Short Review of Journal Abstracts for Casualty Care 2020–2022

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This brief collection of articles is based on the review conducted since 2008 by Tactical Combat Casualty Care (CoTCCC), considered relevant to the tactical, operational, and prehospital care communities. This publication known as "Journal watch" can be accessed through the link www.deployed medicine.com.

In this compilation, you will find important publications that refer to topics that are dealt with both in training and in daily practice. The focus is to present the most recent evidence from the years 2020 to 2022, whose objective is none other than to serve as a refresher for anyone who faces patients in austere or "unconventional" environments, although many of them can serve as guidance in prehospital and/or civilian hospital settings.

The evidence gathers from the importance of the correct indication of the tourniquet; doses, routes of administration, and results of the administration of tranexamic acid; complications from correct measurement and placement of the nasopharyngeal airway; the importance of early administration of whole blood and blood products to increase survival; the technique and correct location of needle thoracostomy or the importance of preventing hypothermia and the devices to be used for prevent it, among others.

I hope, therefore, that this work will help and improve both the training and the care of our wounded warriors and patients.

Evidence-based principles of time, triage and treatment: refining the initial medical response to massive casualty incidents

Stacy A. Shackelford, MD, Michael A. Remley, NRP, Sean Keenan, MD, Russ S. Kotwal, MD, MPH, Jay B. Baker, MD, Jennifer Gurney, MD, Stephen Rush, MD, and Paul Friedrichs, MD

J Trauma Acute Care Surg. 2022;93(2S Suppl 1): S160–S164.

Background: The overall approach to massive casualty triage has changed little in the past 200 years. As the military and civilian organizations prepare for the possibility of future large-scale combat operations, terrorist attacks and natural disasters, potentially involving hundreds or even thousands of casualties, a modified approach is needed to conduct effective triage, initiate treatment, and save as many lives as possible. **Methods:** Military experience and review of analyses from the Department of Defense Trauma Registry are combined to introduce new concepts in triage and initial casualty management. **Results:** The classification of the scale of massive casualty (MASCAL) incidents, timeline of life-saving interventions, immediate first pass actions prior to formal triage decisions during the first hour after injury, simplification of triage decisions, and the understanding that ultra-MASCAL will primarily require casualty movement and survival needs with few prehospital life-saving medical interventions are discussed. **Conclusion:** Self aid, bystander, and first responder interventions are paramount and should be trained and planned extensively. Military and disaster planning should not only train these concepts, but should seek innovations to extend the timelines of effectiveness and to deliver novel capabilities within the timelines to the greatest extent possible. (*J Trauma Acute Care Surg.* 2022;93(2S Suppl): S160–S164.)

Prehospital tourniquets placed on limbs without major vascular injuries, has the pendulum swung too far?

Timothy Legare, MD, Rebecca Schroll, MD, John P Hunt, MD, Juan Duchesne, MD, Alan Marr, MD, Jonathan Schoen, MD, MPH, Patrick Greiffenstein, MD, Lance Stuke, MD, Alison Smith, MD, PhD

Am Surg. 2022; 88(9):2103–2107.

Background: Combat applications of tourniquets for extremity trauma have led to increased civilian prehospital tourniquet use. Studies have demonstrated that appropriate prehospital tourniquet application can decrease the incidence of arrival in shock without increasing limb complications. The aim of this study was to examine outcomes of prehospital tourniquet placement without definitive vascular injury. **Methods:** Retrospective review was performed of a prospectively maintained database by the American Association for the Surgery of Trauma from 29 trauma centers. Patients in this subset analysis did not have a significant vascular injury as determined by imaging or intraoperatively. Patients who received prehospital tourniquets (PHTQ) were compared to patients without prehospital tourniquets (No-PHTQ). Outcomes were amputation rates, nerve palsy, compartment syndrome, and in-hospital mortality. **Results:** A total of 622 patients had no major vascular injury. The incidence of patients without major vascular injury was higher in the PHTQ group (n = 585/962, 60.8 vs n = 37/88, 42.0%, $p < .001$). Cohorts were similar in age, gender, penetrating mechanism, injury severity scores (ISS), abbreviated injury score (AIS), and mortality ($p > .05$). Amputation rates were 8.3% (n = 49/585) in the PHTQ group compared to 0% (n = 0/37) in the No-PHTQ group. Amputation rates were higher in PHTQ than No-PHTQ with similar ISS and AIS ($p = .96$, $p = .59$). The incidence of nerve palsy and compartment syndrome was not different ($p > .05$). **Conclusions:** This study showed a significant amount of prehospital tourniquets are being placed on patients without vascular injuries. Further studies are needed to elucidate the appropriateness of prehospital tourniquets, including targeted education of tourniquet placement.

Use of haemostatic devices for the control of junctional and abdominal traumatic haemorrhage: a systematic review

Rhiannon Humphries, David N. Naumann, Zubair Ahmed

Trauma Care. 2022;2(1):23–34.

Abstract: Catastrophic haemorrhage accounts for up to 40% of global trauma related mortality and is the leading cause of preventable deaths on the battlefield. Controlling abdominal and junctional haemorrhage is challenging, especially in the pre-hospital

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setting or 'under fire', yet there is no haemostatic agent that satisfies the seven characteristics of an 'ideal haemostat'. We conducted a systematic search of Embase, Medline, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Web of Science to evaluate the feasibility and efficacy of three types of haemostatic devices. Participants included any trauma patient in a pre-hospital setting, perfused human cadavers, or healthy human volunteer simulations. The haemostatic devices reviewed were REBOA, iTClamp, and four junctional tourniquets: AAJT, CRoC, JETT, and SJT. The SJT had the best user survey performance of the junctional tourniquets, and the four junctional tourniquets had an overall efficacy of 26.6–100% and an application time of 10–203 s. The iTClamp had an efficacy of 60–100% and an application time of 10–60 s. REBOA had an efficacy of 71–100% and an application time ranging from 5 min to >80 min. In civilian and military trauma patients, with the use of junctional tourniquets, iTClamp, or REBOA, mortality varied from 0–100%. All of these studies were deemed low to very low in quality; hence, the reliability of data presented in each of the studies is called into question. We conclude that despite limited data for these devices, their use in the pre-hospital environment or 'under fire' is feasible with the correct training, portable imaging, and patient selection algorithms. However, higher quality studies are required to confirm the true efficacy of these devices.

Studies on the correct length of nasopharyngeal airways in adults: a literature review

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J Spec Oper Med. 21(3):45–50.

The use of a nasopharyngeal airway (NPA) as an adjunct airway device can be critically important in emergency medicine. When placed correctly, the device can prevent upper airway obstruction. The goal of our review was to learn whether there is scientific evidence about the correct length and the insertion depth, and also possible facial landmarks, that can predict the appropriate length of the NPA. There has been no real consensus on how to measure the appropriate tube length for the NPA. Several studies have been able to demonstrate correlations between facial landmarks and body dimensions; however, we did not find any scientific evidence on this matter. The reviewed studies do not indicate evidence to support current recommended guidelines. This could potentially lead to both military and civilian emergency training programs not having the most accurate scientific information for training on anatomic structures and also not having a better overall understanding of intraoral dimensions. Emergency personnel should be taught validated scientific knowledge of NPAs so as to quickly determine the correct tube length and how to use anatomic correlations. This might require further studies on the correlations and perhaps radiographic measurements. A further approach includes adjusting the tube to its correct length according to the sufficient assessment and management of the airway problem.

Needle thoracentesis decompression: observations from postmortem computed tomography and autopsy

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J Spec Oper Med. 13(4):53–58.

Background: Needle thoracentesis decompression (NTD) is a recommended emergency treatment for tension pneumothorax. Current doctrine recognizes two suitable sites: the second intercostal space in the midclavicular line and the fourth or fifth intercostal space in the anterior axillary line. **Methods:** A review was conducted of postmortem computed tomography and autopsy results in 16 cases where NTD was performed as an emergency procedure. **Results:** In 16 cases with 23 attempted procedures, the outcome was confirmed in 17 attempts. In 7 placements, the catheter was in the pleural cavity; in 7 placements, the catheter never entered the pleural cavity; and in 3 placements, cavity penetration was verified at autopsy even though the catheter was no longer in the cavity. Success was noted in 6 of 13 anterior attempts and 4 of 4 lateral attempts, for an overall success rate of 59% (10 of 17). In the remaining 6 attempted procedures, a catheter was noted in the soft tissue on imaging; however, presence or absence of pleural cavity penetration was equivocal. All placements were attempted in the combat environment; no information is available about specifically where or by whom. **Conclusion:** NTD via a lateral approach was more successful than that via an anterior approach, although it was used in fewer cases. This supports the revisión of the Tactical Combat Casualty Care Guidelines specifying the lateral approach as an alternative to an anterior approach.

Optimal anatomical location for needle chest decompression for tension pneumothorax: a multicenter prospective cohort study

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Injury. 2020;S0020-1383(20)30888-3.

Objective: Tension pneumothorax (TP) can occur as a potentially life-threatening complication of chest trauma. Both the 2nd intercostal space in the midclavicular line (ICS2-MCL) and the 4th/5th intercostal space in the anterior axillary line (ICS 4/5-AAL) have been proposed as preferred locations for needle decompression (ND) of a TP. In the present study, we aimed to determine chest wall thickness (CWT) at ICS2-MCL and ICS4/5-AAL in normal weight-, overweight-, and obese patients, and to calculate theoretical success rates of ND for these locations based on standard catheter length. **Methods:** We performed a prospective multicenter study of a convenience sample of adult patients presenting in emergency departments (EDs) of 2 university hospitals and 6 teaching hospitals participating in the PRIDE consortium. CWT was measured bilaterally in ISC2-MCL and ISC4/5-AAL with point of care ultrasound (POCUS), and hypothetical success rates of ND were calculated for both locations based on standard equipment used for ND. **Results:** A total of 392 patients was included during a 2-week period. Mean age was 51 years (range, 18–89), 52% were male, and mean BMI was 25.5 (range, 16.3–45.0). Median CWT was 26 [IQR, 21-32] (range, 9-52) mm in ISC2-MCL, and 26 [21–33] (range, 10–78) mm in ICS4/5-AAL ($p < 0.001$). CWT in ISC2-MCL was significantly thinner than ICS4/5-AAL in overweight (BMI 25-30, $p < 0.001$) and obese (BMI >30, $p = 0.016$) subjects, but not in subjects with a normal BMI. Hypothetical failure rates for 45mm Venflon and 50mm angiocatheter were 2.5% and 0.8% for ICS2-MCL and 6.2% and 2.5% for ISC4/5-AAL ($p = 0.016$ and $p = 0.052$, respectively). **Conclusion:** In overweight and obese subjects, the chest wall is thicker in ICS 4/5-AAL than in ICS2-MCL, and theoretical chances of successful needle decompression of a tension pneumothorax are significantly higher in ICS2-MCL compared to ICS 4/5-AAL.

Paramedic understanding of tension pneumothorax and needle thoracostomy (NT) site selection

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Cureus. 2020;14(7):e27013.

Introduction: Tension pneumothorax is an immediate threat to life. Treatment in the prehospital setting is usually achieved by needle thoracostomy (NT). Prehospital personnel are taught to perform NT, frequently in the second intercostal space (ICS) at the mid-clavicular line (MCL). Previous literature has suggested that emergency physicians have difficulty identifying this anatomic location

correctly. We hypothesized that paramedics would also have difficulty accurately identifying the proper location for NT. **Methods:** A prospective, observational study was performed to assess paramedic ability to identify the location for treatment with NT. Participants were recruited during a statewide Emergency Medical Services (EMS) conference. Subjects were asked the anatomic site for NT and asked to mark the site on a shirtless male volunteer. The site was copied onto a transparent sheet lined up against predetermined points on the volunteer's chest. It was then compared against the correct location that had been identified using palpation, measuring tape, and ultrasound. **Results:** 29 paramedics participated, with 24 (83%) in practice for more than five years and 23 (79%) doing mostly or all 9-1-1 response. All subjects (100%) reported training in NT, although six (21%) had never performed a NT in the field. Nine paramedics (31%) recognized the second ICS at the MCL as the desired site for NT, with 12 (41%) specifying only the second ICS, 11 (38%) specifying second or third ICS, and six (21%) naming a different location (third, fourth, or fifth ICS). None (0%) of the 29 paramedics identified the exact second ICS MCL on the volunteer. Mean distance from the second ICS MCL was 1.37-cm (interquartile range [IQR]: 0.7-1.90) in the medial-lateral direction and 2.43-cm in the superior-inferior direction (IQR: 1.10-3.70). Overall mean distance was 3.12cm from the correct location (IQR: 1.90-4.50). Most commonly, the identified location was too inferior (93%). Allowing for a 2-cm radius from the correct position, eight (28%) approximated the correct placement. 25 (86%) were within a 5-cm radius. **Conclusion** In this study, paramedics had difficulty identifying the correct anatomic site for NT. EMS medical directors may need to rethink training or consider alternative techniques.

Intraosseous access in the resuscitation of trauma patients: a literatura review

Tyler JA, Perkins Z, De'Ath HD.

Eur J Trauma Emerg Surg. 2021;47(1):47–55.

Purpose: Intraosseous (IO) catheters continue to be recommended in trauma resuscitation. Their utility has recently been debated due to concerns regarding inadequate flow rates during blood transfusion and the potential for haemolysis. The objectives of this review was to examine the evidence for intraosseous catheters in trauma resuscitation and to highlight areas for future research. **Methods:** A PubMed and Embase search for articles published from January 1990 to August 2018 using the terms ("intra-osseous access" or "intraosseous access" or "IO access") AND trauma was performed. Original articles describing the use of an IO catheter in the resuscitation of one or more trauma patients were eligible. Animal, cadaveric studies, and those involving healthy volunteers were excluded. **Results:** Nine studies, comprising 1218 trauma patients and 1432 device insertions, were included. The insertion success rate was 95% and the incidence of complications 0.9%. Flow-rate data and evidence of haemolysis were poorly reported. **Conclusion:** Intraosseous catheters have high insertion success rates and a low incidence of complications in trauma patients. Existing evidence suggests that IO transfusion is not associated with haemolysis; however, further studies in humans are needed. There is a paucity of Flow-rate data for blood transfusion via IO catheters in this population, although much anecdotal evidence advocating their use exists.

Sternal intraosseous devices: review of the literature

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West J Emerg Med. 2021;22(3):690–695.

Introduction: The intraosseous (IO) route is one of the primary means of vascular access in critically ill and injured patients. The most common sites used are the proximal humerus, proximal tibia, and sternum. Sternal IO placement remains an often-overlooked option in emergency and prehospital medicine. Due to the conflicts in Afghanistan and Iraq, the use of sternal IOs have increased. **Methods:** The authors conducted a limited review, searching the PubMed and Google Scholar databases for "sternal IO," "sternal intraosseous," and "intraosseous," without specific date limitations. A total of 47 articles was included in this review. **Results:** Sternal IOs are currently FDA approved for ages 12 and older. Sternal IO access offers several anatomical, pharmacokinetic, hemodynamic, and logistical advantages over peripheral intravenous and other IO points of access. Sternal IO use carries many of the same risks and limitations as the humeral and tibial sites. Sternal IO gravity flow rates are sufficient for transfusing blood and resuscitation. In addition, studies demonstrated sternal IOs are safe during active CPR. **Conclusion:** The sternal IO route remains underutilized in civilian settings. When considering IO vascular access in adults or older children, medical providers should consider the sternum as the recommended IO access, particularly if the user is a novice with IO devices, increased flow rates are required, the patient has extremity trauma, or administration of a lipid soluble drug is anticipated.

Military experience in the management of pelvic fractures from OIF/OEF

Parker W, Despain RW, Bailey J, Elster E, Rodriguez CJ, Bradley M

BMJ Mil Health. 2020-001469.

Introduction: Pelvic fractures are a common occurrence in combat trauma. However, the fracture patterns and management within the most recent conflicts, i.e., Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF), have yet to be described, especially in the context of dismounted complex blast injury. Our goal was to identify the incidence, patterns of injury, and management of pelvic fractures. **Methods:** We conducted a retrospective review on all combat-injured patients who arrived at our military treatment hospital between November 2010 and November 2012. Basic demographics, Young-Burgess fracture pattern classification, and treatment strategies were examined. **Results:** Of 562 patients identified within the study time period, 14% (81 of 562) were found to have a pelvic fracture. The vast majority (85%) were secondary to an improvised explosive device. The average Injury Severity Score for patients with pelvic fracture was 31 ± 12, and 70% were classified as open. Of the 228 patients with any traumatic lower extremity amputation, 23% had pelvic fractures, while 30% of patients with bilateral above-knee amputations also sustained a pelvic fracture. The most common Young-Burgess injury pattern was anteroposterior compression (APC) (57%), followed by lateral compression (LC) (36%) and vertical shear (VS) (7%). Only 2% (nine of 562) of all patients were recorded as having pelvic binders placed in the prehospital setting. 49% of patients with pelvic fracture required procedural therapy, the most common of which was placement of a pelvic external fixator (34 of 40; 85%), followed by preperitoneal packing (16 of 40; 40%) and angioembolisation (three of 40; 0.75%). 17 (42.5%) patients required combinations of these three treatment modalities, the majority of which were a combination of external fixator and preperitoneal packing. The likelihood to need procedural therapy was impacted by injury pattern, as 72% of patients with an APC injury, 100% of patients with a VS injury, and 25% of patients with an LC injury required procedural therapy. **Conclusions:** Pelvic fractures were common concomitant injuries following blast-induced traumatic lower extremity amputations. APC was the most common pelvic fracture pattern identified. While procedural therapy was frequent, the majority of patients underwent conservative therapy. However, placement of an external fixator was the most frequently used modality. Considering angioembolisation was used in less than 1% of cases, in the forward deployed military environment, management

should focus on pelvic external fixation ± preperitoneal packing. Finally, prehospital pelvic binder application may be an area for further process improvement.

The use of tranexamic acid in Tactical Combat Casualty Care: TCCC Proposed Change 20-02

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J Spec Oper Med. 20(3):36–43.

The literature continues to provide strong support for the early use of tranexamic acid (TXA) in severely injured trauma patients. Questions persist, however, regarding the optimal medical and tactical/logistical use, timing, and dose of this medication, both from the published TXA literature and from the TCCC user community. The use of TXA has been explored outside of trauma, new dosing strategies have been pursued, and expansion of retrospective use data has grown, as well. These questions emphasize the need for a reexamination of TXA by the CoTCCC. The most significant updates to the TCCC Guidelines are (i) including significant traumatic brain injury (TBI) as an indication for TXA, (ii) changing the dosing protocol to a single 2g IV/IO administration, and (iii) recommending TXA administration via slow IV/IO push.

Case series on 2g tranexamic acid flush from the 75th Ranger Regiment casualty database

Christopher Patrick Androski, Jr, MD; William Bianchi, DO, MSc; Douglas L Robinson, DO, MS; Gregory J Zarow, PhD; Charles H Moore, MD; Travis G Deaton, MD; Brendon Drew, DO; Simon Corona Gonzalez; Ryan M Knight, MD

J Spec Oper Med. 20(4):85–91.

Early tranexamic acid (TXA) administration for resuscitation of critically injured warfighters provides a mortality benefit. The 2019 Tactical Combat Casualty Care (TCCC) recommendations of a 1g drip over 10 minutes, followed by 1g drip over 8 hours, is intended to limit potential TXA side-effects, including hypotension, seizures, and anaphylaxis. However, this slow and cumbersome TXA infusion protocol is difficult to execute in the tactical care environment. Additionally, the side-effect cautions derive from studies of elderly or cardiothoracic surgery patients, not young healthy warfighters. Therefore, the 75th Ranger Regiment developed and implemented a 2g intravenous or intraosseous (IV/IO) TXA flush protocol. We report on the first six cases of this protocol in the history of the Regiment. After-action reports revealed no incidences of post-TXA hypotension, seizures, or anaphylaxis. Combined, the results of this case series are encouraging and provide a foundation for larger studies to fully determine the safety of the novel 2g IV/IO TXA flush protocol toward preserving the lives of traumatically injured warfighters.

Association between prehospital tranexamic acid administration and outcomes of severe traumatic brain injury

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JAMA Neurol. 2021;78(3):338–345.

Importance: The development and expansion of intracranial hematoma are associated with adverse outcomes. Use of tranexamic acid might limit intracranial hematoma formation, but its association with outcomes of severe traumatic brain injury (TBI) is unclear. **Objective:** To assess whether prehospital administration of tranexamic acid is associated with mortality and functional outcomes in a group of patients with severe TBI. **Design, setting, and participants:** This multicenter cohort study is an analysis of prospectively collected observational data from the Brain Injury: Prehospital Registry of Outcome, Treatments and Epidemiology of Cerebral Trauma (BRAIN-PROTECT) study in the Netherlands. Patients treated for suspected severe TBI by the Dutch Helicopter Emergency Medical Services between February 2012 and December 2017 were included. Patients were followed up for 1 year after inclusion. Data were analyzed from January 10, 2020, to September 10, 2020. **Exposures:** Administration of tranexamic acid during prehospital treatment. **Main outcomes and measures:** The primary outcome was 30-day mortality. Secondary outcomes included mortality at 1 year, functional neurological recovery at discharge (measured by Glasgow Outcome Scale), and length of hospital stay. Data were also collected on demographic factors, preinjury medical condition, injury characteristics, operational characteristics, and prehospital vital parameters. **Results:** A total of 1827 patients were analyzed, of whom 1283 (70%) were male individuals, and the median (interquartile range) age was 45 (23–65) years. In the unadjusted analysis, higher 30-day mortality was observed in patients who received prehospital tranexamic acid (odds ratio [OR], 1.34; 95% CI, 1.16-1.55; $p < .001$) compared with patients who did not receive prehospital tranexamic acid. After adjustment for confounders, no association between prehospital administration of tranexamic acid and mortality was found across the entire cohort of patients. However, a substantial increase in the odds of 30-day mortality persisted in patients with severe isolated TBI who received prehospital tranexamic acid (OR, 4.49; 95% CI, 1.57–12.87; $p = .005$) and after multiple imputations (OR, 2.05; 95% CI, 1.22-3.45; $p = .007$). **Conclusions and relevance:** This study found that prehospital tranexamic acid administration was associated with increased mortality in patients with isolated severe TBI, suggesting the judicious use of the drug when no evidence for extracranial hemorrhage is present.

Update on applications and limitations of perioperative tranexamic acid

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Anesth Analg. 2022;135(3):460–473.

Tranexamic acid (TXA) is a potent antifibrinolytic with documented efficacy in reducing blood loss and allogeneic red blood cell transfusion in several clinical settings. With a growing emphasis on patient blood management, TXA has become an integral aspect of perioperative blood conservation strategies. While clinical applications of TXA in the perioperative period are expanding, routine use in select clinical scenarios should be supported by evidence for efficacy. Furthermore, questions regarding optimal dosing without increased risk of adverse events such as thrombosis or seizures should be answered. Therefore, ongoing investigations into TXA utilization in cardiac surgery, obstetrics, acute trauma, orthopedic surgery, neurosurgery, pediatric surgery, and other perioperative settings continue. The aim of this review is to provide an update on the current applications and limitations of TXA use in the perioperative period.

Clinical use of tranexamic acid: evidences and controversies

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Braz J Anesthesiol. 2022;72(6):795–812.

Tranexamic acid (TXA) significantly reduces blood loss in a wide range of surgical procedures and improves survival rates in obstetric and trauma patients with severe bleeding. Although it mainly acts as a fibrinolysis inhibitor, it also has an anti-inflammatory effect, and may help attenuate the systemic inflammatory response syndrome found in some cardiac surgery patients. However, the administration of high doses of TXA has been associated with seizures and other adverse effects that increase the cost of care, and the administration of TXA to reduce perioperative bleeding needs to be standardized. Tranexamic acid is generally well tolerated, and most adverse reactions are considered mild or moderate. Severe events are rare in clinical trials, and literature reviews have shown TXA to be safe in several different surgical procedures. However, after many years of experience with TXA in various fields, such as orthopedic surgery, clinicians are now querying whether the dosage, route and interval of administration currently used and the methods used to control and analyze the antifibrinolytic mechanism of TXA are really optimal. These issues need to be evaluated and reviewed using the latest evidence to improve the safety and effectiveness of TXA in treating intracranial hemorrhage and bleeding in procedures such as liver transplantation and cardiac, trauma, and obstetric surgery.

Pharmacokinetics of intramuscular tranexamic acid in bleeding trauma patients: a clinical trial

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Br J Anaesth. 2021;126(1):201–209.

Background: Intravenous tranexamic acid (TXA) reduces bleeding deaths after injury and childbirth. It is most effective when given early. In many countries, pre-hospital care is provided by people who cannot give IV injections. We examined the pharmacokinetics of intramuscular TXA in bleeding trauma patients. **Methods:** We conducted an open-label pharmacokinetic study in two UK hospitals. Thirty bleeding trauma patients received a loading dose of TXA 1g IV, as per guidelines. The second TXA dose was given as two 5mL (0.5g each) IM injections. We collected blood at intervals and monitored injection sites. We measured TXA concentrations using liquid chromatography coupled to mass spectrometry. We assessed the concentration time course using non-linear mixed-effect models with age, sex, ethnicity, body weight, type of injury, signs of shock, and glomerular filtration rate as possible covariates. **Results:** Intramuscular TXA was well tolerated with only mild injection site reactions. A two-compartment open model with first-order absorption and elimination best described the data. For a 70-kg patient, aged 44 yr without signs of shock, the population estimates were 1.94 h^{-1} for IM absorption constant, 0.77 for IM bioavailability, 7.1L h^{-1} for elimination clearance, 11.7L h^{-1} for intercompartmental clearance, 16.1L volume of central compartment, and 9.4L volume of the peripheral compartment. The time to reach therapeutic concentrations (5 or 10mg L^{-1}) after a single intramuscular TXA 1g injection is 4 or 11 min, with the time above these concentrations being 10 or 5.6 h, respectively. **Conclusions:** In bleeding trauma patients, intramuscular TXA is well tolerated and rapidly absorbed.

The risk of thromboembolic events with early intravenous 2 and 4g bolus dosing of tranexamic acid compared to placebo in patients with severe traumatic bleeding: a secondary analysis of a randomized, double-blind, placebo-controlled, single-center trial

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Transfusion. 2022;62 Suppl 1:S139–S150.

Background: Screening for the risk of thromboembolism (TE) due to tranexamic acid (TXA) in patients with severe traumatic injury has not been performed in randomized clinical trials. Our objective was to determine if TXA dose was independently associated with thromboembolism. **Methods:** This is a secondary analysis of a single-center, double-blinded, randomized controlled trial comparing placebo to a 2g or 4g intravenous TXA bolus dose in trauma patients with severe injury. We used multivariable discrete-time Cox regression models to identify associations with risk for thromboembolic events within 30 days post-enrollment. Event curves were created using discrete-time Cox regression. **Results:** There were 50 patients in the placebo group, 49 in the 2g, and 50 in the 4g TXA group. In adjusted analyses for thromboembolism, a 2g dose of TXA had a hazard ratio (HR, 95% confidence interval [CI]) of 3.20 (1.12–9.11) (p = .029), and a 4g dose of TXA had an HR (95% CI) of 5.33 (1.94–14.63) (p = .001). Event curves demonstrated a higher probability of thromboembolism for both doses of TXA compared to placebo. Other parameters independently associated with thromboembolism include time from injury to TXA administration, body mass index, and total blood products transfused. **Discussion:** In patients with severe traumatic injury, there was a dose-dependent increase in the risk of at least one thromboembolic event with TXA. TXA should not be withheld, but thromboembolism screening should be considered for patients receiving a dose of at least 2g TXA intravenously for traumatic hemorrhage.

Effect of out-of-hospital tranexamic acid vs placebo on 6-month functional neurologic outcomes in patients with moderate or severe traumatic brain injury

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Importance: Traumatic brain injury (TBI) is the leading cause of death and disability due to trauma. Early administration of tranexamic acid may benefit patients with TBI. **Objective:** To determine whether tranexamic acid treatment initiated in the out-of-hospital setting within 2 hours of injury improves neurologic outcome in patients with moderate or severe TBI**. Design, setting, and participants:** Multicenter, double-blinded, randomized clinical trial at 20 trauma centers and 39 emergency medical services agencies in the US and Canada from May 2015 to November 2017. Eligible

participants (N = 1280) included out-of-hospital patients with TBI aged 15 years or older with Glasgow Coma Scale score of 12 or less and systolic blood pressure of 90mmHg or higher. **Interventions:** Three interventions were evaluated, with treatment initiated within 2 hours of TBI: out-of-hospital tranexamic acid (1g) bolus and in-hospital tranexamic acid (1g) 8-hour infusion (bolus maintenance group; n = 312), out-of-hospital tranexamic acid (2g) bolus and in-hospital placebo 8-hour infusion (bolus only group; n = 345), and out-of-hospital placebo bolus and in-hospital placebo 8-hour infusion (placebo group; n = 309). **Main outcomes and measures:** The primary outcome was favorable neurologic function at 6 months (Glasgow Outcome Scale-Extended score >4 [moderate disability or good recovery]) in the combined tranexamic acid group vs the placebo group. Asymmetric significance thresholds were set at 0.1 for benefit and 0.025 for harm. There were 18 secondary end points, of which 5 are reported in this article: 28-day mortality, 6-month Disability Rating Scale score (range, 0 [no disability] to 30 [death]), progression of intracranial hemorrhage, incidence of seizures, and incidence of thromboembolic events. **Results:** Among 1063 participants, a study drug was not administered to 96 randomized participants and 1 participantwas excluded, resulting in 966 participants in the analysis population (mean age, 42 years; 255 [74%] male participants; mean Glasgow Coma Scale score, 8). Of these participants, 819 (84.8%) were available for primary outcome analysis at 6-month followup. The primary outcome occurred in 65% of patients in the tranexamic acid groups vs 62% in the placebo group (difference, 3.5%; [90% 1-sided confidence limit for benefit, –0.9%]; p = .16; [97.5% 1-sided confidence limit for harm, 10.2%]; p = .84). There was no statistically significant difference in 28-day mortality between the tranexamic acid groups vs the placebo group (14% vs 17%; difference, –2.9% [95% CI, –7.9% to 2.1%]; p = .26), 6-month Disability Rating Scale score (6.8 vs 7.6; difference, –0.9 [95% CI, –2.5 to 0.7]; p = .29), or progression of intracranial hemorrhage (16% vs 20%; difference, –5.4% [95% CI, –12.8% to 2.1%]; p = .16). **Conclusions and relevance:** Among patients with moderate to severe TBI, out-of-hospital tranexamic acid administration within 2 hours of injury compared with placebo did not significantly improve 6-month neurologic outcome as measured by the Glasgow Outcome Scale-Extended.

Tranexamic acid during prehospital transport in patients at risk for hemorrhage after injury: a double-blind, placebo-controlled, randomized clinical trial

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JAMA Surg. 2020;156(1):11–20.

Importance: In-hospital administration of tranexamic acid after injury improves outcomes in patients at risk for hemorrhage. Data demonstrating the benefit and safety of the pragmatic use of tranexamic acid in the prehospital phase of care are lacking for these patients. **Objective:** To assess the effectiveness and safety of tranexamic acid administered before hospitalization compared with placebo in injured patients at risk for hemorrhage. **Design, setting, and participants:** This pragmatic, phase 3, multicenter, double-blind, placebo-controlled, superiority randomized clinical trial included injured patients with prehospital hypotension (systolic blood pressure ≤90mmHg) or tachycardia (heart rate ≥110/min) before arrival at 1 of 4 US level 1 trauma centers, within an estimated 2 hours of injury, from May 1, 2015, through October 31, 2019. **Interventions:** Patients received 1g of tranexamic acid before hospitalization (447 patients) or placebo (456 patients) infused for 10 minutes in 100mL of saline. The randomization scheme used prehospital and in-hospital phase assignments, and patients administered tranexamic acid were allocated to abbreviated, standard, and repeat bolus dosing regimens on trauma center arrival. **Main outcomes and measures:** The primary outcome was 30-day all-cause mortality. **Results:** In all, 927 patients (mean [SD] age, 42 [18] years; 686 [74.0%] male) were eligible for prehospital enrollment (460 randomized to tranexamic acid intervention; 467 to placebo intervention). After exclusions, the intention-to-treat study cohort comprised 903 patients: 447 in the tranexamic acid arm and 456 in the placebo arm. Mortality at 30 days was 8.1% in patients receiving tranexamic acid compared with 9.9% in patients receiving placebo (difference, –1.8%; 95% CI, –5.6% to 1.9%; p = .17). Results of Cox proportional hazards regression analysis, accounting for site, verified that randomization to tranexamic acid was not associated with a significant reduction in 30-day mortality (hazard ratio, 0.81; 95% CI, 0.59–1.11, p = .18). Prespecified dosing regimens and post hoc subgroup analyses found that prehospital tranexamic acid were associated with significantly lower 30-day mortality. When comparing tranexamic acid effect stratified by time to treatment and qualifying shock severity in a post hoc comparison, 30-day mortality was lower when tranexamic acid was administered within 1 hour of injury (4.6% vs 7.6%; difference, –3.0%; 95% CI, –5.7% to –0.3%; p < .002). Patients with severe shock (systolic blood pressure ≤70mmHg) who received tranexamic acid demonstrated lower 30-day mortality compared with placebo (18.5% vs 35.5%; difference, –17%; 95% CI, –25.8% to –8.1%; p < .003). **Conclusions and relevance:** In injured patients at risk for hemorrhage, tranexamic acid administered before hospitalization did not result in significantly lower 30-day mortality. The prehospital administration of tranexamic acid after injury did not result in a higher incidence of thrombotic complications or adverse events. Tranexamic acid given to injured patients at risk for hemorrhage in the prehospital setting is safe and associated with survival benefit in specific subgroups of patients.

Efficacy and safety of tranexamic acid administration in traumatic brain injury patients: a systematic review and meta-analysis

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J Intensive Care. 2020;8:46.

Background: The exacerbation of intracranial bleeding is critical in traumatic brain injury (TBI) patients. Tranexamic acid (TXA) has been used to improve outcomes in TBI patients. However, the effectiveness of TXA treatment remains unclear. This study aimed to assess the effect of administration of TXA on clinical outcomes in patients with TBI by systematically reviewing the literature and synthesizing evidence of randomized controlled trials (RCTs). **Methods:** MEDLINE, the Cochrane Central Register of Controlled Trials, and Igaku Chuo Zasshi (ICHUSHI) Web were searched. Selection criteria included randomized controlled trials with clinical outcomes of adult TBI patients administered TXA or placebo within 24 hr after admission. Two investigators independently screened citations and conducted data extraction. The primary "critical" outcome was all-cause mortality. The secondary "important" outcomes were good neurological outcome rates, enlargement of bleeding, incidence of ischemia, and hemorrhagic intracranial complications. Random effect estimators with weights calculated by the inverse variance method were used to report risk ratios (RRs). **Results:** A total of 640 records were screened. Seven studies were included for quantitative analysis. Of 10,044 patients

from seven of the included studies, 5076 were randomly assigned to the TXA treatment group, and 4968 were assigned to placebo. In the TXA treatment group, 914 patients (18.0%) died, while 961 patients (19.3%) died in the placebo group. There was no significant difference between groups (RR, 0.93; 95% confidence interval, 0.86–1.01). No significant differences between the groups in other important outcomes were observed. **Conclusions:** TXA treatment demonstrated a tendency to reduce head trauma-related deaths in the TBI population, with no significant incidence of thromboembolic events. TXA treatment may therefore be suggested in the initial TBI care.

Fluid resuscitation in Tactical Combat Casualty Care TCCC Guidelines Change 21-01. 4 November 2021

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J Spec Oper Med. 21(4):126–137.

Hemorrhagic shock in combat trauma remains the greatest life threat to casualties with potentially survivable injuries. Advances in external hemorrhage control and the increasing use of damage control resuscitation have demonstrated significant success in decreasing mortality in combat casualties. Presently, an expanding body of literature suggests that fluid resuscitation strategies for casualties in hemorrhagic shock that include the prehospital use of cold-stored or fresh whole blood when available, or blood components when whole blood is not available, are superior to crystalloid and colloid fluids. On the basis of this recent evidence, the Committee on Tactical Combat Casualty Care (TCCC) has conducted a review of fluid resuscitation for the combat casualty who is in hemorrhagic shock and made the following new recommendations: (1) cold stored low-titer group O whole blood (CS-LTOWB) has been designated as the preferred resuscitation fluid, with fresh LTOWB identified as the first alternate if CS-LTOWB is not available; (2) crystalloids and Hextend are no longer recommended as fluid resuscitation options in hemorrhagic shock; (3) target systolic blood pressure (SBP) resuscitation goals have been redefined for casualties with and without traumatic brain injury (TBI) coexisting with their hemorrhagic shock; and (4) empiric prehospital calcium administration is now recommended whenever blood product resuscitation is required.

Balanced crystalloids versus saline in critically ill adults—a systematic review with meta-analysis

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NEJM Evid. 2022;1(2)

Background: The comparative efficacy and safety of balanced crystalloid solutions and saline for fluid therapy in critically ill adults remain uncertain. **Methods:** We systematically reviewed randomized clinical trials (RCTs) comparing the use of balanced crystalloids with saline in critically ill adults. The primary outcome was 90-day mortality after pooling data from low-risk-of-bias trials using a random-effects model. We also performed a Bayesian meta-analysis to describe the primary treatment effect in probability terms. Secondary outcomes included the incidence of acute kidney injury (AKI), new treatment with renal replacement therapy (RRT), and ventilator-free and vasopressor-free days to day 28. **Results:** We identified 13 RCTs, comprising 35,884 participants. From six trials (34,450 participants) with a low risk of bias, the risk ratio (RR) for 90-day mortality with balanced crystalloids versus saline was 0.96 (95% confidence interval [CI], 0.91 to 1.01; I^2 = 12.1%); using vague priors, the posterior probability that balanced crystalloids reduce mortality was 89.5%. The RRs of developing AKI and of being treated with RRT with balanced crystalloids versus saline were 0.96 (95% CI, 0.89 to 1.02) and 0.95 (95% CI, 0.81 to 1.11), respectively. Ventilator-free days (mean difference, 0.18 days; 95% CI, 20.45 to 0.81) and vasopressor-free days (mean difference, 0.19 days; 95% CI, 20.14 to 0.51) were similar between groups. **Conclusions:** The estimated effect of using balanced crystalloids versus saline in critically ill adults ranges from a 9% relative reduction to a 1% relative increase in the risk of death, with a high probability that the average effect of using balanced crystalloids is to reduce mortality.

Low titer group O whole blood resuscitation: military experience from the point of injury

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J Trauma Acute Care Surg. 2020;89(4):834–841.

Introduction: In the far forward combat environment, the use of whole blood is recommended for the treatment of hemorrhagic shock after injury. In 2016, US military special operations teams began receiving low titer group O whole blood (LTOWB) for use at the point of injury (POI). This is a case series of the initial 15 patients who received LTOWB on the battlefield. **Methods:** Patients were identified in the Department of Defense Trauma Registry, and charts were abstracted for age, sex, nationality, mechanism of injury, injuries and physiologic criteria that triggered the transfusion, treatments at the POI, blood products received at the POI and the damage-control procedures done by the first surgical team, next level of care, initial interventions by the second surgical team, Injury Severity Score, and 30-day survival. Descriptive statistics were used to characterize the clinical data when appropriate. **Results:** Of the 15 casualties, the mean age was 28, 50% were US military, and 63% were gunshot wounds. Thirteen patients survived to discharge, one died of wounds after arrival at the initial resuscitative surgical care, and two died prehospital. The mean Injury Severity Score was 21.31 (SD, 18.93). Eleven (68%) of the causalities received additional blood products during evacuation/role 2 and/or role 3. Vital signs were available for 10 patients from the prehospital setting and 9 patients upon arrival at the first surgical capable facility. The mean systolic blood pressurewas 80.5 prehospital and 117mmHg (p = 0.0002) at the first surgical facility. The mean heart rate was 105 beats per minute prehospital and 87.4 beats per minute (p = 0.075) at the first surgical facility. The mean hospital stay was 24 days. **Conclusion:** The use of cold-stored LTOWB at POI is feasible during combat operations. Further data are needed to validate and inform best practice for POI transfusion.

Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial

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Lancet Haematol. 2020;9(4):e250–e261.

Background: Time to treatment matters in traumatic haemorrhage but the optimal prehospital use of blood in major trauma remains uncertain. We investigated whether use of packed red blood cells (PRBC) and lyophilised plasma (LyoPlas) was superior to use of 0.9% sodium chloride for improving tissue perfusion and reducing mortality in trauma-related haemorrhagic shock**. Methods:** Resuscitation with pre-hospital blood products (RePHILL) is a multicentre, allocation concealed, open-label, parallel group, randomised, controlled, phase 3 trial done in four civilian prehospital critical care services in the UK. Adults (age ≥16 years) with trauma-related haemorrhagic shock and hypotension (defined as systolic blood pressure <90mmHg or absence of palpable radial pulse) were assessed for eligibility by prehospital critial care teams. Eligible participants were randomly assigned to receive either up to two units each of PRBC and LyoPlas or up to 1L of 0.9% sodium chloride administered through the intravenous or intraosseous route. Sealed treatment packs which were identical in external appearance, containing PRBC–LyoPlas or 0.9% sodium chloride, were prepared by blood banks and issued to participating sites according to a randomisation schedule prepared by the coordinating centre (1:1 ratio, stratified by site). The primary outcome was a composite of episode mortality or impaired lactate clearance, or both, measured in the intention-to-treat population. This study is completed and registered with ISRCTN.com, ISRCTN62326938. **Findings:** From Nov 29, 2016, to Jan 2, 2021, prehospital critical care teams randomly assigned 432 participants to PRBC–LyoPlas (n=209) or to 0.9% sodium chloride (n=223). Trial recruitment was stopped before it achieved the intended sample size of 490 participants due to disruption caused by the COVID-19 pandemic. The median follow-up was 9 days (IQR 1 to 34) for participants in the PRBC–LyoPlas group and 7 days (0 to 31) for people in the 0.9% sodium chloride group. Participants were mostly white (62%) and male (82%), had a median age of 38 years (IQR 26 to 58), and were mostly involved in a road traffic collision (62%) with severe injuries (median injury severity score 36, IQR 25 to 50). Before randomisation, participants had received on average 430mL crystalloid fluids and tranexamic acid (90%). The composite primary outcome occurred in 128 (64%) of 199 participants randomly assigned to PRBC–LyoPlas and 136 (65%) of 210 randomly assigned to 0.9% sodium chloride (adjusted risk difference –0.025% [95% CI –9.0 to 9.0], p=0.996). The rates of transfusion-related complications in the first 24 hr after ED arrival were similar across treatment groups (PRBC–LyoPlas 11 [7%] of 148 compared with 0.9% sodium chloride nine [7%] of 137, adjusted relative risk 1.05 [95% CI 0.46–2.42]). Serious adverse events included acute respiratory distress syndrome in nine (6%) of 142 patients in the PRBC–LyoPlas group and three (2%) of 130 in 0.9% sodium chloride group, and two other unexpected serious adverse events, one in the PRBC-LyoPlas (cerebral infarct) and one in the 0.9% sodium chloride group (abnormal liver function test). There were no treatment-related deaths. **Interpretation:** The trial did not show that prehospital PRBC–LyoPlas resuscitation was superior to 0.9% sodium chloride for adult patients with trauma related haemorrhagic shock. Further research is required to identify the characteristics of patients who might benefit from prehospital transfusion and to identify the optimal outcomes for transfusion trials in major trauma. The decision to commit to routine prehospital transfusion will require careful consideration by all stakeholders. **Funding:** National Institute for Health Research Efficacy and Mechanism Evaluation.

Use of cold-stored whole blood is associated with improved mortality in hemostatic resuscitation of major bleeding: a multicenter study

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Ann Surg. 2022:276(4):579–588.

Objective: The aim of this study was to identify a mortality benefit with the use of whole blood (WB) as part of the resuscitation of bleeding trauma patients. **Background:** Blood component therapy (BCT) is the current standard for resuscitating trauma patients, with WB emerging as the blood product of choice. We hypothesized that the use of WB versus BCT alone would result in decreased mortality. **Methods:** We performed a 14-center, prospective observational study of trauma patients who received WB versus BCT during their resuscitation. We applied a generalized linear mixed-effects model with a random effect and controlled for age, sex, mechanism of injury (MOI), and injury severity score. All patients who received blood as part of their initial resuscitation were included. Primary outcome was mortality, and secondary outcomes included acute kidney injury, deep vein thrombosis/pulmonary embolism, pulmonary complications, and bleeding complications. **Results:** A total of 1623 [WB: 1180 (74%), BCT: 443(27%)] patients who sustained penetrating (53%) or blunt (47%) injury were included. Patients who received WB had a higher shock index (0.98 vs 0.83), more comorbidities, and more blunt MOI (all p<0.05). After controlling for center, age, sex, MOI, and injury severity score, we found no differences in the rates of acute kidney injury, deep vein thrombosis/pulmonary embolism or pulmonary complications. WB patients were 9% less likely to experience bleeding complications and were 48% less likely to die than BCT patients (p<0.0001). **Conclusions:** Compared with BCT, the use of WB was associated with a 48% reduction in mortality in trauma patients. Our study supports the use of WB use in the resuscitation of trauma patients.

Transfusion strategies in bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine

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Intensive Care Med. 2021;47(12):1368–1392.

Purpose: To develop evidence-based clinical practice recommendations regarding transfusion practices and transfusion in bleeding critically ill adults. **Methods:** A taskforce involving 15 international experts and 2 methodologists used the GRADE approach to guideline development. The taskforce addressed three main topics: transfusion support in massively and non-massively bleeding critically ill patients (transfusion ratios, blood products, and point of care testing) and the use of tranexamic acid. The panel developed and answered structured guideline questions using the population, intervention, comparison, and outcomes (PICO) format. **Results:** The taskforce generated 26 clinical practice recommendations (2 strong recommendations, 13 conditional recommendations, 11 no recommendation), and identified 10 PICOs with insufficient evidence to make a recommendation. **Conclusions:** This clinical practice

guideline provides evidence-based recommendations for the management of massively and non-massively bleeding critically ill adult patients and identifies areas where further research is needed.

Prehospital lyophilized plasma transfusion for trauma-induced coagulopathy in patients at risk for hemorrhagic shock: a randomized clinical trial

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JAMA Netw Open. 2020;5(7):e2223619.

Importance: Blood transfusion is a mainstay of therapy for trauma-induced coagulopathy, but the optimal modalities for plasma transfusion in the prehospital setting remain to be defined. **Objective:** To determine whether lyophilized plasma transfusion can reduce the incidence of trauma-induced coagulopathy compared with standard care consisting of normal saline infusion. **Design, setting, and participants**: This randomized clinical trial was performed at multiple centers in France involving prehospital medical teams. Participants included 150 adults with trauma who were at risk for hemorrhagic shock and associated coagulopathy between April 1, 2016, and September 30, 2019, with a 28-day follow-up. Data were analyzed from November 1, 2019, to July 1, 2020. **Intervention:** Patients were randomized in a 1:1 ratio to receive either plasma or standard care with normal saline infusion (control). **Main outcomes and measures:** The primary outcome was the international normalized ratio (INR) on arrival at the hospital. Secondary outcomes included the need for massive transfusion and 30-day survival. As a safety outcome, prespecified adverse events included thrombosis, transfusion-related acute lung injury, and transfusion-associated circulatory overload. **Results:** Among 150 randomized patients, 134 were included in the analysis (median age, 34 [IQR, 26–49] years; 110 men [82.1%]), with 68 in the plasma group and 66 in the control group. Median INR values were 1.21 (IQR, 1.12–1.49) in the plasma group and 1.20 (IQR, 1.10–1.39) in the control group (median difference, –0.01 [IQR, –0.09 to 0.08]; p = .88). The groups did not differ significantly in the need for massive transfusion (7 [10.3%] vs 4 [6.1%]; relative risk, 1.78 [95% CI, 0.42-8.68]; p = .37) or 30-day survival (hazard ratio for death, 1.07 [95% CI, 0.44-2.61]; p = .89). In the full intention-to-treat population (n = 150), the groups did not differ in the rates of any of the prespecified adverse events. **Conclusions and relevance:** In this randomized clinical trial including severely injured patients at risk for hemorrhagic shock and associated coagulopathy, prehospital transfusion of lyophilized plasma was not associated with significant differences in INR values vs standard care with normal saline infusion. Nevertheless, these findings show that lyophilized plasma transfusion is a feasible and safe procedure for this patient population.

Whole blood vs blood component therapy for transfusion in trauma patients: a prospective, multicenter study

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Objective: Currently, blood component therapy (BCT) is standard practice for the resuscitation of trauma patients, but recently whole blood (WB) transfusion has emerged as the resuscitation strategy of choice at select US trauma centers. Much of the data regarding WB is limited to small prospective or retrospective studies which have failed to demonstrate a significant benefit of WB versus BCT. We hypothesized that the use of WB transfusion vs BCT alone would result in decreased mortality in trauma patients. **Methods**: We performed a multicenter (14 verified trauma centers), prospective-observational study of patients who received WB vs BCT during their initial trauma resuscitation. We applied a generalized linear mixed-effects model with a random effect (to control for center) and also controlled for age, sex, mechanism of injury (MOI) and injury severity score (ISS). Trauma patients of any age who received a blood transfusion as part of their initial resuscitation were included. Primary outcome was in-hospital mortality and secondary outcomes included acute kidney injury (AKI), deep venous thrombosis (DVT), pulmonary complications, bleeding complications, and length of stay (LOS). **Results:** A total of 1,623 trauma patients who sustained either penetrating (53%) or blunt (47%) injury were included. Of the 1,623 patients, 1,180 (73%) received at least one unit of WB while 443 (27%) received only BCT. Median age was 40y (IQR 11-30), 83% were male and median ISS was 22 (IQR 11-30). Patients who received WB had a higher shock index (1.08 vs 0.94), more comorbid conditions, and more likely had a blunt MOI (all $p < 0.05$). After controlling for center, age, sex, prehospital blood products, MOI, and ISS, we found no differences in the rates of AKI, DVT/PE, pulmonary complications, or LOS between groups. Patients who received WB were 9% less likely to experience a bleeding complication and were 48% less likely to die than those who received BCT alone ($p<0.0001$). **Conclusions:** Compared with standard blood component therapy, the use of whole blood transfusion resulted in a 48% reduction in mortality in trauma patients. Our study supports the universal use of whole blood during the initial resuscitation of trauma patients who require a transfusion.

Hypocalcemia as a predictor of mortality and transfusion. A scoping review of hypocalcemia in trauma and hemostatic resuscitation

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Background: Calcium plays an essential role in physiologic processes, including trauma's "Lethal Diamond." Thus, inadequate serum calcium in trauma patients exacerbates the effects of hemorrhagic shock secondary to traumatic injury and subsequently poorer outcomes compared to those with adequate calcium levels. Evidence to date supports the consideration of calcium derangements when assessing the risk of mortality and the need for blood product transfusion in trauma patients. This review aims to further elucidate the predictive strength of this association for future treatment guidelines and clinical trials. **Methods:** Publications were collected on the relationship between i-Ca and the outcomes

of traumatic injuries from PubMed, Web of Science, and CINAHL. Manuscripts were reviewed to select for English language studies. Hypocalcemia was defined as i-Ca <1.2mmol/L. **Results:** Using PRISMA guidelines, we reviewed 300 studies, 7 of which met our inclusion criteria. Five papers showed an association between hypocalcemia and mortality. **Conclusions:** In adult trauma patients, there has been an association seen between hypocalcemia, mortality, and the need for increased blood product transfusions. It is possible we are now seeing an association between low calcium levels prior to blood product administration and an increased risk for mortality and need for transfusion. Hypocalcemia may serve as a biomarker to show these needs.

Therefore, hypocalcemia could potentially be used as an independent predictor for multiple transfusions such that ionized calcium measurements could be used predictively, allowing faster administration of blood products

Management of hypothermia in Tactical Combat Casualty Care: TCCC Guideline Proposed Change 20-01 (June 2020)

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As an outcome of combat injury and hemorrhagic shock, trauma-induced hypothermia (TIH) and the associated coagulopathy and acidosis result in significantly increased risk for death. In an effort to manage TIH, the Hypothermia Prevention and Management Kit™ (HPMK) was implemented in 2006 for battlefield casualties. Recent feedback from operational forces indicates that limitations exist in the HPMK to maintain thermal balance in cold environments, due to the lack of insulation. Consequently, based on lessons learned, some US Special Operations Forces are now upgrading the HPMK after short-term use (60 minutes) by adding insulation around the casualty during training in cold environments. Furthermore, new research indicates that the current HPMK, although better than no hypothermia protection, was ranked last in objective and subjective measures in volunteers when compared with commercial and user-assembled external warming enclosure systems. On the basis of these observations and research findings, the Committee on Tactical Combat Casualty Care decided to review the hypothermia prevention and management guidelines in 2018 and to update them on the basis of these facts and that no update has occurred in 14 years. Recommendations are made for minimal costs, low cube and weight solutions to create an insulated HPMK, or when the HPMK is not readily available, to create an improvised hypothermia (insulated) enclosure system.

Hypothermia in the combat trauma population

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Background: The MARCH (Massive hemorrhage, Airway, Respirations, Circulation, and Hypothermia/Head injuries) algorithm taught to military medics includes interventions to prevent hypothermia. As possible sequelae from major trauma, hypothermia is associated with coagulopathy and lower survival. This paper sought to define hypothermia within our combat trauma population using an outcomes-based method, and determine clinical variables associated with hypothermia. **Methods:** This is a secondary analysis of a previously described dataset from the Department of Defense Trauma Registry focused on casualties who received prehospital care. A receiver operating curve was constructed and Youden's index was used to define hypothermia within the predetermined population based on mortality risk. A multivariable regression model was used to identify associations. **Results:** There were 23,243 encounters that met the inclusion criteria for this study with patients having received prehospital care and documentation of at least one emergency department temperature. An optimal threshold of 36.2°C was found to predict mortality; 3,159 casualties had temperatures below this threshold (14%). Survival to discharge was lower among casualties with hypothermia (91% versus 98%). Hypothermic casualties were less likely to undergo blanket application (38% versus 40%). However, they had higher proportions with Hypothermia Prevention and Management Kit application (11% versus 7%) and radiant warming (2% versus 1%). On multivariable regression modeling, none of the hypothermia interventions were associated with a decreased likelihood of hypothermia. Non-hypothermia interventions associated with hypothermia included prehospital intubation (OR 1.57, 95% CI 1.45–1.69) and blood product administration. **Conclusions:** Hypothermia, including a single recorded low temperature in the patient care record, was associated with worse outcomes in this combat trauma population. Prehospital intubation was most strongly associated with developing hypothermia. Prehospital warming interventions were not associated with a reduction in hypothermia risk. Our dataset suggests that current methods for prehospital warming are inadequate.

Epidemiology, patterns of care and outcomes of traumatic brain injury in deployed military settings: implications for future military operations

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J Trauma Acute Care Surg. 2022;93(2):220–228.

Background: Traumatic brain injury (TBI) is prevalent and highly morbid among Service Members. A better understanding of TBI epidemiology, outcomes, and care patterns in deployed settings could inform potential approaches to improve TBI diagnosis and management. **Methods:** A retrospective cohort analysis of Service Members Defense Health Agency TCCC All Service Members Course. Members who sustained a TBI in deployed settings between 2001 and 2018 was conducted. Among individuals hospitalized with TBI, we compared the demographic characteristics, mechanism of injury, injury type, and severity between combat and noncombat injuries. We compared diagnostic tests and procedures, evacuation patterns, return to duty rates and days in care between individuals with concussion and those with severe TBI. **Results:** There were 46,309 Servicemembers with TBI and 9,412 who were hospitalized; of those hospitalized, 55% (4,343) had isolated concussion and 9% (796) had severe TBI, of whom 17% (132/796) had multiple injuries. Overall mortality was 2% and ranged from 0.1% for isolated concussion to 18% for severe TBI. The vast majority of TBI were evacuated by rotary wing to role 3 or higher, including those with isolated concussion. As compared with severe TBI, individuals with isolated concussion had fewer diagnostic or surgical procedures performed. Only 6%of Servicemembers with severe TBI were able to return to duty as compared with 54% of those with isolated concussion. Traumatic brain injury resulted in 123,677 lost duty days; individuals with isolated concussion spent a median of 2 days in care and those with severe TBI spent a median of 17 days in care and a median of 6 days in the intensive care unit. **Conclusion:** While most TBI in the deployed setting are mild, TBI is frequently associated with hospitalization and multiple injuries. Overtriage of mild TBI is common. Improved TBI capabilities applicable to forward settings will be critical to the success of future multidomain operations with limitations in air superiority.

23.4% hypertonic saline: a tactical option for the management of severe traumatic brain injury with impending or ongoing herniation

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There are limited options available to the combat medic for management of traumatic brain injury (TBI) with impending or ongoing herniation. Current pararescue and Tactical Combat Casualty Care (TCCC) guidelines prescribe a bolus of 3% or 5% hypertonic saline. However, this fluid bears a tactical burden of weight (~570g) and pack volume (~500 cm^3). Thus, 23.4% hypertonic saline is an attractive option, because it has a lighter weight (80g) and pack volume (55 cm^3), and it provides a similar osmotic load per dose. Current literature supports the use of 23.4% hypertonic saline in the management of acute TBI, and evidence indicates that it is safe to administer via peripheral and intraosseous cannulas. Current combat medic TBI treatment algorithms should be updated to include the use of 23.4% hypertonic saline as an alternative to 3% and 5% solutions, given its effectiveness and tactical advantages.

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