With Reduced Mortality in Critical Illness*

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Critical Care Medicine: October 2018 - Volume 46 - Issue 10 - p 1600–1607
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Clinical Investigations

OBJECTIVES:

To characterize current practice in fluid administration and deresuscitation (removal of fluid using diuretics or renal replacement therapy), the relationship between fluid balance, deresuscitative measures, and outcomes and to identify risk factors for positive fluid balance in critical illness.

DESIGN:

Retrospective cohort study.

SETTING:

Ten ICUs in the United Kingdom and Canada.

PATIENTS:

Adults receiving invasive mechanical ventilation for a minimum of 24 hours.

INTERVENTIONS:

None.

MEASUREMENTS AND MAIN RESULTS:

Four-hundred patients were included. Positive cumulative fluid balance (fluid input greater than output) occurred in 87.3%: the largest contributions to fluid input were from medications and maintenance fluids rather than resuscitative IV fluids. In a multivariate logistic regression model, fluid balance on day 3 was an independent risk factor for 30-day mortality (odds ratio 1.26/L [95% CI, 1.07-1.46]), whereas negative fluid balance achieved in the context of deresuscitative measures was associated with lower mortality. Independent predictors of greater fluid balance included treatment in a Canadian site.

CONCLUSIONS:

Fluid balance is a practice-dependent and potentially modifiable risk factor for adverse outcomes in critical illness. Negative fluid balance achieved with dereuscitation on day 3 of ICU stay is associated with improved patient outcomes. Minimization of day 3 fluid balance by limiting maintenance fluid intake and drug diluents, and using dereuscitative measures, represents a potentially beneficial therapeutic strategy which merits investigation in randomized trials.

Moderate and Severe Acute Respiratory Distress Syndrome: Hemodynamic and Cardiac Effects of an Open Lung Strategy With Recruitment Maneuver Analyzed Using Echocardiography*

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Critical Care Medicine: October 2018 - Volume 46 - Issue 10 - p 1608–1616
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Clinical Investigations

OBJECTIVES:

Open lung ventilation with a recruitment maneuver could be beneficial for acute respiratory distress syndrome patients. However, the increased airway pressures resulting from the recruitment maneuver may induce cardiac dysfunction, limiting the benefit of this maneuver. We analyzed the effect of a recruitment maneuver and decremental positive end-expiratory pressure titration on cardiac function.

SETTINGS:

Medical ICU Amiens, France.

PATIENTS:

Twenty patients with moderate to severe acute respiratory distress syndrome INTERVENTIONS:: Patients underwent a stepwise recruitment maneuver with respiratory evaluation and echocardiography assessment of cardiac function including longitudinal strain at baseline, peak positive end-expiratory pressure of recruitment maneuver (positive end-expiratory pressure 40 cm H₂O), and at "optimal" positive end-expiratory pressure. The patients were divided into two groups based on change on the PaO₂/FIO₂ ratio (nonresponders < 50%; responders ≥ 50%).

MEASUREMENTS AND MAIN RESULTS:

At peak positive end-expiratory pressure during the recruitment maneuver, the arterial pressure, cardiac output, left ventricular size decreased and right ventricular size increased. The left ventricular ejection fraction decreased from 60% ± 13% to 48% ± 18% (p = 0.05). Both left and right ventricular global longitudinal strain were impaired (-15.8% ± 4.5% to -11% ± 4.7% and -19% ± 5% to -14% ± 6% [p = 0.05] respectively). Fifty percent of patients were nonresponders and demonstrated a lower hemodynamic tolerance to the recruitment maneuver than responders. Optimal positive end-expiratory pressure was 14 ± 5 cm H₂O (vs 11 ± 4 cm H₂O at baseline), and PaO₂/FIO₂ ratio increased from 111 ± 25 to 197 ± 89 mm Hg (p < 0.0001). All hemodynamic variables returned to their baseline value after the recruitment maneuver despite a higher positive end-expiratory pressure.

CONCLUSIONS:

An open lung strategy with a stepwise recruitment maneuver permitted a higher positive end-expiratory pressure and improved oxygenation without any cardiac impairment. The recruitment maneuver was associated with mild and transient, cardiac dysfunction, with nonresponders demonstrating poorer tolerance.

Evaluation of Effect of Probiotics on Cytokine Levels in Critically Ill Children With Severe Sepsis: A Double-Blind, Placebo-Controlled Trial*

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Pediatric Critical Care

OBJECTIVES:

To evaluate the effect of probiotics on cytokines in children with severe sepsis.

DESIGN:

Randomized, double-blind, placebo-controlled trial.

SETTING:

ICU of a tertiary care teaching hospital in North India.

PATIENTS:

Children 3 months to 12 years old with severe sepsis.

INTERVENTIONS:

Enrolled children were randomized to probiotic (n = 50) and placebo (n = 50) groups. Probiotic group received VSL#3 (Danisco-Dupont USA, Madison, WI) (Lactobacillus paracasei, L. plantarum, L. acidophilus, L. delbrueckii, Bifidobacterium longum, B. infantis, B. breve, Streptococcus salivarius; maltose and silicon dioxide), and placebo group received maltose and silicon dioxide. Dose was 1 sachet twice daily for 7 days. Blood was collected on days 1 and 7 for estimation of interleukin-6, interleukin-12p70, interleukin-17, tumor necrosis factor- α , interleukin-10, and transforming growth factor - β 1. "Primary outcome": Change in cytokine levels in probiotic and placebo groups from day 1 to 7. "Secondary outcomes": Sequential Organ Failure Assessment score, healthcare-associated infections, ICU stay, and mortality.

MEASUREMENTS AND MAIN RESULTS:

On day 7, probiotic group had significantly lower levels of proinflammatory cytokines (interleukin-6 [80 vs 186 pg/mL, $p = 0.001$]; interleukin-12p70 [44 vs 79 pg/mL, $p = 0.001$]; interleukin-17 [217 vs 293 pg/mL, $p = 0.01$]; and tumor necrosis factor- α [192 vs 348 pg/mL, $p = 0.01$]) and higher levels of antiinflammatory cytokines (interleukin-10 [320 vs 240 pg/mL, $p = 0.02$] and transforming growth factor- β 1 [311 vs 221 ng/mL, $p = 0.01$]) than placebo group. From day 1 to 7, probiotic group showed significant decrease in proinflammatory cytokines (interleukin-6 [196-80 pg/mL, $p = 0.001$]; interleukin-12p70 [71-44 pg/mL, $p = 0.01$]; interleukin-17 [258-217 pg/mL, $p = 0.01$]; and tumor necrosis factor- α [347-192 pg/mL, $p = 0.001$]) and increase in antiinflammatory cytokines (interleukin-10 [198-320 pg/mL, $p = 0.001$] and transforming growth factor- β 1 [216-311 ng/mL, $p = 0.001$]) as compared to placebo group. Sequential Organ Failure Assessment score on day 7 was significantly less in probiotic group (1 vs 3). There was a nonsignificant trend toward lower incidence of healthcare-associated infections (14% vs 20%) and duration of ICU stay (6.5 vs 9 d) in probiotic group. Mortality was similar in two groups.

CONCLUSIONS:

Probiotics supplementation for 7 days resulted in significant decrease in proinflammatory and increase in antiinflammatory cytokines in children with severe sepsis.

Effect of Thiamine Administration on Lactate Clearance and Mortality in Patients With Septic Shock*

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Clinical Investigations

OBJECTIVES:

Mounting evidence has shown that critically ill patients are commonly thiamine deficient. We sought to test the hypothesis that critically ill patients with septic shock exposed to thiamine would demonstrate improved lactate clearance and more favorable clinical outcomes compared with those not receiving thiamine.

DESIGN:

Retrospective, single-center, matched cohort study.

SETTING:

Tertiary care academic medical center.

PATIENTS:

Adult patients admitted with an International Classification of Diseases, 9th Edition, or International Classification of Diseases, 10th Edition, diagnosis code of septic shock to either the medicine or surgery ICU.

INTERVENTIONS:

None.

MEASUREMENTS AND MAIN RESULTS:

Patients who received IV thiamine supplementation within 24 hours of hospital admission were identified and compared with a matched cohort of patients not receiving thiamine. The primary objective was to determine if thiamine administration was associated with a reduced time to lactate clearance in septic shock. Secondary outcomes included 28-day mortality, acute kidney injury, and need for renal replacement therapy, and vasopressor and mechanical ventilation-free days. Two-thousand two-hundred seventy-two patients were screened, of whom 1,049 were eligible. The study consisted of 123 thiamine-treated patients matched with 246 patients who did not receive thiamine. Based on the Fine-Gray survival model, treatment with thiamine was associated with an improved likelihood of lactate clearance (subdistribution hazard ratio, 1.307; 95% CI, 1.002-1.704). Thiamine administration was also associated with a reduction in 28-day mortality (hazard ratio, 0.666; 95% CI, 0.490-0.905). There were no differences in any secondary outcomes.

CONCLUSIONS:

Thiamine administration within 24 hours of admission in patients presenting with septic shock was associated with improved lactate clearance and a reduction in 28-day mortality compared with matched controls.