

## POST-ADMISSION CRITICAL CARE LITERATURE REVIEW

### ORIGINAL ARTICLES

#### **01. Defining the surgical critical care research agenda: results of a gaps analysis from the Critical Care Committee of the American Association for the Surgery of Trauma** Kim DY, et al., Critical

Care Committee of the AAST. J Trauma Acute Care Surg. 2019 Oct 31. doi: 10.1097/TA.0000000000002532

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/31688786>

#### **BACKGROUND:**

There has been an unprecedented increase in critical care research recently and there is a need for an organized and systematic approach to surgical critical care research planning. The purpose of this paper was to establish a surgical critical care research agenda via a systematic review of the literature and needs assessment.

#### **METHODS:**

A systematic review of the literature was performed to identify high-impact critical care articles since 1999 on the basis of citation data. Using a standardized data abstraction tool, surgical representation in the literature was analyzed. A needs assessment was performed using a modified Delphi approach in three rounds to obtain consensus among members of the Critical Care Committee of the American Association for the Surgery of Trauma (n=30) regarding research priorities in surgical critical care.

#### **RESULTS:**

Of 1,019 articles screened, 645 underwent full-text review, and 276 papers were included in the final analysis. Surgical patients were identified in 177 studies (64.1%), whereas trauma patients were identified in 82 (31.7%). Key categories identified during the first round of the Delphi included end of life care, traumatic brain injury (TBI), delirium, post-ICU syndrome, hemodynamic monitoring, and volume/fluid balance. During the second and third rounds, 10 topics were classified as high priority. The three highest ranked topics were: addressing goals of care in the acute care setting ( $4.44 \pm 0.70$ ); improving prognostic indicators in patients with severe TBI ( $4.38 \pm 0.85$ ); and interventions to mitigate the post-ICU syndrome ( $4.22 \pm 0.65$ ). There was a strong positive correlation in ratings ( $R_s$  value = 0.90,  $p = 0.001$ ) between rounds 2 and 3.

#### **CONCLUSIONS:**

The results of this study highlight the recent surgical critical care research literature and may serve as a platform for future research endeavors in surgical critical care.

#### **02. The research agenda for trauma critical care.** Asehnoune K, et al. Intensive Care Med. 2017 Sep;43(9):1340-1351. doi: 10.1007/s00134-017-4895-9. Epub 2017 Jul 29.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/28756471>

In this research agenda on the acute and critical care management of trauma patients, we concentrate on the major factors leading to death, namely haemorrhage and traumatic brain injury (TBI). In haemostasis biology, the results of randomised controlled trials have led to the therapeutic focus moving away from the augmentation of coagulation factors (such as recombinant factor VIIa) and towards fibrinogen supplementation and administration of antifibrinolytics such as tranexamic acid. Novel diagnostic techniques need to be evaluated to determine whether an individualised precision approach is superior to current empirical practice. The timing and efficacy of platelet transfusions remain in question, while new blood products need to be developed and evaluated, including whole blood variants, lyophilised products and novel red cell storage modalities. The current cornerstones of

TBI management are intracranial pressure control, maintenance of cerebral perfusion pressure and avoidance of secondary insults (such as hypotension, hypoxaemia, hyperglycaemia and pyrexia). Therapeutic hypothermia and decompressive craniectomy are controversial therapies. Further research into these strategies should focus on identifying which subgroups of patients may benefit from these interventions. Prediction of the long-term outcome early after TBI remains challenging. Early magnetic resonance imaging has recently been evaluated for predicting the long-term outcome in mild and severe TBI. Novel biomarkers may also help in outcome prediction and may predict chronic neurological symptoms. For trauma in general, rehabilitation is complex and multidimensional, and the optimal timing for commencement of rehabilitation needs investigation. We propose priority areas for clinical trials in the next 10 years.

**03. Late immune consequences of combat trauma: a review of trauma-related immune dysfunction and potential therapies.** Thompson KB, et al. *Mil Med Res.* 2019 Apr 24;6(1):11. doi: 10.1186/s40779-019-0202-0.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/31014397>

With improvements in personnel and vehicular body armor, robust casualty evacuation capabilities, and damage control resuscitation strategies, more combat casualties are surviving to reach higher levels of care throughout the casualty evacuation system. As such, medical centers are becoming more accustomed to managing the deleterious late consequences of combat trauma related to the dysregulation of the immune system. In this review, we aim to highlight these late consequences and identify areas for future research and therapeutic strategies. Trauma leads to the dysregulation of both the innate and adaptive immune responses, which places the injured at risk for several late consequences, including delayed wound healing, late onset sepsis and infection, multi-organ dysfunction syndrome, and acute respiratory distress syndrome, which are significant for their association with the increased morbidity and mortality of wounded personnel. The mechanisms by which these consequences develop are complex but include an imbalance of the immune system leading to robust inflammatory responses, triggered by the presence of damage-associated molecules and other immune-modifying agents following trauma. Treatment strategies to improve outcomes have been difficult to develop as the immunophenotype of injured personnel following trauma is variable, fluid and difficult to determine. As more information regarding the triggers that lead to immune dysfunction following trauma is elucidated, it may be possible to identify the immunophenotype of injured personnel and provide targeted treatments to reduce the late consequences of trauma, which are known to lead to significant morbidity and mortality.

**04. Update in sepsis guidelines: what is really new?** Plevin R, et al. *Trauma Surg Acute Care Open.* 2017 Sep 7;2(1):e000088. doi: 10.1136/tsaco-2017-000088. eCollection 2017.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29766091>

Sepsis remains a highly lethal entity resulting in more than 200 000 deaths in the USA each year. The in-hospital mortality approaches 30% despite advances in critical care during the last several decades. The direct health care costs in the USA exceed \$24 billion dollars annually and continue to escalate each year especially as the population ages. The Surviving Sepsis Campaign published their initial clinical practice guidelines for the management of severe sepsis and septic shock in 2004. Updated versions were published in 2008, 2012 and most recently in 2016 following the convening of the Third International Consensus Definitions Task Force. This task force was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine to address prior criticisms of the multiple definitions used clinically for sepsis-related illnesses. In the 2016 guidelines, sepsis is redefined by the

taskforce as a life-threatening organ dysfunction caused by a dysregulated host response to infection. In addition to using the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score to more rapidly identify patients with sepsis, the task force also proposed a novel scoring system to rapidly screen for patients outside the ICU who are at risk of developing sepsis: the 'quickSOFA' (qSOFA) score. To date, the largest reductions in mortality have been associated with early identification of sepsis, initiation of a 3-hour care bundle and rapid administration of broad-spectrum antibiotics. The lack of progress in mortality reduction in sepsis treatment despite extraordinary investment of research resources underscores the variability in patients with sepsis. No single solution is likely to be universally beneficial, and sepsis continues to be an entity that should receive high priority for the development of precision health approaches for treatment.

**05. Sepsis and Septic Shock Strategies.** Armstrong BA, et al. Surg Clin North Am. 2017 Dec;97(6):1339-1379. doi: 10.1016/j.suc.2017.07.003. Epub 2017 Oct 5.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29132513>

Three therapeutic principles most substantially improve organ dysfunction and survival in sepsis: early, appropriate antimicrobial therapy; restoration of adequate cellular perfusion; timely source control. The new definitions of sepsis and septic shock reflect the inadequate sensitivity, specificity, and lack of prognostication of systemic inflammatory response syndrome criteria. Sequential (sepsis-related) organ failure assessment more effectively prognosticates in sepsis and critical illness. Inadequate cellular perfusion accelerates injury and reestablishing perfusion limits injury. Multiple organ systems are affected by sepsis and septic shock and an evidence-based multipronged approach to systems-based therapy in critical illness results in improved outcomes.

**06. Acute kidney injury in trauma patients admitted to the ICU: a systematic review and meta-analysis.** Søvik S, et al. Intensive Care Med. 2019 Apr;45(4):407-419. doi: 10.1007/s00134-019-05535-y. Epub 2019 Feb 6.

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*PURPOSE:*

To perform a systematic review and meta-analysis of acute kidney injury (AKI) in trauma patients admitted to the intensive care unit (ICU).

*METHODS:*

We conducted a systematic literature search of studies on AKI according to RIFLE, AKIN, or KDIGO criteria in trauma patients admitted to the ICU (PROSPERO CRD42017060420). We searched PubMed, Cochrane Database of Systematic Reviews, UpToDate, and NICE through 3 December 2018. Data were collected on incidence of AKI, risk factors, renal replacement therapy (RRT), renal recovery, length of stay (LOS), and mortality. Pooled analyses with random effects models yielded mean differences, OR, and RR, with 95% CI.

*RESULTS:*

Twenty-four observational studies comprising 25,182 patients were included. Study quality (Newcastle-Ottawa scale) was moderate. Study heterogeneity was substantial. Incidence of post-traumatic AKI in the ICU was 24% (20-29), of which 13% (10-16) mild, 5% (3-7) moderate, and 4% (3-6) severe AKI. Risk factors for AKI were African American descent, high age, chronic hypertension, diabetes mellitus, high Injury Severity Score, abdominal injury, shock, low Glasgow Coma Scale (GCS) score, high APACHE II score, and sepsis. AKI patients had 6.0 (4.0-7.9) days longer ICU LOS and increased risk of death [RR 3.4 (2.1-5.7)] compared to non-AKI patients. In patients with AKI, RRT was used in 10% (6-15). Renal recovery occurred in 96% (78-100) of patients.

*CONCLUSIONS:*

AKI occurred in 24% of trauma patients admitted to the ICU, with an RRT use among these of 10%. Presence of AKI was associated with increased LOS and mortality, but renal recovery in AKI survivors was good.

**07. Acute kidney injury in trauma patients.** Harrois A, et al. *Curr Opin Crit Care.* 2017 Dec;23(6):447-456. doi: 10.1097/MCC.0000000000000463.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29035925>

*PURPOSE OF REVIEW:*

To review epidemiology and pathophysiology of acute kidney injury (AKI) in trauma patients and propose strategies that aim at preventing AKI after trauma.

*RECENT FINDINGS:*

AKI in trauma patients has been reported to be as frequent as 50% with an association to a prolonged length of stay and a raise in mortality. Among the specific risk factors encountered in trauma patients, hemorrhagic shock, rhabdomyolysis severity, age, and comorbidities are independently associated with AKI occurrence. Resuscitation with balanced solutes seems to have beneficial effects on renal outcome compared with NaCl 0.9%, particularly in the context of rhabdomyolysis. However, randomized clinical studies are needed to confirm this signal. Abdominal compartment syndrome (ACS) is rare but has to be diagnosed to initiate a dedicated therapy.

*SUMMARY:*

The high incidence of AKI in trauma patients should lead to early identification of those at risk of AKI to establish a resuscitation strategy that aims at preventing AKI.

**08. WSES consensus conference guidelines: monitoring and management of severe adult traumatic brain injury patients with polytrauma in the first 24 hours.** Picetti E, et al. *World J Emerg Surg.* 2019 Nov 29;14:53. doi: 10.1186/s13017-019-0270-1. eCollection 2019.

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The acute phase management of patients with severe traumatic brain injury (TBI) and polytrauma represents a major challenge. Guidelines for the care of these complex patients are lacking, and worldwide variability in clinical practice has been documented in recent studies. Consequently, the World Society of Emergency Surgery (WSES) decided to organize an international consensus conference regarding the monitoring and management of severe adult TBI polytrauma patients during the first 24 hours after injury. A modified Delphi approach was adopted, with an agreement cut-off of 70%. Forty experts in this field (emergency surgeons, neurosurgeons, and intensivists) participated in the online consensus process. Sixteen recommendations were generated, with the aim of promoting rational care in this difficult setting.

**09. Pre-Clinical Testing of Therapies for Traumatic Brain Injury.** DeWitt DS, et al. *J Neurotrauma.* 2018 Dec 1;35(23):2737-2754. doi: 10.1089/neu.2018.5778. Epub 2018 Aug 30.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29756522>

Despite the large number of promising neuroprotective agents identified in experimental traumatic brain injury (TBI) studies, none has yet shown meaningful improvements in long-term outcome in clinical trials. To develop recommendations and guidelines for pre-clinical testing of pharmacological or biological therapies for TBI, the Moody Project for Translational Traumatic Brain Injury Research hosted a symposium attended by investigators with extensive experience in pre-clinical TBI testing. The

symposium participants discussed issues related to pre-clinical TBI testing including experimental models, therapy and outcome selection, study design, data analysis, and dissemination. Consensus recommendations included the creation of a manual of standard operating procedures with sufficiently detailed descriptions of modeling and outcome measurement procedures to permit replication. The importance of the selection of clinically relevant outcome variables, especially related to behavior testing, was noted. Considering the heterogeneous nature of human TBI, evidence of therapeutic efficacy in multiple, diverse (e.g., diffuse vs. focused) rodent models and a species with a gyrencephalic brain prior to clinical testing was encouraged. Basing drug doses, times, and routes of administration on pharmacokinetic and pharmacodynamic data in the test species was recommended. Symposium participants agreed that the publication of negative results would reduce costly and unnecessary duplication of unsuccessful experiments. Although some of the recommendations are more relevant to multi-center, multi-investigator collaborations, most are applicable to pre-clinical therapy testing in general. The goal of these consensus guidelines is to increase the likelihood that therapies that improve outcomes in pre-clinical studies will also improve outcomes in TBI patients.

**10. Standard of care, controversies, and innovations in the medical treatment of severe traumatic brain injury.** Scerrati A, et al. *J Neurosurg Sci.* 2018 Oct;62(5):574-583. doi: 10.23736/S0390-5616.18.04462-4. Epub 2018 Apr 18.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29671294>

Severe traumatic brain injury (STBI) is characterized by a primary injury which cannot be reversed and a secondary injury that can be prevented or reversed. Management of STBI patients in intensive care mainly aims at preventing the secondary injury. Treatment aims to: reducing ICP pressure (that can result in an ischemic insult); avoiding hypotension, hyperthermia, or hypoxemia; maintaining a normal electrolytes homeostasis; treating the autonomic dysfunction syndrome, coagulopathies, acute kidney injury and maintaining an adequate nutrition. Many treatment protocols are already well established, while many others are still debated. Moreover, new frontiers in STBI management are represented by the neurovascular regeneration and neurorestoration, which are showing very promising results even if most of them still need a clinical validation. In this paper we review standard of care, controversies and innovations in the medical treatment of STBI.

**11. Pathophysiology and Management of Intracranial Hypertension and Tissue Brain Hypoxia After Severe Traumatic Brain Injury: An Integrative Approach.** Godoy DA, et al. *Neurosurg Clin N Am.* 2018 Apr;29(2):195-212. doi: 10.1016/j.nec.2017.12.001.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29502711>

Monitoring intracranial pressure in comatose patients with severe traumatic brain injury (TBI) is considered necessary by most experts. Acute intracranial hypertension (IHT), when severe and sustained, is a life-threatening complication that demands emergency treatment. Yet, secondary anoxic-ischemic injury after brain trauma can occur in the absence of IHT. In such cases, adding other monitoring modalities can alert clinicians when the patient is in a state of energy failure. This article reviews the mechanisms, diagnosis, and treatment of IHT and brain hypoxia after TBI, emphasizing the need to develop a physiologically integrative approach to the management of these complex situations.

**12. Management of severe traumatic brain injury (first 24hours).** Geeraerts T, et al.; French Society of Anaesthesia; Intensive Care Medicine; in partnership with Association de neuro-anesthésie-réanimation de langue française (Anarlf); French Society of Emergency Medicine (Société Française de Médecine d'urgence (SFMU); Société française de neurochirurgie (SFN); Groupe francophone de réanimation et

d'urgences pédiatriques (GFRUP); Association des anesthésistes-réanimateurs pédiatriques d'expression française (Adarpef). *Anaesth Crit Care Pain Med*. 2018 Apr;37(2):171-186. doi: 10.1016/j.accpm.2017.12.001. Epub 2017 Dec 27.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/29288841>

The latest French Guidelines for the management in the first 24 hours of patients with severe traumatic brain injury (TBI) were published in 1998. Due to recent changes (intracerebral monitoring, cerebral perfusion pressure management, treatment of raised intracranial pressure), an update was required. Our objective has been to specify the significant developments since 1998. These guidelines were conducted by a group of experts for the French Society of Anesthesia and Intensive Care Medicine (Société française d'anesthésie et de réanimation [SFAR]) in partnership with the Association de neuro-anesthésie-réanimation de langue française (ANARLF), The French Society of Emergency Medicine (Société française de médecine d'urgence (SFMU)), the Société française de neurochirurgie (SFN), the Groupe francophone de réanimation et d'urgences pédiatriques (GFRUP) and the Association des anesthésistes-réanimateurs pédiatriques d'expression française (ADARPEF). The method used to elaborate these guidelines was the Grade<sup>®</sup> method. After two Delphi rounds, 32 recommendations were formally developed by the experts focusing on the evaluation the initial severity of traumatic brain injury, the modalities of prehospital management, imaging strategies, indications for neurosurgical interventions, sedation and analgesia, indications and modalities of cerebral monitoring, medical management of raised intracranial pressure, management of multiple trauma with severe traumatic brain injury, detection and prevention of post-traumatic epilepsy, biological homeostasis (osmolarity, glycaemia, adrenal axis) and paediatric specificities.

**13. Severe traumatic brain injury: targeted management in the intensive care unit.** Stocchetti N, et al. *Lancet Neurol*. 2017 Jun;16(6):452-464. doi: 10.1016/S1474-4422(17)30118-7.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/28504109>

Severe traumatic brain injury (TBI) is currently managed in the intensive care unit with a combined medical-surgical approach. Treatment aims to prevent additional brain damage and to optimise conditions for brain recovery. TBI is typically considered and treated as one pathological entity, although in fact it is a syndrome comprising a range of lesions that can require different therapies and physiological goals. Owing to advances in monitoring and imaging, there is now the potential to identify specific mechanisms of brain damage and to better target treatment to individuals or subsets of patients. Targeted treatment is especially relevant for elderly people-who now represent an increasing proportion of patients with TBI-as preinjury comorbidities and their therapies demand tailored management strategies. Progress in monitoring and in understanding pathophysiological mechanisms of TBI could change current management in the intensive care unit, enabling targeted interventions that could ultimately improve outcomes.

**14. Critical care management of traumatic brain injury.** Menon DK, Ercole A. *Handb Clin Neurol*. 2017;140:239-274. doi: 10.1016/B978-0-444-63600-3.00014-3.

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Traumatic brain injury (TBI) is a growing global problem, which is responsible for a substantial burden of disability and death, and which generates substantial healthcare costs. High-quality intensive care can save lives and improve the quality of outcome. TBI is extremely heterogeneous in terms of clinical presentation, pathophysiology, and outcome. Current approaches to the critical care management of TBI are not underpinned by high-quality evidence, and many of the current therapies in use have not

shown benefit in randomized control trials. However, observational studies have informed the development of authoritative international guidelines, and the use of multimodality monitoring may facilitate rational approaches to optimizing acute physiology, allowing clinicians to optimize the balance between benefit and risk from these interventions in individual patients. Such approaches, along with the emerging impact of advanced neuroimaging, genomics, and protein biomarkers, could lead to the development of precision medicine approaches to the intensive care management of TBI.

**15. Critical Care Management of the Patient with Traumatic Brain Injury.** Reddy GD, et al. *Semin Neurol.* 2016 Dec;36(6):570-576. Epub 2016 Dec 1.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/27907961>

The critical care management of patients with traumatic brain injury is complex. The primary goal is to minimize the effects of secondary injury that would otherwise serve to further worsen neurologic function. This requires an understanding of the abnormal brain physiology that is found in these patients. In this article the authors discuss this physiology and describe suggested treatment strategies for these patients based on evidence-based guidelines.

**16. A State-of-the-Science Overview of Randomized Controlled Trials Evaluating Acute Management of Moderate-to-Severe Traumatic Brain Injury.** Bragge P, et al. *J Neurotrauma.* 2016 Aug 15;33(16):1461-78. doi: 10.1089/neu.2015.4233. Epub 2016 Mar 18.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/26711675>

Moderate-to-severe traumatic brain injury (TBI) remains a major global challenge, with rising incidence, unchanging mortality and lifelong impairments. State-of-the-science reviews are important for research planning and clinical decision support. This review aimed to identify randomized controlled trials (RCTs) evaluating interventions for acute management of moderate/severe TBI, synthesize key RCT characteristics and findings, and determine their implications on clinical practice and future research. RCTs were identified through comprehensive database and other searches. Key characteristics, outcomes, risk of bias, and analysis approach were extracted. Data were narratively synthesized, with a focus on robust (multi-center, low risk of bias,  $n > 100$ ) RCTs, and three-dimensional graphical figures also were used to explore relationships between RCT characteristics and findings. A total of 207 RCTs were identified. The 191 completed RCTs enrolled 35,340 participants (median, 66). Most (72%) were single center and enrolled less than 100 participants (69%). There were 26 robust RCTs across 18 different interventions. For 74% of 392 comparisons across all included RCTs, there was no significant difference between groups. Positive findings were broadly distributed with respect to RCT characteristics. Less than one-third of RCTs demonstrated low risk of bias for random sequence generation or allocation concealment, less than one-quarter used covariate adjustment, and only 7% employed an ordinal analysis approach. Considerable investment of resources in producing 191 completed RCTs for acute TBI management has resulted in very little translatable evidence. This may result from broad distribution of research effort, small samples, preponderance of single-center RCTs, and methodological shortcomings. More sophisticated RCT design, large multi-center RCTs in priority areas, increased focus on pre-clinical research, and alternatives to RCTs, such as comparative effectiveness research and precision medicine, are needed to fully realize the potential of acute TBI research to benefit patients.

**17. Extracorporeal membrane oxygenation for adult respiratory distress syndrome in trauma patients: A case series and systematic literature review.** Robba C, et al. *J Trauma Acute Care Surg.* 2017 Jan;82(1):165-173. doi: 10.1097/TA.0000000000001276.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/27779577>

**BACKGROUND:**

Venovenous extracorporeal membrane oxygenation (vv-ECMO) is an established salvage therapy for severe respiratory failure, and may provide an alternative form of treatment for trauma-induced adult respiratory distress syndrome (ARDS) when conventional treatments have failed. The need for systemic anticoagulation is a relative contraindication for patients with bleeding risks, especially in multitraumatic injury.

**METHODS:**

We describe a case series of four trauma patients with ARDS who were managed with ECMO admitted to the neuro critical care unit at Addenbrooke's Hospital, Cambridge (UK), from January 2000 to January 2016. We performed a systematic review of the available literature to investigate the safety and efficacy of vv-ECMO in posttraumatic ARDS, focusing on the use of different anticoagulation strategies and risk of bleeding on patients with multiple injuries.

**RESULTS:**

Thirty-one patients were included. A heparin bolus was given in 16 cases. Eleven patients developed complications during treatment with ECMO with three cases of major bleeding. In all documented cases of bleeding a bolus and infusion of heparin was administered, aiming for an activated clotting time (ACT) target longer than 150 seconds. Two patients treated with heparin-free ECMO developed thromboembolic complications. Four patients died, and death was never directly or indirectly related to use of ECMO.

**CONCLUSION:**

vv-ECMO can be lifesaving in respiratory failure. Our experience and our literature review suggest that vv-ECMO should be considered as a rescue treatment for the management of severe hypoxemic respiratory failure secondary to ARDS in trauma patients. For patients with a high risk of bleeding, the use of ECMO with no initial anticoagulation could be considered a valid option. For patients with a moderate risk of bleeding, use of a heparin infusion keeping an ACT target shorter than 150 seconds can be appropriate.

**18. Strategies for ventilation in acute, severe lung injury after combat trauma.** Brogden TG, et al. J R Army Med Corps. 2015 Mar;161(1):14-21. doi: 10.1136/jramc-2013-000159. Epub 2013 Nov 12.

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Post-traumatic Acute Respiratory Distress Syndrome (ARDS) continues to be a major critical care challenge with a high associated mortality and extensive morbidity for those who survive. This paper explores the evolution in recognition and management of this condition and makes some recommendations for treatment of post-combat ARDS for military practitioners. It is aimed at the generalist in disciplines other than critical care, but will also be of interest to intensivists.

**19. Enteral versus parenteral nutrition and enteral versus a combination of enteral and parenteral nutrition for adults in the intensive care unit.** Lewis SR, et al. Cochrane Database Syst Rev. 2018 Jun 8;6:CD012276. doi: 10.1002/14651858.CD012276.pub2.

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**BACKGROUND:**

Critically ill people are at increased risk of malnutrition. Acute and chronic illness, trauma and inflammation induce stress-related catabolism, and drug-induced adverse effects may reduce appetite or increase nausea and vomiting. In addition, patient management in the intensive care unit (ICU) may

also interrupt feeding routines. Methods to deliver nutritional requirements include provision of enteral nutrition (EN), or parenteral nutrition (PN), or a combination of both (EN and PN). However, each method is problematic. This review aimed to determine the route of delivery that optimizes uptake of nutrition.

**OBJECTIVES:**

To compare the effects of enteral versus parenteral methods of nutrition, and the effects of enteral versus a combination of enteral and parenteral methods of nutrition, among critically ill adults, in terms of mortality, number of ICU-free days up to day 28, and adverse events.

**SEARCH METHODS:**

We searched CENTRAL, MEDLINE, and Embase on 3 October 2017. We searched clinical trials registries and grey literature, and hand-searched reference lists of included studies and related reviews.

**SELECTION CRITERIA:**

We included randomized controlled studies (RCTs) and quasi-randomized studies comparing EN given to adults in the ICU versus PN or versus EN and PN. We included participants that were trauma, emergency, and postsurgical patients in the ICU.

**DATA COLLECTION AND ANALYSIS:**

Two review authors independently assessed studies for inclusion, extracted data, and assessed risk of bias. We assessed the certainty of evidence with GRADE.

**CONCLUSIONS:**

We found insufficient evidence to determine whether EN is better or worse than PN, or than combined EN and PN for mortality in hospital, at 90 days and at 180 days, and on the number of ventilator-free days and adverse events. We found fewer deaths at 30 days when studies gave combined EN and PN, and reduced sepsis for EN rather than PN. We found no studies that reported number of ICU-free days up to day 28. Certainty of the evidence for all outcomes is either low or very low. The 11 studies awaiting classification may alter the conclusions of the review once assessed.

**20. Controversies in Critical Care Nutrition Support.** Patel JJ, Codner P. Crit Care Clin. 2016 Apr;32(2):173-89. doi: 10.1016/j.ccc.2015.11.002. Epub 2016 Feb 4.

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Critical illness predisposes individuals to highly variable metabolic and immune responses, leading to muscle mass loss, impaired healing, immobility, and susceptibility to infections and cognitive impairment. Recommendations for nutrition in critically ill patients are supported by observational studies, small randomized controlled trials, and mechanistic data. There is no standardization of nutritional therapy in critically ill patients and controversies in the type, quantity, and timing of nutrition support persist. This article reviews the physiologic basis for nutrition support, the concept of nutritional risk, and various controversies in critical care nutrition support.

**21. Palliative care in the trauma ICU.** O'Connell K, Maier R. Curr Opin Crit Care. 2016 Dec;22(6):584-590.

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**PURPOSE OF REVIEW:**

The benefits of palliative care for critically ill patients are well recognized, yet acceptance into surgical culture is lagging. With the increasing proportion of geriatric trauma patients, integration of palliative medicine within daily intensive care services to facilitate goal-concordant care is imperative.

**RECENT FINDINGS:**

Misconceptions of palliative medicine as it applies to trauma patients linger among trauma surgeons and many continue to practice without routine consultation of a palliative care service. Aggressive end-

of-life care does not correlate with an improved family perception of medical care received near death. Additionally, elderly patients near the end of life often prefer palliative treatments over life-extending therapy, and their treatment preferences are often not achieved. A new geriatric-specific prognosis calculator estimates the risk of mortality after trauma, which is useful in starting goals of care discussions with older patients and their families.

**SUMMARY:**

Shifting our quality focus from 30-day mortality rates to measurements of symptom control and achievement of patient treatment preferences will prioritize patient beneficence and autonomy. Ownership of surgical palliative care as a service provided by acute care surgeons will ensure that our patients with incurable injury and illness will receive optimal patient-centered care.

**22. Care of the Critically Ill Burn Patient. An Overview from the Perspective of Optimizing**

**Palliative Care.** Ray DE, et al.; Improving Palliative Care in the Intensive Care Unit (IPAL-ICU) Project Advisory Board. *Ann Am Thorac Soc.* 2017 Jul;14(7):1094-1102. doi: 10.1513/AnnalsATS.201607-577PS. PDF: No Free PDF available

URL: <https://www.ncbi.nlm.nih.gov/pubmed/28590164>

Burn specialists have long recognized the need for and have role modeled a comprehensive approach incorporating relief of distress as part of care during critical illness. More recently, palliative care specialists have become part of the healthcare team in many U.S. hospitals, especially larger academic institutions that are more likely to have designated burn centers. No current literature describes the intersection of palliative care and burn care or integration of primary and specialist palliative care in this unique context. This Perspective gives an overview of burn care; focuses on pain and other symptoms in burn intensive care unit settings; addresses special needs of critically ill burned patients, their families, and clinicians for high-quality palliative care; and highlights potential benefits of integrating primary and specialist palliative care in burn critical care. MEDLINE and the Cumulative Index to Nursing and Allied Health Literature were searched, and an e-mail survey was used to obtain information from U.S. Burn Fellowship Program directors about palliative medicine training. The Improving Palliative Care in the Intensive Care Unit Project Advisory Board synthesized published evidence with their own research and clinical experience in preparing this article. Mortality and severe morbidity for critically ill burned patients remains high. American Burn Association guidelines lay the foundation for a robust system of palliative care delivery, embedding palliative care principles and processes in intensive care by burn providers. Understanding basic burn care, challenges for symptom management and communication, and the culture of the particular burn unit, can optimize quality and integration of primary and specialist palliative care in this distinctive setting.

**23. Fibrinolysis and antifibrinolytic treatment in the trauma patient.** Gall LS, Davenport RA. *Curr Opin Anaesthesiol.* 2018 Apr;31(2):227-233. doi: 10.1097/ACO.0000000000000561.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/29324486>

**PURPOSE OF REVIEW:**

The role of antifibrinolytics in trauma haemorrhage and early coagulopathy remains controversial with respect to patient selection, dosage, timing of treatment, and risk of thrombotic complications. This review presents our current understanding of the mechanisms of fibrinolysis in trauma, diagnostic evaluation, and the evidence base for treatment.

**RECENT FINDINGS:**

Excessive fibrinolysis following severe injury is a major component of acute traumatic coagulopathy and contributes to the high mortality from trauma haemorrhage. The protein C pathway, endothelial dysfunction, platelet activity, shock, and tissue injury are key to the development of hyper fibrinolysis

in trauma. D-dimer and viscoelastic haemostatic assays (rotational thromboelastometry, TEG) remain the best available diagnostic modalities but have a number of limitations compared with plasma biomarkers of fibrinolytic activation, for example, plasmin- $\alpha$ 2-antiplasmin complex. Current evidence supports the continued empiric use of tranexamic acid in major trauma haemorrhage.

**SUMMARY:**

Improving the outcomes for bleeding trauma patients requires a deeper understanding of the mechanisms driving hyperfibrinolysis and the subsequent switch toward a prothrombotic state. Discovering the interplay between platelet activity, fibrinogen utilization, the immune response, and the fibrinolytic system may lead to development of novel therapeutics.

**24. Early haemorrhage control and management of trauma-induced coagulopathy: the importance of goal-directed therapy.** Stensballe J, et al. *Curr Opin Crit Care*. 2017 Dec;23(6):503-510. doi:

10.1097/MCC.0000000000000466.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/29059118>

**PURPOSE OF REVIEW:**

The aim of this study was to discuss the recent developments in trauma-induced coagulopathy and the evolution of goal-directed therapy.

**RECENT FINDINGS:**

Mortality from major trauma continues to be a worldwide problem, and massive haemorrhage remains a major cause in 40% of potentially preventable trauma deaths. Development of trauma-induced coagulopathy challenges 25-35% of the patients further increasing trauma mortality. The pathophysiology of coagulopathy in trauma reflects at least two distinct mechanisms: Acute traumatic coagulopathy, consisting of endogenous heparinization, activation of the protein C pathway, hyperfibrinolysis and platelet dysfunction, and resuscitation associated coagulopathy. Clear fluid resuscitation with crystalloids and colloids is associated with dilutional coagulopathy and poor outcome in trauma. Haemostatic resuscitation is now the backbone of trauma resuscitation using a ratio-driven strategy aiming at 1:1:1 of red blood cells, plasma and platelets while applying goal-directed therapy early and repeatedly to control trauma-induced coagulopathy.

**SUMMARY:**

Trauma resuscitation should focus on early goal-directed therapy with use of viscoelastic haemostatic assays while initially applying a ratio 1:1:1 driven transfusion therapy (with red blood cells, plasma and platelets) in order to sustain normal haemostasis and control further bleeding.

**25. Acute traumatic coagulopathy: pathophysiology and resuscitation.** Simmons JW, Powell MF. *Br J Anaesth*. 2016 Dec;117(suppl 3):iii31-iii43.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/27940454>

Acute Traumatic Coagulopathy occurs immediately after massive trauma when shock, hypoperfusion, and vascular damage are present. Mechanisms for this acute coagulopathy include activation of protein C, endothelial glycocalyx disruption, depletion of fibrinogen, and platelet dysfunction. Hypothermia and acidaemia amplify the endogenous coagulopathy and often accompany trauma. These multifactorial processes lead to decreased clot strength, autoheparinization, and hyperfibrinolysis. Furthermore, the effects of aggressive crystalloid administration, haemodilution from inappropriate blood product transfusion, and prolonged surgical times may worsen clinical outcomes.

We review normal coagulation using the cell-based model of haemostasis and the pathophysiology of acute traumatic coagulopathy. Developed trauma systems reduce mortality, highlighting critical goals for the trauma patient in different phases of care. Once patients reach a trauma hospital, certain

triggers reliably indicate when they require massive transfusion and specialized trauma care. These triggers include base deficit, international normalized ratio (INR), systolic arterial pressure, haemoglobin concentration, and temperature. Early identification for massive transfusion is critically important, as exsanguination in the first few hours of trauma is a leading cause of death. To combat derangements caused by massive haemorrhage, damage control resuscitation is a technique that addresses each antagonist to normal haemostasis. Components of damage control resuscitation include damage control surgery, permissive hypotension, limited crystalloid administration, haemostatic resuscitation, and correction of hyperfibrinolysis.

**26. Haemostatic resuscitation in trauma: the next generation.** Stensballe J, et al. *Curr Opin Crit Care*. 2016 Dec;22(6):591-597.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/27811561>

*PURPOSE OF REVIEW:*

To discuss the recent developments in and evolution of next generation haemostatic resuscitation in bleeding trauma.

*RECENT FINDINGS:*

Mortality from major trauma is a worldwide problem, and massive haemorrhage remains a major cause of potentially preventable deaths. Development of coagulopathy further increases trauma mortality emphasizing that coagulopathy is a key target in the phase of bleeding. The pathophysiology of coagulopathy in trauma reflects at least three distinct mechanisms that may be present isolated or coexist: acute traumatic coagulopathy, coagulopathy associated with the lethal triad, and consumptive coagulopathy. The concepts of 'damage control surgery' and 'damage control resuscitation' have been developed to ensure early control of bleeding and coagulopathy to improve outcome in bleeding trauma. Haemostatic resuscitation aims at controlling coagulopathy and consists of a ratio driven strategy aiming at 1 : 1 : 1, using tranexamic acid according to CRASH-2, and applying haemostatic monitoring enabling a switch to a goal-directed approach when bleeding slows. Haemostatic resuscitation is the mainstay of trauma resuscitation and is associated with improved survival.

*SUMMARY:*

The next generation of haemostatic resuscitation aims at applying a ratio 1 : 1 : 1 driven strategy while using antifibrinolytics, haemostatic monitoring and avoiding critical fibrinogen deficiency by substitution.

**27. Targeted Coagulation Management in Severe Trauma: The Controversies and the Evidence.**

Winearls J, et al. *Anesth Analg*. 2016 Oct;123(4):910-24. doi: 10.1213/ANE.0000000000001516.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/27636575>

Hemorrhage in the setting of severe trauma is a leading cause of death worldwide. The pathophysiology of hemorrhage and coagulopathy in severe trauma is complex and remains poorly understood. Most clinicians currently treating trauma patients acknowledge the presence of a coagulopathy unique to trauma patients-trauma-induced coagulopathy (TIC)-independently associated with increased mortality. The complexity and incomplete understanding of TIC has resulted in significant controversy regarding optimum management. Although the majority of trauma centers utilize fixed-ratio massive transfusion protocols in severe traumatic hemorrhage, a widely accepted "ideal" transfusion ratio of blood to blood products remains elusive. The recent use of viscoelastic hemostatic assays (VHAs) to guide blood product replacement has further provoked debate as to the optimum transfusion strategy. The use of VHA to quantify the functional contributions of individual components of the coagulation system may permit targeted treatment of TIC but remains controversial and is unlikely

to demonstrate a mortality benefit in light of the heterogeneity of the trauma population. Thus, VHA-guided algorithms as an alternative to fixed product ratios in trauma are not universally accepted, and a hybrid strategy starting with fixed-ratio transfusion and incorporating VHA data as they become available is favored by some institutions. We review the current evidence for the management of coagulopathy in trauma, the rationale behind the use of targeted and fixed-ratio approaches and explore future directions.

**28. Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) for trauma induced coagulopathy in adult trauma patients with bleeding.** Hunt H, et al. Cochrane Database Syst Rev. 2015 Feb 16;(2):CD010438. doi: 10.1002/14651858.CD010438.pub2.

PDF: No free PDF available

URL: <https://www.ncbi.nlm.nih.gov/pubmed/25686465>

**BACKGROUND:**

Trauma-induced coagulopathy (TIC) is a disorder of the blood clotting process that occurs soon after trauma injury. A diagnosis of TIC on admission is associated with increased mortality rates, increased burdens of transfusion, greater risks of complications and longer stays in critical care. Current diagnostic testing follows local hospital processes and normally involves conventional coagulation tests including prothrombin time ratio/international normalized ratio (PTR/INR), activated partial prothrombin time and full blood count. In some centres, thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are standard tests, but in the UK they are more commonly used in research settings.

**OBJECTIVES:**

The objective was to determine the diagnostic accuracy of thromboelastography (TEG) and rotational thromboelastometry (ROTEM) for TIC in adult trauma patients with bleeding, using a reference standard of prothrombin time ratio and/or the international normalized ratio.

**SEARCH METHODS:**

We ran the search on 4 March 2013. Searches ran from 1970 to current. We searched The Cochrane Library, MEDLINE (OvidSP), EMBASE Classic and EMBASE, eleven other databases, the web, and clinical trials registers. The Cochrane Injuries Group's specialised register was not searched for this review as it does not contain diagnostic test accuracy studies. We also screened reference lists, conducted forward citation searches and contacted authors.

**SELECTION CRITERIA:**

We included all cross-sectional studies investigating the diagnostic test accuracy of TEG and ROTEM in patients with clinically suspected TIC, as well as case-control studies. Participants were adult trauma patients in both military and civilian settings. TIC was defined as a PTR/INR reading of 1.2 or greater, or 1.5 or greater.

**DATA COLLECTION AND ANALYSIS:**

We piloted and performed all review stages in duplicate, including quality assessment using the QUADAS-2 tool, adhering to guidance in the Cochrane Handbook for Diagnostic Test Accuracy Reviews. We analysed sensitivity and specificity of included studies narratively as there were insufficient studies to perform a meta-analysis.

**AUTHORS' CONCLUSIONS:**

We found no evidence on the accuracy of TEG and very little evidence on the accuracy of ROTEM. The value of accuracy estimates are considerably undermined by the small number of included studies, and concerns about risk of bias relating to the index test and the reference standard. We are unable to offer advice on the use of global measures of haemostatic function for trauma based on the evidence on test accuracy identified in this systematic review. This evidence strongly suggests that at present these tests

should only be used for research. We consider more thoroughly what this research could be in the Discussion section.

**29. Hemodynamic monitoring of the injured patient: From central venous pressure to focused echocardiography.** Strumwasser A, et al.; American Association for the Surgery of Trauma Committee on Critical Care. J Trauma Acute Care Surg. 2016 Mar;80(3):499-510. doi: 10.1097/TA.0000000000000938.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/26713977>

No abstract

**30. Non-invasive hemodynamic monitoring in trauma patients.** Kuster M, et al. World J Emerg Surg. 2015 Mar 8;10:11. doi: 10.1186/s13017-015-0002-0. eCollection 2015.a

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/25774210>

*BACKGROUND:*

The assessment of hemodynamic status is a crucial task in the initial evaluation of trauma patients. However, blood pressure and heart rate are often misleading, as multiple variables may impact these conventional parameters. More reliable methods such as pulmonary artery thermodilution for cardiac output measuring would be necessary, but its applicability in the Emergency Department is questionable due to their invasive nature. Non-invasive cardiac output monitoring devices may be a feasible alternative.

*METHODS:*

A systematic literature review was conducted. Only studies that explicitly investigated non-invasive hemodynamic monitoring devices in trauma patients were considered.

*RESULTS:*

A total of 7 studies were identified as suitable and were included into this review. These studies evaluated in a total of 1,197 trauma patients the accuracy of non-invasive hemodynamic monitoring devices by comparing measurements to pulmonary artery thermodilution, which is the gold standard for cardiac output measuring. The correlation coefficients  $r$  between the two methods ranged from 0.79 to 0.92. Bias and precision analysis ranged from  $-0.02 \pm 0.78$  l/min/m<sup>2</sup> to  $-0.14 \pm 0.73$  l/min/m<sup>2</sup>. Additionally, data on practicality, limitations and clinical impact of the devices were collected.

*CONCLUSION:*

The accuracy of non-invasive cardiac output monitoring devices in trauma patients is broadly satisfactory. As the devices can be applied very early in the shock room or even preclinically, hemodynamic shock may be recognized much earlier and therapeutic interventions could be applied more rapidly and more adequately. The devices can be used in the daily routine of a busy ED, as they are non-invasive and easy to master.

## **GUIDELINES**

**31. Monitoring modalities and assessment of fluid status: A practice management guideline from the Eastern Association for the Surgery of Trauma.** Plurad DS, et al. J Trauma Acute Care Surg. 2018 Jan;84(1):37-49. doi: 10.1097/TA.0000000000001719.

PDF: [Read PDF Here](#)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/29019796>

**BACKGROUND:**

Fluid administration in critically ill surgical patients must be closely monitored to avoid complications. Resuscitation guided by invasive methods are not consistently associated with improved outcomes. As such, there has been increased use of focused ultrasound and Arterial Pulse Waveform Analysis (APWA) to monitor and aid resuscitation. An assessment of these methods using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework is presented.

**METHODS:**

A subsection of the Surgical Critical Care Task Force of the Practice Management Guideline Committee of EAST conducted two systematic reviews to address the use of focused ultrasound and APWA in surgical patients being evaluated for shock. Six population, intervention, comparator, and outcome (PICO) questions were generated. Critical outcomes were prediction of fluid responsiveness, reductions in organ failures or complications and mortality. Forest plots were generated for summary data and GRADE methodology was used to assess for quality of the evidence. Reviews are registered in PROSPERO, the International Prospective Register of Systematic Reviews (42015032402 and 42015032530).

**RESULTS:**

Twelve focused ultrasound studies and 20 APWA investigations met inclusion criteria. The appropriateness of focused ultrasound or APWA-based protocols to predict fluid responsiveness varied widely by study groups. Results were mixed in the one focused ultrasound study and 9 APWA studies addressing reductions in organ failures or complications. There was no mortality advantage of either modality versus standard care. Quality of the evidence was considered very low to low across all PICO questions.

**CONCLUSION:**

Focused ultrasound and APWA compare favorably to standard methods of evaluation but only in specific clinical settings. Therefore, conditional recommendations are made for the use of these modalities in surgical patients being evaluated for shock.

**MILITARY PRIORITIES**

**32. The Top 10 Research and Development priorities for battlefield surgical care**

Martin, M. et al. 2019 Journal of Trauma and Acute Care Surgery.

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URL: <https://www.ncbi.nlm.nih.gov/pubmed/31246901>