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Sepsis
Current Awareness Bulletin
February 2020

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Title: Development of a Simple Sequential Organ Failure Assessment Score for Risk Assessment of Emergency Department Patients With Sepsis.

Citation: Journal of Intensive Care Medicine (Sage Publications Inc.); Mar 2020; vol. 35 (no. 3); p. 270-278

Author(s): Guirgis, Faheem W.; Puskarich, Michael A.; Smotherman, Carmen; Sterling, Sarah A.; Gautam, Shiva; Moore, Frederick A.; Jones, Alan E.

Objectives: Sepsis-3 recommends using the quick Sequential Organ Failure Assessment (qSOFA) score followed by SOFA score for sepsis evaluation. The SOFA is complex and unfamiliar to most emergency physicians, while qSOFA is insensitive for sepsis screening and may result in missed cases of sepsis. The objective of this study was to devise an easy-to-use simple SOFA score for use in the emergency department (ED).

Methods: Retrospective study of ED patients with sepsis with in-hospital mortality as the primary outcome. A simple SOFA score was derived and validated and compared with SOFA and qSOFA.

Results: A total of 3297 patients with sepsis were included, and in-hospital mortality was 10.1%. Simple SOFA had a sensitivity and specificity of 88% and 44% in the derivation set and 93% and 44% in the validation set for in-hospital mortality, respectively. The sensitivity and specificity of qSOFA was 38% and 86% and for SOFA was 90% and 50%, respectively. There were 2760 (84%) of 3297 qSOFA-negative (<2) patients. In this group, simple SOFA had a sensitivity and specificity of 86% and 48% in the derivation set and 91% and 48% in the validation set, respectively. Sequential Organ Failure Assessment was 86% sensitive and 57% specific in qSOFA-negative patients. For all encounters, the areas under the receiver–operator characteristic curves (AUROC) were 0.82 for SOFA, 0.78 (derivation) and 0.82 (validation) for simple SOFA, and 0.68 for qSOFA. In qSOFA-negative patients, the AUROCs were 0.80 for SOFA and 0.76 (derivation) and 0.82 (validation) for simple SOFA.

Conclusions: Simple SOFA demonstrates similar predictive ability for in-hospital mortality from sepsis compared to SOFA. External validation of these findings is indicated.

Title: Effect of magnesium supplementation on lactate clearance in critically ill patients with severe sepsis: a randomized clinical trial.

Citation: European Journal of Clinical Pharmacology; Feb 2020; vol. 76 (no. 2); p. 175-184

Author(s): Noormandi, Afsaneh; Khalili, Hossein; Mohammadi, Mostafa; Abdollahi, Alireza

Objectives: In this study, changes in lactate clearance following magnesium supplementation were evaluated in critically ill patients with severe sepsis.

Methods: Fifty-eight patients with severe sepsis were randomly assigned to receive either magnesium (n = 30) or placebo (n = 28). Patients in the magnesium group received intravenous magnesium sulfate to maintain serum magnesium level around 3 mg/dL for 3 days. The placebo group received the same volume of normal saline. Change in lactate clearance was considered primary outcome of the study.

Results: Mean increase in the lactate clearance in the magnesium group was significantly higher than the placebo group on day 2 (27.53% vs. 23.79% respectively, $p < 0.001$) and day 3 (49.83% vs. 37.02% respectively, $p < 0.001$). Time to lactate clearance was also significantly shorter in the magnesium group than the placebo group (47.28 ± 20.59 vs. 61.20 ± 24.31 h respectively, $p = 0.03$). Sepsis-related mortality was not significantly different but median length of ICU stay was significantly shorter in the magnesium group than the placebo group (8 vs. 15 days respectively, $p < 0.01$).

Conclusions: Magnesium supplementation increased lactate clearance in critically ill patients with severe sepsis. Optimizing serum magnesium level near the upper limit of the normal range may improve severe sepsis outcomes.

Title: Sepsis and Early Warning Score Systems.

Citation: Journal of Nursing; Feb 2020; vol. 67 (no. 1); p. 12-18

Author(s): Shu-Fen Lu; Ru-Yu Lien; Shin-Shang Chou

Abstract: Sepsis is a significant cause of morbidity and mortality worldwide. Early diagnosis and management of sepsis is critical to improving patient prognoses. Surviving sepsis campaign guidelines issued in 2016 encourage health institutions to establish a screening system to identify patients who are at risk of sepsis. In 2012, the Royal College of Physicians in the UK began to advocate replacing local and regional scoring systems with the National Early Warning Score (NEWS), which is optimized for the identification of sepsis. Although many hospitals continue to use other scoring systems, all healthcare organizations are being encouraged to adopt a standardized scoring system to better promote patient safety by facilitating rapid diagnoses and screenings and thus, subsequently, improving decisionmaking by clinical staffs. NEWS plays a very important role in the treatment of sepsis patients. Although research findings related to this scoring system differ somewhat, they provide an important reference for clinical nursing staffs. Intelligent systems are not comprehensive in terms of their capabilities. However, combining human intelligence with system features and further optimizing the system should contribute significantly to the reduction of mortality risk in patients with sepsis.

Title: Improving community recognition of sepsis using early warning scores.

Citaiton: Nursing Times; Jan 2020; vol. 116 (no. 1); p. 20-22

Author(s): Pope, Daniel Thomas

Abstract: Around 70% of sepsis cases originate in the community and, although the National Early Warning Score is mandatory in secondary care, its use has not been extended to primary and community care. Community NEWS scoring was introduced in an acute clinical team to improve patient outcomes and reduce patient mortality through better detection and treatment of sepsis. Staff confidence in recognising acute deterioration and sepsis increased from 77% to 92%, and community NEWS is now being rolled out to all community services in Wales.

Title: Maternal sepsis update: current management and controversies.

Citation: Obstetrician & Gynaecologist; Jan 2020; vol. 22 (no. 1); p. 45-55

Author(s): Greer, Orene; Shah, Nishel Mohan; Johnson, Mark R

Key content: Sepsis is a leading cause of maternal morbidity and mortality, globally and in the UK.In pregnancy and the puerperium, women may be more susceptible to rapid deterioration of illness following an infection.Sepsis has a complex pathophysiology and the immunological and cardiovascular adaptations of normal pregnancy may have an adverse impact on the maternal response to infection. Furthermore, physiological changes of pregnancy, which mimic those of sepsis, often delay recognition and optimal management.'Bedside' identification of pathogens and their antibiotic resistance patterns may help to improve clinical outcomes.Recent updates in sepsis management, areas of controversy and the importance of translational research and clinical trials for pregnancy and the puerperium are discussed. Learning objectives: To highlight the difficulties of diagnosing sepsis in pregnancy.To highlight recent updates, new definitions and controversies of current sepsis management.To highlight the potential for research to develop novel biomarkers and therapeutic agents specific to the pregnant woman. Ethical issues: Sepsis research involving new technologies differentially benefits high-income countries compared with low-/middle-income countries despite the greatest burden of maternal sepsis being in the latter.With the current rapid evolution of omic technology platforms, greater affordability will provide greater accessibility.

Title: Epidemiology of intra-abdominal infection and sepsis in critically ill patients: "AbSeS", a multinational observational cohort study and ESICM Trials Group Project.

Citation: Intensive Care Medicine; Dec 2019; vol. 45 (no. 12); p. 1703-1717

Author(s): Blot, Stijn; Antonelli, Massimo; Arvaniti, Kostoula; Blot, Koen; Creagh-Brown, Ben; de Lange, Dylan; De Waele, Jan; Deschepper, Mieke; Dikmen, Yalim; Dimopoulos, George; Eckmann, Christian; Francois, Guy; Girardis, Massimo; Koulenti, Despoina; Labeau, Sonia; Lipman, Jeffrey; Lipovestky, Fernando; Maseda, Emilio; Montravers, Philippe; Mikstacki, Adam

Purpose: To describe the epidemiology of intra-abdominal infection in an international cohort of ICU patients according to a new system that classifies cases according to setting of infection acquisition (community-acquired, early onset hospital-acquired, and late-onset hospital-acquired), anatomical disruption (absent or present with localized or diffuse peritonitis), and severity of disease expression (infection, sepsis, and septic shock).

Methods: We performed a multicenter (n = 309), observational, epidemiological study including adult ICU patients diagnosed with intra-abdominal infection. Risk factors for mortality were assessed by logistic regression analysis.

Results: The cohort included 2621 patients. Setting of infection acquisition was community-acquired in 31.6%, early onset hospital-acquired in 25%, and late-onset hospital-acquired in 43.4% of patients. Overall prevalence of antimicrobial resistance was 26.3% and difficult-to-treat resistant Gram-negative bacteria 4.3%, with great variation according to geographic region. No difference in prevalence of antimicrobial resistance was observed according to setting of infection acquisition. Overall mortality was 29.1%. Independent risk factors for mortality included late-onset hospital-acquired infection, diffuse peritonitis, sepsis, septic shock, older age, malnutrition, liver failure, congestive heart failure, antimicrobial resistance (either methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, extended-spectrum beta-lactamase-producing Gram-negative bacteria, or carbapenem-resistant Gram-negative bacteria) and source control failure evidenced by either the need for surgical revision or persistent inflammation.

Conclusion: This multinational, heterogeneous cohort of ICU patients with intra-abdominal infection revealed that setting of infection acquisition, anatomical disruption, and severity of disease expression are disease-specific phenotypic characteristics associated with outcome, irrespective of the type of infection. Antimicrobial resistance is equally common in community-acquired as in hospital-acquired infection.

Title: Vitamin C and Thiamine Are Associated with Lower Mortality in Sepsis.

Citation: The journal of trauma and acute care surgery; Feb 2020

Author(s): Byerly, Saskya; Parreco, Joshua; Soe-Lin, Hahn; Parks, Jonathan; Lee, Eugenia E; Shnaydman, Ilya; Mantero, Alejandro; Yeh, D Dante; Namias, Nicholas; Rattan, Rishi

Introduction: The efficacy of vitamin C (VitC) and thiamine (THMN) in patients admitted to the intensive care unit (ICU) with sepsis is unclear. The purpose of this study was to evaluate the effect of VitC and THMN on mortality and lactate clearance in ICU patients. We hypothesized that survival and lactate clearance would be improved when treated with thiamine and/or vitamin C.

Methods: The Philips eICU database version 2.0 was queried for patients admitted to the ICU in 2014-2015 for ≥48 hours and patients with sepsis and an elevated lactate≥2.0 mmol/L. Subjects were categorized according to the receipt of VitC, THMN, both, or neither. The primary outcome was in-hospital mortality. Secondary outcome was lactate clearance defined as lactate<2.0 mmol/L achieved after maximum lactate. Univariable comparisons included age, gender, race, Acute Physiology Score III, APACHE IVa score, SOFA, surgical ICU admission status, intubation status, hospital region, liver disease, vasopressors, steroids, VitC and THMN orders. Kaplan-Meier curves, logistic regression, propensity score matching and competing risks modeling were constructed.

Results: Of 146,687 patients from 186 hospitals, 7.7% (n=11,330) were included. Overall mortality was 25.9% (n=2,930). Evidence in favor of an association between VitC and/or THMN administration

and survival was found on log rank test (all p<0.001). After controlling for confounding factors, VitC (AOR:0.69[0.50-0.95]) and THMN (AOR:0.71[0.55-0.93]) were independently associated with survival and THMN was associated with lactate clearance (AOR:1.50 [1.22-1.96]). On competing risk model VitC (AOR:0.675 [0.463-0.983]), THMN (AOR:0.744 [0.569-0.974]), and VitC+THMN (AOR:0.335 [0.13-0.865]) were associated with survival but not lactate clearance. For subgroup analysis of patients on vasopressors, VitC+THMN were associated with lactate clearance (AOR:1.85 [1.05-3.24]) and survival (AOR:0.223 [0.0678-0.735]).

Conclusions: VitC+THMN is associated with increased survival in septic ICU patients. Randomized, multicenter trials are needed to better understand their effects on outcomes.

Level of Evidence: Therapeutic Study, Level IV.

Title: Efficacy of vitamin C in patients with sepsis: An updated meta-analysis.

Citation: European journal of pharmacology; Feb 2020; vol. 868 ; p. 172889

Author(s): Wei, Xue-Biao; Wang, Zhong-Hua; Liao, Xiao-Long; Guo, Wei-Xin; Wen, Jian-Yi; Qin, Tie-He; Wang, Shou-Hong

Abstract: Previous studies have suggested the beneficial effects of vitamin C in patients with sepsis. However, the results could not be reproduced in the subsequent studies. This meta-analysis aimed to reevaluate the value of vitamin C treatment in patients with sepsis. Electronic databases were searched from inception to August 2019 for the studies comparing the effect of vitamin C versus non-vitamin C infusion in patients with sepsis. Data from 10 studies (4 randomized controlled trials [RCTs] and 6 retrospective studies) involving 1671 patients (495 in the vitamin C treatment group and 1176 in the control group) were included. The use of vitamin C did not reduce the risk of 28-day (OR = 0.84, P = 0.611, I2 = 56.3%), intensive care unit (ICU; OR = 0.79, P = 0.319, I2 = 46.2%), or in-hospital mortality (OR = 0.76, P = 0.251, I2 = 51.0%). No difference in the duration of vasopressor usage and the length of ICU or hospital stay was present. The subgroup analysis for two RCTs suggested that vitamin C treatment showed reduced 28-day mortality (OR = 0.22, P = 0.014, I2 = 35.7%), whereas this beneficial effect did not occur in subgroup analysis for three retrospective studies (OR = 1.11, P = 0.527, I2 = 0%). Retrospective meta-analysis could not reveal the beneficial effect of vitamin C on patients with sepsis. Therefore, in order to clarify the role of vitamin C in sepsis the high-quality RCTs will be required in the future study.

Title: Current and emerging treatments for neonatal sepsis.

Citation: Expert opinion on pharmacotherapy; Feb 2020 ; p. 1-8

Author(s): Carbone, Federico; Montecucco, Fabrizio; Sahebkar, Amirhossein

Introduction: Mortality due to sepsis is still prevalent, peaking at extreme ages of life including infancy. Despite many efforts, the peculiarity of the infant immune system has limited further advances in its treatment. Indeed, neonates experience a dramatic physiological transition from immune tolerance to the maternal antigens to functional maturity. Such a transition is extremely dynamic, as is the pathophysiology of infant sepsis, which is dependent on many infant, maternal, and environmental factors.

Areas covered: In this review, the authors critically update and summarize the current paradigm of immunomodulation in infant sepsis. They confirm how exogenous stimulation of the immune system through intravenous immunoglobulin, colony stimulating factors, and granulocyte transfusion have failed to impact on the prognosis of infant sepsis. They also strongly support the beneficial effects of supplementation/replacement therapies with products naturally contained within maternal milk as well as antioxidant compounds.

Expert opinion: Breastfeeding is beneficial against sepsis. Knowledge of the neonatal immune system is indeed too limited to effectively strengthen immune response by exogenous interventions, especially in preterm and low-birth-weight infants. Awareness of this limitation should pave the way

for future studies (e.g. gender- and omics-based) aimed at better characterizing the infant immune system and promoting a more tailored approach.

Title: Nutrition in Sepsis: A Bench-to-Bedside Review.

Citation: Nutrients; Feb 2020; vol. 12 (no. 2)

Author(s): De Waele, Elisabeth; Malbrain, Manu L N G; Spapen, Herbert

Abstract: Nutrition therapy in sepsis is challenging and differs from the standard feeding approach in critically ill patients. The dysregulated host response caused by infection induces progressive physiologic alterations, which may limit metabolic capacity by impairing mitochondrial function. Hence, early artificial nutrition should be ramped-up and emphasis laid on the post-acute phase of critical illness. Caloric dosing is ideally guided by indirect calorimetry, and endogenous energy production should be considered. Proteins should initially be delivered at low volume and progressively increased to 1.3 g/kg/day following shock symptoms wane. Both the enteral and parenteral route can be (simultaneously) used to cover caloric and protein targets. Regarding pharmaconutrition, a low dose glutamine seems appropriate in patients receiving parenteral nutrition. Supplementing arginine or selenium is not recommended. High-dose vitamin C administration may offer substantial benefit, but actual evidence is too limited for advocating its routine use in sepsis. Omega-3 polyunsaturated fatty acids to modulate metabolic processes can be safely used, but non-inferiority to other intravenous lipid emulsions remains unproven in septic patients. Nutrition stewardship, defined as the whole of interventions to optimize nutritional approach and treatment, should be pursued in all septic patients but may be difficult to accomplish within a context of profoundly altered cellular metabolic processes and organ dysfunction caused by time-bound excessive inflammation and/or immune suppression. This review aims to provide an overview and practical recommendations of all aspects of nutritional therapy in the setting of sepsis.

Title: Early Recognition and Emergency Treatment of Sepsis and Septic Shock in Children.

Citation: Pediatric emergency care; Feb 2020; vol. 36 (no. 2); p. 101-106

Author(s): Hilarius, Kristel W E; Skippen, Peter W; Kissoon, Niranjan

Abstract: Early diagnosis and treatment of sepsis and septic shock in children results in improved outcomes. However, diagnosis is hampered by lack of specific diagnostic tests and relies on the recognition of the alterations of vital signs and protean systemic manifestations associated with infections, signs that mimic many critical illnesses. As a result, the early diagnosis of sepsis is usually presumptive and is based on the suspicion or presence of an infection in combination with the systemic changes. Suspicion should be heightened in vulnerable risk groups such as those with immune compromise due to underlying disease or medication use. Thus, on many occasions, treatment of sepsis is initiated on clinical suspicion pending the outcomes of ongoing evaluations and laboratory findings.What is of relevance to the emergency clinicians is the initial recognition, resuscitation, and treatment in the first few hours of presentation. To best accomplish these tasks, contemporary guidelines suggest that the use of a "recognition bundle" containing a trigger tool for rapid identification, a "resuscitation and stabilization bundle" to enable adherence to best practice, and a "performance bundle" to identify and overcome barriers to best practice be used.Although there are no universally acceptable tools to accomplish these tasks, the various iterations used in quality improvement initiatives have consistently demonstrated better care processes and outcomes. In this article, we outline the contemporary approach to sepsis in the first hours after presentation.

Title: Evaluating a digital sepsis alert in a London multisite hospital network: a natural experiment using electronic health record data.

Citation: Journal of the American Medical Informatics Association : JAMIA; Feb 2020; vol. 27 (no. 2); p. 274-283

Author(s): Honeyford, Kate; Cooke, Graham S; Kinderlerer, Anne; Williamson, Elizabeth; Gilchrist, Mark; Holmes, Alison; Sepsis Big Room; Glampson, Ben; Mulla, Abdulrahim; Costelloe, Ceire

Objective: The study sought to determine the impact of a digital sepsis alert on patient outcomes in a UK multisite hospital network.

Materials and Methods: A natural experiment utilizing the phased introduction (without randomization) of a digital sepsis alert into a multisite hospital network. Sepsis alerts were either visible to clinicians (patients in the intervention group) or running silently and not visible (the control group). Inverse probability of treatment-weighted multivariable logistic regression was used to estimate the effect of the intervention on individual patient outcomes.

Outcomes: In-hospital 30-day mortality (all inpatients), prolonged hospital stay (≥7 days) and timely antibiotics (≤60 minutes of the alert) for patients who alerted in the emergency department.RESULTSThe introduction of the alert was associated with lower odds of death (odds ratio, 0.76; 95% confidence interval [CI], 0.70-0.84; n = 21 183), lower odds of prolonged hospital stay ≥7 days (OR, 0.93; 95% CI, 0.88-0.99; n = 9988), and in patients who required antibiotics, an increased odds of receiving timely antibiotics (OR, 1.71; 95% CI, 1.57-1.87; n = 4622).

Discussion: Current evidence that digital sepsis alerts are effective is mixed. In this large UK study, a digital sepsis alert has been shown to be associated with improved outcomes, including timely antibiotics. It is not known whether the presence of alerting is responsible for improved outcomes or whether the alert acted as a useful driver for quality improvement initiatives.

Conclusions: These findings strongly suggest that the introduction of a network-wide digital sepsis alert is associated with improvements in patient outcomes, demonstrating that digital based interventions can be successfully introduced and readily evaluated.

Title: Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children.

Citaiton: Intensive care medicine; Feb 2020; vol. 46 ; p. 10-67

Author(s): Weiss, Scott L; Peters, Mark J; Alhazzani, Waleed; Agus, Michael S D; Flori, Heidi R; Inwald, David P; Nadel, Simon; Schlapbach, Luregn J; Tasker, Robert C; Argent, Andrew C; Brierley, Joe; Carcillo, Joseph; Carrol, Enitan D; Carroll, Christopher L; Cheifetz, Ira M; Choong, Karen; Cies, Jeffry J; Cruz, Andrea T; De Luca, Daniele; Deep, Akash; Faust, Saul N; De Oliveira, Claudio Flauzino; Hall, Mark W; Ishimine, Paul; Javouhey, Etienne; Joosten, Koen F M; Joshi, Poonam; Karam, Oliver; Kneyber, Martin C J; Lemson, Joris; MacLaren, Graeme; Mehta, Nilesh M; Møller, Morten Hylander; Newth, Christopher J L; Nguyen, Trung C; Nishisaki, Akira; Nunnally, Mark E; Parker, Margaret M; Paul, Raina M; Randolph, Adrienne G; Ranjit, Suchitra; Romer, Lewis H; Scott, Halden F; Tume, Lyvonne N; Verger, Judy T; Williams, Eric A; Wolf, Joshua; Wong, Hector R; Zimmerman, Jerry J; Kissoon, Niranjan; Tissieres, Pierre

Objectives: To develop evidence-based recommendations for clinicians caring for children (including infants, school-aged children, and adolescents) with septic shock and other sepsis-associated organ dysfunction.

Design: A panel of 49 international experts, representing 12 international organizations, as well as three methodologists and three public members was convened. Panel members assembled at key international meetings (for those panel members attending the conference), and a stand-alone meeting was held for all panel members in November 2018. A formal conflict-of-interest policy was developed at the onset of the process and enforced throughout. Teleconferences and electronic-based discussion among the chairs, co-chairs, methodologists, and group heads, as well as within subgroups, served as an integral part of the guideline development process.

Methods: The panel consisted of six subgroups: recognition and management of infection, hemodynamics and resuscitation, ventilation, endocrine and metabolic therapies, adjunctive therapies, and research priorities. We conducted a systematic review for each Population, Intervention, Control, and Outcomes question to identify the best available evidence, statistically summarized the evidence, and then assessed the quality of evidence using the Grading of Recommendations Assessment, Development, and Evaluation approach. We used the evidence-to-decision framework to formulate recommendations as strong or weak, or as a best practice statement. In addition, "in our practice" statements were included when evidence was inconclusive to issue a recommendation, but the panel felt that some guidance based on practice patterns may be appropriate.

Results: The panel provided 77 statements on the management and resuscitation of children with septic shock and other sepsis-associated organ dysfunction. Overall, six were strong recommendations, 49 were weak recommendations, and nine were best-practice statements. For 13 questions, no recommendations could be made; but, for 10 of these, "in our practice" statements were provided. In addition, 52 research priorities were identified.

Conclusions: A large cohort of international experts was able to achieve consensus regarding many recommendations for the best care of children with sepsis, acknowledging that most aspects of care had relatively low quality of evidence resulting in the frequent issuance of weak recommendations. Despite this challenge, these recommendations regarding the management of children with septic shock and other sepsis-associated organ dysfunction provide a foundation for consistent care to improve outcomes and inform future research.

Title: Antithrombin III expression predicts acute kidney injury in elderly patients with sepsis.

Citation: Experimental and therapeutic medicine; Feb 2020; vol. 19 (no. 2); p. 1024-1032

Author(s): Xie, Yun; Tian, Rui; Jin, Wei; Xie, Hui; Du, Jiang; Zhou, Zhigang; Wang, Ruilan

Abstract: Elderly people represent the age group most frequently affected by acute kidney injury (AKI). The potential of Antithrombin III (ATIII) level for predicting AKI among elderly patients with sepsis is yet to be elucidated. Therefore, the purpose of the present study was to evaluate the ability of ATIII to predict AKI nondevelopment and prognosis in elderly patients with sepsis, in an intensive care unit (ICU). The present study was retrospective and included 107 elderly patients with sepsis who had been admitted to ICUs between October 2015 and March 2018. An assessment of renal function was performed daily by measuring serum creatinine (Cr) level and urine output, and ATIII level was obtained within 48 h of sepsis diagnosis. Among all enrolled patients, 29 (27.1%) developed AKI. ATIII expression was a predictor of AKI nondevelopment [Area under the curve (AUC)-Receiving operator characteristic (ROC)=0.729; sensitivity, 0.700; specificity, 0.714], and the ATIII/Creatine ratio was also a predictor of AKI nondevelopment (AUC-ROC=0.971; sensitivity, 0.900; specificity, 1). The accuracy of ATIII (AUC-ROC=0.681; sensitivity, 0.802; specificity, 0.542) and ATIII/Cr (AUC-ROC=0.804; sensitivity, 0.596; specificity, 0.875) in predicting survival was intermediate. However, the ATIII serum level was able to accurately predict AKI nondevelopment in elderly patients with sepsis, who were admitted to ICUs. Patients were divided into low- and high-ATIII groups using either 66.95% or 55.7% as cut-off values, both of which were used for further analysis. By comparison, the ICU stay was significantly lower in the high-ATIII group [P=0.020 (69.95%) and 0.049 (55.7%)] and off mechanical ventilation time, off continuous renal replacement therapy time and survival time were significantly higher in the high ATIII group [P=0.049, 0.048, and 0.014, respectively (66.95%); and P=0.041, 0.036, and 0.021, respectively (55.7%)]. The current study indicated that ATIII serum level predicts AKI in elderly patients with sepsis, and that low ATIII levels predicted a poorer prognosis.

Title: Lactate, bicarbonate and anion gap for evaluation of patients presenting with sepsis to the emergency department: A prospective cohort study.

Citation: Emergency medicine Australasia : EMA; Feb 2020; vol. 32 (no. 1); p. 20-24

Author(s): Mitra, Biswadev; Roman, Cristina; Charters, Kate E; O'Reilly, Gerard; Gantner, Dashiell; Cameron, Peter A

Objective: A serum lactate level >2 mmol/L has been chosen as the preferred cut-off value for screening of patients with suspected sepsis. In patients with suspected sepsis presenting to the ED, we aimed to determine the outcomes of patients with initial lactate levels ≤2 mmoL/L, but abnormal bicarbonate or anion gaps (AGs).

Methods: This prospective cohort study enrolled patients from an adult tertiary referral hospital who presented with suspected sepsis. The predictive value of lactate, bicarbonate and the AG for intensive care unit (ICU) admission and death at hospital discharge were evaluated using area under the receiver operating characteristic curves (AUROC).

Results: There were 441 patients with suspected sepsis enrolled from February 2016 to June 2017. There were 96 (22.0%) patients who were admitted to the ICU and at hospital discharge, 42 (9.6%) patients had died. There was no statistically significant difference between the AUROCs of lactate or bicarbonate level or AG to predict ICU admission (P = 0.17). There was no statistically significant difference between the AUROCs of lactate or bicarbonate level or AG to predict mortality at hospital discharge (P = 0.44). Among the 73 patients with normal lactate levels, but abnormal bicarbonate or AG, there were seven (9.6%) deaths.

Conclusions: A normal lactate level alone should not be used to exclude life-threatening sepsis. Patients with metabolic acidosis characterised by low bicarbonate or high AG levels, but with normal lactate levels, have high rates of ICU requirement and mortality and should also be considered for early, aggressive therapy.

Title: Health economic evaluations of sepsis interventions in critically ill adult patients: A systematic review

Citation: Journal of Intensive Care; Jan 2020; vol. 8 (no. 1)

Author(s): Higgins A.M.; Brooker J.E.; MacKie M.; Cooper D.J.; Harris A.H.

Background: Sepsis is a global health priority. Interventions to reduce the burden of sepsis need to be both effective and cost-effective. We performed a systematic review of the literature on health economic evaluations of sepsis treatments in critically ill adult patients and summarised the evidence for cost-effectiveness.

Method(s): We systematically searched MEDLINE, Embase, and the Cochrane Library using thesaurus (e.g. MeSH) and free-text terms related to sepsis and economic evaluations. We included all articles that reported, in any language, an economic evaluation of an intervention for the management of sepsis in critically ill adult patients. Data extracted included study details, intervention details, economic evaluation methodology, and outcomes. Included studies were appraised for reporting quality using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

Result(s): We identified 50 records representing 46 economic evaluations for a variety of interventions including antibiotics (n = 5), fluid therapy (n = 2), early goal-directed therapy and other resuscitation protocols (n = 8), immunoglobulins (n = 2), and interventions no longer in clinical use such as monoclonal antibodies (n = 7) and drotrecogin alfa (n = 13). Twelve (26%) evaluations were of excellent reporting quality. Incremental cost-effectiveness ratios (ICERs) ranged from dominant (lower costs and higher effectiveness) for early goal-directed therapy, albumin, and a multifaceted sepsis education program to dominated (higher costs and lower effectiveness) for polymerase chain reaction assays (LightCycler SeptiFast testing MGRADE, SepsiTestTM, and IRIDICA BAC BSI assay). ICERs varied widely across evaluations, particularly in subgroup analyses.

Conclusion(s): There is wide variation in the cost-effectiveness of sepsis interventions. There remain important gaps in the literature, with no economic evaluations identified for several interventions routinely used in sepsis. Given the high economic and social burden of sepsis, high-quality economic evaluations are needed to increase our understanding of the cost-effectiveness of these interventions in routine clinical practice and to inform decision makers.

Title: Fluid resuscitation in patients with end-stage renal disease on hemodialysis presenting with severe sepsis or septic shock: A case control study

Citation: Journal of Critical Care; Feb 2020; vol. 55 ; p. 157

Author(s): Rajdev, Kartikeya; Leifer, Lazer; Sandhu, Gurkirat; Mann, Benjamin; Pervaiz, Sami; Habib, Saad; Siddiqui, Abdul Hasan; Bino, Joseph; Demissie, Seleshi; El-Sayegh, Suzanne

Abstract: Due to the potential risk of volume overload, physicians are hesitant to aggressively fluid-resuscitate septic patients with end-stage renal disease (ESRD) on hemodialysis (HD). Primary objective: To calculate the percentage of ESRD patients on HD (Case) who received ≥30 mL/Kg fluid resuscitation within the first 6 h compared to non-ESRD patients (Control) that presented with severe sepsis (SeS) or septic shock (SS). Secondary objectives: Effect of fluid resuscitation on intubation rate, need for urgent dialysis, hospital length of stay (LOS), intensive care unit (ICU) admission and LOS, need for vasopressors, and hospital mortality. Medical records of 715 patients with sepsis, SeS, SS, and ESRD were reviewed. We identified 104 Case and 111 Control patients. In the Case group, 23% of patients received ≥30 mL/Kg fluids compared to 60% in the Control group ($p < 0.001$). There was no significant difference in in-hospital mortality, need for urgent dialysis, intubation rates, ICU LOS, or hospital LOS between the two groups. Subgroup analysis between ESRD patients who received ≥30 mL/Kg (N = 80) vs those who received <30 mL/Kg (N = 24) showed no significant difference in any of the secondary outcomes. Compliance with 30 mL/Kg fluids was low for all patients but significantly lower for ESRD patients. Aggressive fluid resuscitation appears to be safe in ESRD patients.

Title: Association of negative fluid balance during the de-escalation phase of sepsis management with mortality: A cohort study

Citation: Journal of Critical Care; Feb 2020; vol. 55 ; p. 16

Author(s): Dhondup, Tsering; Jong-Chie, Claudia Tien; Marquez, Alberto; Kennedy, Cassie C; Gajic, Ognjen; Kashani, Kianoush B

Purpose: We aimed to evaluate the impact of negative fluid balance during the fluid de-escalation phase of sepsis management.

Material and Methods: This is a historical cohort study of adult intensive care units (ICU) patients with septic shock and severe sepsis in a quaternary medical center, from January 2007 through December 2009. We used regression modeling to assess the impact of negative volume balance on mortality after adjustments for age, comorbidities, and illness severity.

Results: Among 633 enrolled patients, 387 patients reached negative fluid balance who in comparison with others had a lower 90-day mortality rate (36% vs. 44%; P = .048), despite higher severity of illness. Each 1-L negative daily fluid balance was associated with reduced ICU, hospital, 90-day and 1-year mortality (hazard ratio [HR] 0.39 [95%CI, 0.28–0.57], 0.76 [95%CI, 0.63–0.94], 0.69 [95%CI, 0.59–0.81], 0.67 [0.58–0.78], respectively; P < .05). This protective effect of negative volume balance was maintained when cumulative ICU fluid balance was utilized.

Conclusions: There is not only a significant association between outcomes of patients who were resuscitated for sepsis and achieving negative fluid balance, but also the amount of daily or cumulative negative fluid balance is associated with lower mortality of these patients. Prospective clinical trials are needed to validate this finding.

Title: Sepsis: Symptoms, Assessment, Diagnosis, and the Hour-1 Bundle in Patients With Cancer.

Citation: Clinical journal of oncology nursing; Feb 2020; vol. 24 (no. 1); p. 99-102

Author(s): Boucher, Jean E; Carpenter, Dawn

Abstract: Sepsis has a higher incidence of hospital stays and poorer morbidity and mortality outcomes in patients with cancer. The development of infection in weakened immune systems and prolonged treatment courses increase the risk for sepsis in patients with cancer. The causes of infection that can lead to sepsis in patients with cancer are further complicated by disease- or therapy-related neutropenia. Early recognition of sepsis is critical for prompt treatment to prevent tissue damage, organ failure, and mortality. The Surviving Sepsis Campaign recommends the Hour-1 bundle as best practice for sepsis management.

Title: Evaluation and management of abdominal sepsis.

Citation: Current opinion in critical care; Jan 2020

Author(s): Sartelli, Massimo

Purpose of Review: The review focuses on the evaluation and management of abdominal sepsis.

Recent Findings: A multitude of surgical approaches towards abdominal sepsis are practized in the world and may be associated with significant morbidity and mortality rates. Despite decades of sepsis research, no specific therapies for sepsis have emerged. Without specific therapies, the management of abdominal sepsis is based on the control of the infection and organ support.

Summary: Early clinical diagnosis, adequate source control to stop ongoing contamination, appropriate antibiotic therapy dictated by patient and infection risk factors, and prompt resuscitation are the cornerstones of its management.

Title: Active antibiotic discontinuation in suspected but not confirmed early-onset neonatal sepsis - a quality-improvement initiative.

Citation: Acta paediatrica (Oslo, Norway : 1992); Jan 2020

Author(s): Dretvik, Thomas; Solevåg, Anne Lee; Finvåg, Andreas; Størdal, Eline Hasselgård; Størdal, Ketil; Klingenberg, Claus

Aim: To study whether a simple targeted intervention could reduce unwarranted antibiotic treatment in near-term and term neonates with suspected, but not confirmed early-onset sepsis.

Methods: A quality-improvement initiative in three Norwegian neonatal intensive care units. The intervention included an inter-hospital clinical practice guideline for discontinuing antibiotics after 36-48 hours if sepsis was no longer suspected and blood cultures were negative in neonates ≥34+0 weeks gestation. Two units used procalcitonin in decision-making. We compared data 12-14 months before and after guideline implementation. The results are presented as median with interquartile ranges.

Results: 284 infants (2.5% of all births ≥34+0 weeks gestation) received antibiotics before and 195 (1.8%) after guideline implementation (p=0.0018). The two units that used procalcitonin discontinued antibiotics earlier after guideline implementation than the unit without procalcitonin. Neonates not diagnosed with sepsis were treated 49 (31-84) hours before and 48 (36-72) hours after guideline implementation (p=0.68). In all infants, including those diagnosed with sepsis, antibiotic treatment duration was reduced from 108 (60-144) to 96 (48-120) hours (p=0.013).

Conclusion: Antibiotic treatment duration for suspected, but not confirmed early-onset sepsis did not change. However, treatment duration for all infants, and the proportion of infants commenced on antibiotics were reduced.

Title: Combination of vitamin C, thiamine and hydrocortisone added to standard treatment in the management of sepsis: results from an open label randomised controlled clinical trial and a review of the literature.

Citation: Infectious diseases (London, England); Jan 2020 ; p. 1-8

Author(s): Wani, Saleem Javaid; Mufti, Showkat A; Jan, Rafi A; Shah, S U; Qadri, Syed Mudassir; Khan, Umar Hafiz; Bagdadi, Farhana; Mehfooz, Nazia; Koul, Parvaiz A

Background: Combination of vitamin C, hydrocortisone and thiamine have recently been used in sepsis but data of efficacy are conflicting and no data are available from developing countries. We sought to study the effect of addition of this combination to standard care in patients with sepsis/septic shock in a north Indian setting.

Methods: In a prospective, open label, randomised fashion, 100 patients with sepsis/septic shock were recruited to receive either standard therapy alone (control group, n = 50) or a combination of vitamin C, thiamine and hydrocortisone (treatment group, n = 50) in addition. The patients were followed for various clinical and laboratory parameters, in-hospital and 30-day mortality, duration of vasopressor use, lactate clearance, duration of hospital stay, and change in serum lactate and the SOFA score over the first 4 days.

Results: The 2 groups were matched for basic characteristics. The in-hospital mortality (28% in controls and 24% in treatment group, p = .82) and 30-day mortality (42% in controls and 40% in treatment group, p = 1.00) was not significantly different in the 2 groups. However, there was a significant difference in duration of vasopressor use (96.13 ± 40.50 h in control group v/s 75.72 ± 30.29 h in treatment group, p value = .010) and lactate clearance (control group: 41.81% v/s treatment group: 56.83%, p value =.031) between 2 groups.

Conclusions: Addition of vitamin C, hydrocortisone, and thiamine into standard care of sepsis does not improve in-hospital or 30 day mortality. However lower vasopressor use and faster lactate clearance is observed with treatment.

Title: Potential of glucocorticoids to treat intestinal inflammation during sepsis.

Citation: Current opinion in pharmacology; Jan 2020; vol. 53 ; p. 1-7

Author(s): Van Looveren, Kelly; Wallaeys, Charlotte; Libert, Claude

Abstract: Glucocorticoids (GCs) are steroid hormones characterized by their anti-inflammatory and immunosuppressive nature. Although GCs are very commonly prescribed, in several diseases, including sepsis, their clinical treatment is hampered by side effects and by the occurrence of glucocorticoid resistance (GCR). Sepsis is defined as a life-threatening organ dysfunction, initiated by a dysregulated systemic host response to infections. With at least 19 million cases per year and a lethality rate of about 25%, sepsis is one of the most urgent unmet medical needs. The gut is critically affected during sepsis and is considered as a driving force in this disease. Despite there is no effective treatment for sepsis, pre-clinical studies show promising results by preserving or restoring gut integrity. Since GC treatment reveals therapeutic effects in Crohn's disease (CD) and in pre-clinical sepsis models, we hypothesize that targeting GCs to the gut or stimulating local GC production in the gut forms an interesting strategy for sepsis treatment. According to recent findings that show that dimerization of the glucocorticoid receptor (GR) is essential in inducing anti-inflammatory effects in pre-clinical sepsis models, we predict that new generation GCs that selectively dimerize the GR, can therefore positively affect the outcome of sepsis treatment.

Title: Rate and risk factors for rehospitalisation in sepsis survivors: systematic review and meta-analysis.

Citation: Intensive care medicine; Jan 2020

Author(s): Shankar-Hari, Manu; Saha, Rohit; Wilson, Julie; Prescott, Hallie C; Harrison, David; Rowan, Kathryn; Rubenfeld, Gordon D; Adhikari, Neill K J

Purpose: Sepsis survivors have a higher risk of rehospitalisation and of long-term mortality. We assessed the rate, diagnosis, and independent predictors for rehospitalisation in adult sepsis survivors.

Methods: We searched for non-randomized studies and randomized clinical trials in MEDLINE, Cochrane Library, Web of Science, and EMBASE (OVID interface, 1992-October 2019). The search strategy used controlled vocabulary terms and text words for sepsis and hospital readmission, limited to humans, and English language. Two authors independently selected studies and extracted data using predefined criteria and data extraction forms.

Results: The literature search identified 12,544 records. Among 56 studies (36 full and 20 conference abstracts) that met our inclusion criteria, all were non-randomised studies. Studies most often report 30-day rehospitalisation rate (mean 21.4%, 95% confidence interval [CI] 17.6-25.4%; N = 36 studies reporting 6,729,617 patients). The mean (95%CI) rehospitalisation rates increased from 9.3% (8.3-10.3%) by 7 days to 39.0% (22.0-59.4%) by 365 days. Infection was the most common rehospitalisation diagnosis. Risk factors that increased the rehospitalisation risk in sepsis survivors were generic characteristics such as older age, male, comorbidities, non-elective admissions, hospitalisation prior to index sepsis admission, and sepsis characteristics such as infection and illness severity, with hospital characteristics showing inconsistent associations. The overall certainty of evidence was moderate for rehospitalisation rates and low for risk factors.

Conclusions: Rehospitalisation events are common in sepsis survivors, with one in five rehospitalisation events occurring within 30 days of hospital discharge following an index sepsis admission. The generic and sepsis-specific characteristics at index sepsis admission are commonly reported risk factors for rehospitalisation.

Registration: PROSPERO CRD 42016039257, registered on 14-06-2016.

Title: Lower versus higher fluid volumes during initial management of sepsis - a systematic review with meta-analysis and trial sequential analysis.

Citation: Chest; Jan 2020

Author(s): Meyhoff, Tine Sylvest; Møller, Morten Hylander; Hjortrup, Peter Buhl; Cronhjort, Maria; Perner, Anders; Wetterslev, Jørn

Purpose: Intravenous fluids are recommended during the initial management of sepsis, but the quality of evidence is low, and clinical equipoise exists. We aimed to assess patient-important benefits and harms of lower versus higher fluid volumes in adult patients with sepsis.

Methods: We conducted a systematic review with meta-analysis and trial sequential analysis (TSA) of randomised clinical trials of intravenous fluid volume separation in adult patients with sepsis. We adhered to our published protocol, the Cochrane Handbook, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and the Grading of Recommendations Assessment, Development and Evaluation statements. The primary outcomes were all-cause mortality, serious adverse events and quality-of-life.

Results: We included 9 trials (n=637); all were published after 2015 and had overall high risk of bias. We found no statistically significant difference between lower versus higher fluid volumes on all-cause mortality (relative risk 0.87, 95% confidence interval (CI) 0.69 to 1.10, I2=0%; TSA adjusted CI 0.34 to 2.22), or serious adverse events (relative risk 0.91 95% CI 0.78 to 1.05, I2=0%; TSA adjusted CI 0.68 to 1.21). No trials reported on quality-of-life. We did not find differences in the secondary or exploratory outcomes. The quality of evidence was very low across all outcomes.

Conclusions: In this systematic review, we found very low quantity and quality of evidence supporting the decision on the volumes of IV fluid therapy in adults with sepsis.

Title: The Emerging Role of Vitamin C as a Treatment for Sepsis.

Citation: Nutrients; Jan 2020; vol. 12 (no. 2)

Author(s): Kashiouris, Markos G; L'Heureux, Michael; Cable, Casey A; Fisher, Bernard J; Leichtle, Stefan W; Iii, Alpha A Fowler

Abstract: Sepsis, a life-threatening organ dysfunction due to a dysregulated host response to infection, is a leading cause of morbidity and mortality worldwide. Decades of research have failed to identify any specific therapeutic targets outside of antibiotics, infectious source elimination, and supportive care. More recently, vitamin C has emerged as a potential therapeutic agent to treat sepsis. Vitamin C has been shown to be deficient in septic patients and the administration of high dose intravenous as opposed to oral vitamin C leads to markedly improved and elevated serum levels. Its physiologic role in sepsis includes attenuating oxidative stress and inflammation, improving vasopressor synthesis, enhancing immune cell function, improving endovascular function, and epigenetic immunologic modifications. Multiple clinical trials have demonstrated the safety of vitamin C and two recent studies have shown promising data on mortality improvement. Currently, larger randomized controlled studies are underway to validate these findings. With further study, vitamin C may become standard of care for the treatment of sepsis, but given its safety profile, current treatment can be justified with compassionate use.

Title: Inhaled Albuterol Use and Impaired Lactate Clearance in Patients With Sepsis: A Retrospective Cohort Study.

Citation: Journal of intensive care medicine; Jan 2020 ; p. 885066619901095

Author(s): Maeda, Tetsuro; Paralkar, Janvi; Kuno, Toshiki; Patrawalla, Paru

Background: Lactate clearance has become important in the management of sepsis. However, factors unrelated to sepsis-induced hyperlactatemia, including β-2 adrenergic agonists, can interfere with lactate clearance.

Objectives: To investigate the association of inhaled albuterol with lactate clearance in patients with sepsis.

Methods: This was a single-center retrospective cohort study. Adult patients with sepsis diagnosed in the emergency department from May 2015 to May 2016 with initial lactate levels >2 mmol/L and serial lactate measurements 2 to 6 hours apart were included. Patients were divided into 2 groups based on whether they received inhaled albuterol between lactate measurements. The primary end point was lactate clearance of 10%. Secondary end points included intensive care unit (ICU) consultation and in-hospital mortality. A multivariate logistic regression analysis was performed to assess the effect of inhaled albuterol on lactate clearance.

Results: Of 269 patients included, 58 (22%) received inhaled albuterol between lactate measurements. This group had a significantly higher prevalence of pulmonary disease and a lower initial lactate compared to those who did not receive inhaled albuterol. They had a significantly lower rate of lactate clearance (45% vs 77%, P < .001); however, ICU consultation (71% vs 57%, P = .066) and in-hospital mortality (19% vs 22%, P = .64) were not significantly different. A multivariate logistic regression analysis adjusting for age, sex, chronic kidney disease, cirrhosis, cancer, septic shock or severe sepsis, and the amount of intravenous fluids received showed that inhaled albuterol was independently associated with impaired lactate clearance (adjusted odds ratio: 0.26, 95% confidence interval: 0.14-0.50, P < .001).

Conclusions: Inhaled albuterol in patients with sepsis was associated with impaired lactate clearance without an increase in ICU consultation or in-hospital mortality. Impaired lactate clearance in patients with sepsis who receive inhaled albuterol should be interpreted with caution.

Title: Improved Outcomes After Regional Implementation of Sepsis Alert: A Novel Triage Model.

Citation: Critical care medicine; Jan 2020

Author(s): Rosenqvist, Mari; Bengtsson-Toni, Maria; Tham, Johan; Lanbeck, Peter; Melander, Olle; Åkesson, Per

Objectives: To assess whether the triage model Sepsis Alert for Emergency Departments results in improved initial care of patients with severe infections.

Design: Interventional study comparing patient care before and after the start of a new triage model, including 90-day follow-up.

Setting: Eight emergency departments in Skåne County, Sweden.SUBJECTSPatients with suspected severe infection.

Interventions: Patients with severely deviating vital signs and suspected infection were triaged into a designated sepsis line called Sepsis Alert, for rapid evaluation supported by an infectious disease specialist. Also, all emergency department staff participated in a designated sepsis education before the model was introduced.

Measurements and Main Results: Medical records were evaluated for a 3-month period 1 year before the triage system was started in 2016 and for a 3-month period 1 year after. Of 195,607 patients admitted to these emergency departments during two 3-month periods, a total of 5,321 patients presented severely abnormal vital signs. Of these, 1,066 patients who presented with fever greater thanor equal to 38°C or history of fever/chills were considered to be patients at risk of having severe sepsis. Among patients triaged according to Sepsis Alert, 89.3% received antibiotic treatment within 1 hour after arrival to the emergency department (median time to antibiotics, 26 min), which was significantly better than before the start of the new triage: 67.9% (median time to antibiotics, 37 min) ($p < 0.001$). Additionally, sepsis treatment quality markers were significantly improved after the introduction of Sepsis Alert, including number of blood cultures and lactate measurements taken, percentage of patients receiving IV fluids, and appropriate initial antibiotic treatment. There were no differences in 28- or 90-day mortality rates.

Conclusions: The implementation of the new triage model Sepsis Alert with special attention to severe sepsis patients led to faster and more accurate antibiotic treatment and improved diagnostic procedures and supportive care.

Sources Used:

The following databases are used in the creation of this bulletin: BNI, CINAHL, EMBASE & Medline.

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