Clinical Policy: Critical Issues in the Evaluation of Adult Patients Presenting to the Emergency Department With Acute Blunt Trauma

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ABSTRACT

This clinical policy from the American College of Emergency Physicians is a revision of the 2018 Clinical Policy: Critical Issues in the Evaluation of Adult Patients Presenting to the Emergency Department with Acute Blunt Abdominal Trauma. A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following clinical questions: 1) In adult patients presenting to the emergency department (ED) with blunt trauma, does whole-body computed tomography improve clinically important outcomes in hemodynamically stable patients? 2) In geriatric patients presenting to the ED with blunt trauma, does age-based, differential trauma triage reduce morbidity and/or mortality? 3) In adult patients presenting to the ED with blunt trauma, what is the ideal blood product ratio to reduce morbidity and/or mortality in patients requiring transfusion? 4) In adult patients presenting to the ED with blunt trauma, does resuscitative endovascular balloon occlusion of the aorta reduce morbidity and/or mortality in arrested or peri-arrest patients compared with ED thoracotomy? Evidence was graded, and recommendations were made based on the strength of the available data.

INTRODUCTION

Trauma is the fourth most common cause of death for all ages in the United States and the most common cause of death for ages 1 to 44.[1] It contributes to more years of potential life lost compared with any other cause of death.[2] Blunt trauma is the most common mechanism of injury. The triage, evaluation, and treatment of these patients is a routine element of the practice of emergency medicine.[3] Consequently, there is substantial opportunity in the emergency department (ED) to minimize preventable morbidity and mortality due to blunt trauma. This policy is an update of the 2011 American College of Emergency Physicians' (ACEP) clinical policy on acute blunt abdominal trauma, which is now expanded to address acute blunt trauma not limited to the abdomen.[4]

Despite the high prevalence of patients with blunt trauma, care of these patients is constantly evolving and continues to present a clinical challenge. For example, occult injury remains common as physical examination has limited accuracy in patients with altered mental status, intoxication, and other distracting injuries or even in asymptomatic patients with a normal sensorium.[5,6] This fact, combined with technical advances in computed tomography (CT), have resulted in changes to cross-sectional imaging protocols since the last clinical policy update. Our understanding of the response of the geriatric population to blunt trauma has also evolved, and this has resulted in the variable incorporation of age into trauma triage. Lastly, lessons learned from military trauma care, such as resuscitation with changing blood product ratios and incorporation of advanced invasive techniques for managing noncompressible torso hemorrhage, have been applied and studied in civilian blunt trauma.

The treatment of the injured patient requires a multidisciplinary team composed of many specialties, including trauma surgery, orthopedic surgery, radiology, interventional radiology, neurology, and nursing. This policy focuses on topics of particular importance for emergency physicians.

This policy will address current challenges in the diagnosis and treatment of adult patients with blunt trauma in the era of evolving cross-sectional imaging approaches, differential trauma triage incorporating age, blood product resuscitation ratios, and resuscitative endovascular balloon aortic occlusion (REBOA).

METHODOLOGY

This ACEP clinical policy was developed by emergency physicians with input from medical librarians and a patient safety advocate. It is based on a systematic review and critical, descriptive analysis of the medical literature and is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[7]

Search and Study Selection

This clinical policy is based on a systematic review with a critical analysis of the medical literature meeting the inclusion criteria. Searches of PubMed, SCOPUS, Embase, Web of Science, and the Cochrane Database of Systematic Reviews were performed by a librarian. Search terms and strategies were peer reviewed by a second librarian. All searches were limited to human studies published in English. Specific key words/phrases, years used in the searches, dates of searches, and study selection are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Two subcommittee members independently read the identified abstracts to assess them for possible inclusion. Of those identified for potential inclusion, each full-length text was reviewed for eligibility. Those identified as eligible were subsequently forwarded to the committee's methodology group (emergency physicians with specific research

methodological expertise) for methodological grading using a Class of Evidence framework (Appendix E1, available at http://www.annemergmed.com).

Assessment of Risk of Bias and Determination of Classes of Evidence

Each study identified as eligible by the subcommittee was independently graded by 2 methodologists. Grading was done with respect to the specific critical questions; thus, the Class of Evidence for any one study may vary according to the question for which it is being considered. For example, an article that is graded an "X" because of "inapplicability" for one critical question may be considered perfectly relevant for another question and graded I to III. As such, it was possible for a single article to receive a different Class of Evidence grade when addressing a different critical question.

Design 1 represents the strongest possible study design to answer the critical question, which relates to whether the focus was therapeutic, diagnostic, prognostic, or meta-analysis. Subsequent design types (ie, design 2 and design 3) represent weaker study designs, respectively. Articles are then graded on dimensions related to the study's methodological features and execution, including but not limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, generalizability, data management, analyses, congruence of results and conclusions, and potential for conflicts of interest.

Using a predetermined process that combines the study's design, methodological quality, and applicability to the critical question, 2 methodologists independently assigned a preliminary Class of Evidence grade for each article. Articles with concordant grades from both methodologists received that grade as their final grade. Any discordance in the preliminary grades was adjudicated through discussion, which involved at least 1 additional methodologist, resulting in a final Class of Evidence assignment (ie, class I, class II, class III, or class X) (Appendix E2, available at http://www.annemergmed.com). Studies identified with significant methodologic limitations and/or ultimately determined to not be applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. However, the content in these articles may have been used to formulate the background and to inform expert consensus in the absence of evidence. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Based on the strength of evidence for each critical question, the subcommittee drafted the recommendations and supporting text, synthesizing the evidence using the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of scientific certainty (eg, based on evidence from one or more Class of Evidence I or multiple Class of Evidence II studies that demonstrate consistent effects or estimates).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate scientific certainty (eg, based on evidence from one or more Class of Evidence II studies or multiple Class of Evidence III studies that demonstrate consistent effects or estimates).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as consistency of results, the uncertainty of effect magnitude, and publication bias, among others, might lead to a downgrading of recommendations. When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) are presented to help the reader better understand how the results may be applied to the individual patient. This can assist the clinician in applying the recommendations to most patients but allow adjustment when applying to patients with extremes of risk (Appendix E3, available at http://www.annemergmed.com).

Evaluation and Review of Recommendations

Once drafted, the policy was distributed for internal review (by members of the entire committee), followed by an external expert review and an open comment period for all ACEP membership. Comments were received during a 60-day open comment period, with notices of the comment period sent electronically to ACEP members, published in *EM Today*, posted on the ACEP website, and sent to other pertinent physician organizations. The responses were used to further refine and enhance this clinical policy, although responses did not imply

endorsement. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly.

Application of the Policy

This policy is not intended to be a complete manual on the evaluation and management of patients with penetrating trauma but rather a focused examination of critical questions that have particular relevance to the current practice of emergency medicine. The potential benefits and harms of implementing recommendations are briefly summarized within each critical question.

It is the goal of the Clinical Policies Committee to provide evidence-based recommendations when the scientific literature provides sufficient quality information to inform recommendations for a critical question. When the medical literature does not contain adequate empirical data to inform a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline provides clinical strategies based on medical literature to inform the critical questions addressed in this policy. ACEP funds all staff support and methodologists; the writing committee is composed of unpaid volunteer members of ACEP who are required to disclose all conflicts in line with the organization's policy statement.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline is intended for nonpregnant adult patients with blunt trauma.

Exclusion Criteria. This guideline is not intended for pediatric, pregnant, or penetrating patients with trauma.

CRITICAL QUESTIONS

1. **In adult patients presenting to the ED with blunt trauma, does whole-body CT improve clinically important outcomes in hemodynamically stable patients?**

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Due to the lack of quality evidence, use clinical judgment and hospital-specific protocols to decide between selective CT and whole-body CT imaging in hemodynamically stable, adult, patients with blunt trauma. [Consensus]

Potential Benefit of Implementing the Recommendations

The spectrum of patients with trauma arriving at the ED is very broad. Given the equipoise in risks and benefits of whole-body CT among hemodynamically stable patients with trauma, using clinical judgment will likely lead to the appropriate resource utilization, minimal radiation exposure, and the best outcome for a given patient.

Potential Harm of Implementing the Recommendations

Without clear decision rules, overuse and underuse of whole-body CT in trauma is possible. Overuse would result in additional cost, unnecessary radiation exposure, and potentially false-positive findings that require further evaluation and unnecessary risks. Underuse could result in missed diagnoses and delays in diagnosis.

Key words/phrases for literature searches: nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, whole body scan, pan scan, computed tomography, CT, whole body imaging, x-ray computed tomography, hemodynamics, stable hemodynamics, hemodynamically stable, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020, and May 20, 2021.

Study Selection

Eight hundred and thirteen articles were identified in the searches. Forty-two articles were identified from the search results for further review. After grading for methodologic rigor, 0 class I studies, 0 class II studies, and 0 class III studies were included for this question.

Main Text

There were 42 articles identified to help answer the question; however, they were all deemed to be either low relevance regarding this critical question or low quality as assessed by the methodologists. No articles were graded as level 3 or higher. Nonetheless, there are insights that may be relevant to emergency physicians.

Whole-body CT has become commonplace in the evaluation of patients with trauma.[8] There are several meta-analyses that demonstrate a mortality benefit for patients who meet "trauma activation criteria" or the need for a trauma team evaluation. In addition, multiple studies also

report the benefit of identifying unexpected findings and change in management.[9,10] Within this cohort that meet trauma activation criteria, the injury severity can vary tremendously, and it is possible that the benefits are driven by the select cohort of more severely injured patients. However, this question focuses on whole-body CT in the hemodynamically stable patient population.

REACT-2, a large, multicenter randomized trial by Sierink et al[11] concluded that whole-body CT compared with selective imaging did not demonstrate a difference in mortality. This widely cited study was excluded from consideration because it provided only indirect evidence to answer our question and had important methodologic limitations. We considered this study indirect evidence as it studied a mixed population of hemodynamically unstable and stable patients. The important methodologic limitations resulting in additional downgrading of this study to an X included the following: randomization without concealment, inability to blind physicians and patients, and approximately 15% of the patients were excluded after randomization without a clearly reported reason.

The additional studies evaluated and graded X did not contribute substantially to our recommendation.[12-14] All demonstrated that injuries of uncertain clinical significance were found by whole-body CT. Some authors concluded that these injuries were not impactful, whereas others concluded that that they were important.[12-14]

Brief Summary

In summary, the yield of clinically important outcomes from whole-body CT among hemodynamically stable patients with trauma is low. However, unexpected significant injuries and emergency interventions are occasionally identified. Whether early identification and intervention for these injuries results in improved clinically important outcomes remains unclear. Consequently, we recommend using clinical judgment, local protocols, or shared decisionmaking when possible in the use of whole-body CT versus selective CT in hemodynamically stable patients with blunt trauma.

Future Research

A large high-quality randomized trial comparing whole-body CT to selective CT for hemodynamically stable patients with trauma with a reliable examination using a clear, widely accepted definition of a clinically important injury is necessary to answer this question and help guide emergency physicians on best practices in CT imaging of patients with trauma.

2. **In geriatric patients presenting to the ED with blunt trauma, does age-based, differential trauma triage reduce morbidity and/or mortality?**

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations.

Emergency physicians should factor age (greater than 65 years) into triage of older adult patients with trauma as they have increased morbidity and mortality compared with similarly injured adults.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

Incorporating age into trauma triage for older adult patients with blunt trauma would enhance early identification of at-risk patients. This could lead to more timely diagnostic evaluation and therapeutic interventions in this time-dependent disease with resultant improved outcomes.

Potential Harm of Implementing the Recommendations

Incorporating age into trauma triage for older adult patients with blunt trauma may decrease the specificity and increase resource utilization without consequent improvement of morbidity and mortality. Additionally, unnecessary diagnostic evaluation and treatment may occur when an older patient is incorrectly triaged to be high risk.

Key words/phrases for literature searches: nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, geriatric, aged, older adult, elder, elderly, gerontology, triage, differential triage, age-based triage, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020, and May 20, 2021.

Study Selection

Eight hundred and sixteen articles were identified in the searches. Seventy-four articles were identified from the search results for further review. After grading for methodologic rigor, 0 class I studies, 0 class II studies, and 6 class III studies were included for this question.

Main Text

Age is a risk factor for mortality in patients with trauma.[15-17] The older population has decreased physiologic reserve compared with their younger counterparts. Additionally, immune function is impaired, and older adults have unique alterations in pulmonary function and cardiovascular response to injury and shock. Polypharmacy is common, and many older patients are receiving anticoagulation therapy. Early identification of an at-risk population is the goal of trauma triage as there is evidence that improved outcomes

occur when early intensive monitoring and aggressive fluid resuscitation is performed.[18-20]

The National Guidelines for the Field Triage of Injured Patients in 2021: Recommendations of the National Expert Panel on Field Triage uses a criterion of age greater than 65 years with a systolic blood pressure (SBP) less than 110 mmHg or pulse rate (PR) greater than SBP for recommending medical care in a specialized trauma centers.[21] This is changed from prior guidelines in which age was considered but there were the same recommendations for SBP as there were for all adults. For older adults, the benefit of specialized tertiary trauma centers is less clear than for children or other adult patients.

The effectiveness of field triage is commonly looked at by the degree of over- and undertriage. Undertriage has been shown to be the highest in older adults and half of seriously injured adults are treated in nontrauma centers in the United States.[22-25] This undertriage suggests that the older adult is not consistently being taken to hospitals best equipped to meet their needs. This is not unique to the United States. Destination noncompliance led to poorer outcomes for older patients with trauma. It has been shown that not only were older adults under triaged compared with their younger counterparts, but a larger proportion of the inhospital deaths occur in centers with no major trauma services compared to major trauma centers.[26]

In a class III, retrospective cohort study by Lim et al,[27] the mortality of older adults, even when risk stratified, was increased by 2.7% for each year of life. Additionally, in a class III study by Ahmed and Greenberg,[16] the authors evaluated patients aged 65 years and older after a fall from ground level at home whose initial evaluation include a normal SBP (90 to 160 mmHg), normal PR (60 to 100 beats per minute), and a Glascow Coma Scale rating of 15. In this study of 40,800 patients, 938 (2.3%) patients died in the hospital. Logistic regression showed older age was associated with a higher risk of inhospital mortality.

The additional class III studies included for review here are also retrospective reviews of trauma databases. They look at modifying the criteria for adult trauma triage based on age to determine either the effects on morbidity and mortality or the criteria's ability to predict morbidity and mortality. As we know that early intervention in severely injured trauma improves morbidity and mortality, these studies can provide only indirect evidence of benefit or harm.[28-31]

The class III study by Ichwan et al[28] defined patients aged 70 years or older as "geriatric." Based on age, this study modified multiple elements of the trauma triage criteria to assess a revised older adult trauma triage. Of 101,577 patients, 33,379 (33%) were aged 70 years or older. This cohort of older adults were less severely injured, with only 13% having an Injury Severity Score (ISS) greater than 15 indicating moderate to severe injury, compared with 29% of younger adults. They were also less likely to have an ICU stay (17% versus 28%) and an operating room procedure within 48 hours (13% versus 29%). Interestingly, despite the older group being less injured (lower ISS, fewer ICU and operating room admissions) the mortality between the 2 groups was similar with 6.8% of older adults and 9.3% of younger adults dying in the ED or hospital. Modification of the adult trauma triage as described improved sensitivity from 61% (95% confidence interval [CI] 60% to 62%) to 93% (95% CI 92% to 94%). There was a concomitant modest decrease in specificity from 61% (95% CI 61% to 62%) to 49% (95% CI 48% to 49%). The improvement in the test performance of this proposed "geriatric" trauma triage compared with nonage-based criteria is demonstrated in the change in likelihood ratios that were calculated based on the study's data. With age-based triage, the positive likelihood ratio improved from 1.6 to 1.8 and the negative likelihood ratio improved more dramatically from 0.8 to 0.1. This suggests the geriatric criteria improve our ability to identify older patients with serious injuries, need for operative or ICU care, or death.

In another class III study, Brown et al[29] evaluated the performance of substituting an SBP of less than 110 mmHg for the current SBP of less than 90 mmHg criterion. The primary outcome was under and overtriage as defined by the ISS, which is an established surrogate for clinical outcome for trauma activation criteria. In this 12-year study, 428,828 older adults were identified, and they found that substituting an SBP of less than 110 mmHg for the current SBP of less than 90 mmHg in older patients achieves a reduction in 4.4% undertriage with a 4.3% increase in overtriage. Regarding mortality, the older patients with SBP of 90 mmHg to 109 mmHg had an odds of mortality similar to older patients with SBP of less than 90 mmHg (adjusted odds ratio 1.03; 95% CI 0.88 to 1.20; P=.71).

Anantha et al[30] evaluated whether a geriatric-specific (age≥65 years) triage protocol appropriately identified severely injured (ISS>15) patients with trauma. The modified criteria for trauma activation included SBP less than 110 mmHg (rather than 90 mmHg), PR less than 50 or greater than 100 beats/min, any motor vehicle collision or fall from any height. They report that 61% of the severely injured older patients were undertriaged despite the geriatric-specific trauma triage protocol. Fortunately, mortality in the undertriaged group was 5% versus 31% in the correctly identified group. They concluded that despite

geriatric triage protocols, older adults remain undertriaged as measured by ISS, but that age-based protocols do capture the highest risk patients.

In 2018, Hung et al[31] published the performance of the activation criteria for the trauma system in Hong Kong where the trauma team activation criteria have been specifically modified for older adults and included risk factors such as rib fractures. In this 10-year cohort study (2006 to 2015), 2,218 patients over the age of 55 were identified.[31] The 30-day mortality was 7.5% for those aged 55 to 70 and 17.7% for those above 70 years of age. The undertriage rate was 59% for age 55 to 70, and 69.1% for those aged above 70. The sensitivity of trauma team activation in identifying severe outcomes decreases as the age increases. This study reinforces that age is an important triage criteria and possibly specific criteria should be developed for patients aged older than 70 years.

Brief Summary

With advancing age in adult patients with blunt trauma, standard trauma triage criteria under perform in predicting severity of illness and outcomes. Age-based trauma triage improves the criteria's ability to prevent undertriage and limit overtriage. As there is evidence of under- and overtriage's impact on morbidity and mortality, there is indirect evidence supporting age-based trauma triage to improve patient outcomes.

Future Research

The definition of geriatric is still variable in research (ranging from an age cutoff of 55 years to 70 years). Future research should focus on an acceptable definition of the older patients with trauma and determine subpopulations who will benefit from triage to major trauma centers. The direct effect on morbidity, mortality, resource utilization, and the effectiveness of trauma system implementation should be prospectively assessed.

Further work incorporating both quantitative and qualitative methods will be required to better understand factors to address how to manage older patients with trauma and identify appropriate remedies and their implementation. This should focus on geographic differences, patient preferences, emergency medical services provider training and preferences, structure of the emergency medical services system, and local facility factors.

3. **In adult patients presenting to the ED with blunt trauma, what is the ideal blood product ratio to reduce morbidity and/or mortality in patients requiring transfusion?**

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations

In adult patients presenting to the ED with blunt trauma, use a fresh frozen plasma (FFP): platelet: packed red blood cells (PRBC) ratio from1:1:1 to 1:1:1.5 to reduce 24-hour mortality without increasing morbidity.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

- Administration of recommended blood product ratios within 6 hours of resuscitation may decrease 24-hour mortality, exsanguination, and hypothermia.
- The identification of optimal goal of blood product ratio will allow trauma centers and blood banks to protocolize massive transfusion protocols (MTPs) to improve consistency of high-quality care.

Potential Harm of Implementing the Recommendations

Increased FFP and platelet ratios may create new needs and stress placed on the existing limited blood product supply.

Key words/phrases for literature searches: nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, blood transfusion, blood product, blood product ratio, leukocyte transfusion, blood platelet transfusion, massive transfusion protocol, autologous blood transfusion, erythrocyte transfusion, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020, and May 20, 2021.

Study Selection

Eight hundred six articles were identified in the searches. Two hundred ninety articles were identified from the search results for further review. After grading for methodologic rigor, 0 class I studies, 0 class II studies, and 5 class III studies were included for this question.

Text

Hemorrhage is a leading cause of death in blunt trauma. MTPs have been utilized to prevent mortality from hemorrhage. Massive transfusion is defined as >10 units of packed red cells over 24 hours.[32-43] Massive transfusion is an independent risk factor for mortality and morbidity and is associated with acute coagulopathy and severe immunologic responses, leading to multiorgan failure and acute respiratory distress syndrome.[44-53] Acute coagulopathy is also a complication in 2% to 34% of patients with blunt trauma receiving MTP and is an independent factor associated with mortality.[45,54,55] Ratios of blood product, specifically FFP:platelets:PRBC, administration in MTP has

evolved over time. Additionally, damage control surgery has changed the utilization of blood products and in recent times, FFP:platelet:PRBC ratios of 1:1:1 are frequently employed in clinical practice based on US military experience.[56-58] Given the complex nature of MTPs, the proportion of FFP:platelets:PRBC is a topic of interest, and varying ratios are employed and recommended by different societies.[59] We performed a comprehensive review of the medical literature comparing adult patients with trauma requiring transfusions in patients with blunt trauma. The literature review yielded 806 publications. Articles were excluded due to poor study design, incorrect population, incorrect intervention, or incorrect outcomes. Of the 25 remaining publications, 20 were deemed to be low relevance with regard to the critical question or low methodologic as assessed by the methodologists and 5 level III studies are included in this policy.[60-64]

To understand the methods and findings of these studies, a point of mathematical nomenclature used in this literature must be clarified. When discussing ratios of units of FFP or platelets to PRBC, a ratio of 1:1 is greater than 1:2, just as 1 divided by 1 is greater than 1 divided by 2. This applies to the nomenclature for multiple ratios as well. Hence a ratio of FFP:platelets:PRBC of 1:1:1 is greater than 1:1:1.5 which is greater than 1:1:2.

The first study by Brown et al[60] was a multicenter prospective cohort study. In this study, a high FFP:PRBC ($\geq$1:1.5) ratio was analyzed as a time-dependent variable and at 6 hours was independently associated with reduction in 6-, 12- and 24-hour mortality, and a high FFP:PRBC ($\geq$1:1.5) ratio at 12 hours was independently associated with a mortality reduction at 12 and 24 hours. In addition, a high ratio at 24 hours was associated with a decline in mortality at 24 hours. Similarly, high platelets:PRBC ($\geq$1:1.5) ratio was associated with an independent reduction in mortality.

A high ratio of FFP:PRBC or platelets:PRBC at 6 and 12 hours did not increase the risk of developing multiorgan failure, nosocomial infection, or acute respiratory distress syndrome during admission. This study showed that early resuscitation using high FFP:PRBC and platelet:PRBC ratios leads to reduced mortality at 6 hours and throughout the first 24 hours from injury. When time-dependent analysis was performed, an increasing FFP:PRBC and platelet:PRBC ratio prevents early death from hemorrhage.[60]

The study by Reynolds et al[61] was also a multicenter prospective cohort study of 1,961 patients, and it suggests that even in those patients requiring massive transfusions who received a high FFP/PRBC transfusion ratio, a temperature lower than 34 °C was not a significant independent risk factor for mortality (OR 1.8, 95% CI 0.9 to 33.5) as opposed to the low FFP:PRBC ratio group with a more than 2-fold higher risk of mortality (OR 2.2, 95% CI 1.1 to 4.2). Hypothermia is common in temperature-induced coagulopathy patients and is associated with a greater independent risk of mortality of more than 85% in patients requiring MTP. This study suggests that the effect of hypothermia can be controlled by the means of adequate resuscitation with a high FFP:RBC ratio and may be the underlying mechanism behind the mortality benefit in the high ratio group.[61]

Hagiwara et al[62] conducted a retrospective observational study across 15 sites in Japan with 189 patients with blunt trauma, and propensity score matching was performed to compare the 2 groups (FFP: PRBC ratio of 1 or more within the first 6 hours and FFP:PRBC ratio of less than 1 within the first 6 hours). Patients with an FFP:PRBC ratio of 1 or more within the first 6 hours had significantly better survival, with an unadjusted hazard ratio of 0.44 and an adjusted hazard ratio of 0.29. Patients with blunt trauma transfused with an FFP:RBC ratio of 1 or more within the first 6 hours after admission had an unadjusted hazard ratio of about 0.4 (95% CI 0.25 to 0.74) and an adjusted hazard ratio of 0.29 (95% CI 0.14 to 0.62). This study suggested a benefit to an early administration of FFP in patients with severe blunt trauma requiring blood transfusion.

Holcomb et al[63] conducted the Pragmatic Randomized Optimal Platelet and Plasma Ratios Randomized clinical trial, a pragmatic, phase 3, multisite, randomized clinical trial of 680 severely injured patients across 12 level I trauma centers. In this trial, administration of FFP, platelets, PRBC in a 1:1:1 ratio compared with a 1:1:2 ratio had no significant differences in 24-hour mortality and 30-day mortality. However, there was a higher rate of hemostasis in the 1:1:1 group and fewer deaths in 24 hours due to exsanguination.

The last study that met inclusion was Sperry et al,[64] a multicenter prospective cohort study evaluating clinical outcomes in blunt injured adults with hemorrhagic shock patients who received an FFP:PRBC transfusion ratio $\geq$1:1.5 compared with patients who received <1:1.5. Patients receiving greater ratios of FFP to PRBC had a significant lower risk of inhospital mortality following massive transfusion, which was most pertinent for mortality within the first 48 hours. Cox proportional hazard regression revealed that receiving a high ratio of FFP:PRBC was independently associated with lower mortality when adjusted for likely confounders (HR 0.48, 95% CI 0.3 to 0.8). This study showed a dose-response relationship for mortality such that as the FFP:PRBC ratio became smaller (less FFP relative to PRBCs), the patients who received minimal or no FFP had the highest early 24-hour mortality.

In adult patients presenting to the ED with blunt trauma, an FFP:platelet:PRBC ratio between 1:1:1 and 1:1:1.5 is ideal to reduce 24-hour mortality. This ratio also decreases exsanguination and FFP:PRBC ratios ≥1:1.5 reduces risk of death by hypothermia in the first 24 hours of resuscitation. FFP should be given within first 6 hours of resuscitation with goal of FFP:RBC ≥1:1.5.

Brief Summary

The literature has recently supported the use of 1:1:1 FFP:platelet:PRBC ratio. There is no significant difference in morbidity in either the 1:1:1 or 1:1:1.5 groups.

Future Research

Laboratory-guided resuscitation has been shown to have equivocal results with 1:1:1 FFP: platelet:RBC ratio with less utilization of non-PRBC blood products, which may not universally available. Future trials to be designed with ≥1:1:1.5 FFP:platelet:RBC ratio, whole blood, and laboratory-guided resuscitation. Furthermore, research is advancing the use of whole blood resuscitation as an alternative to component blood products.[65] However, currently only 24.5% of ACR-verified trauma centers have the capability and resources to transfuse whole blood.[66] Additional research and blood bank capabilities are needed to advance this practice.

4. **In adult patients presenting to the ED with blunt trauma, does REBOA reduce morbidity and/or mortality in arrested or periarrest patients compared to ED thoracotomy?**

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations.

In arrested or periarrest adult, patients with blunt trauma, do not routinely use REBOA over ED thoracotomy.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

Prevention of potential harms of REBOA if no benefit.

Potential Harm of Implementing the Recommendations

Select, as of yet undefined, populations may benefit from REBOA.

Key words/phrases for literature searches: nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, REBOA, Resuscitative endovascular balloon occlusion of the aorta, Cardiac Arrest, Thoracotomy, cardiopulmonary arrest, asystoles, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020, and May 20, 2021.

Study Selection

Eight hundred articles were identified in the searches. One hundred and sixty-eight articles were identified from the search results for further review; 30 articles were sent to the methodologists for grading. After grading for methodologic rigor, 0 class I studies, 0 class II studies, and 2 class III studies were included for this question.

Text

Traumatic arrest from noncompressible abdominopelvic hemorrhage due to blunt trauma has a high mortality.[67,68] Hemorrhage control using ED resuscitative thoracotomy (RT) results in low survival rates in arrested or peri-arrest patients with blunt trauma.[69] REBOA has been proposed as an alternative to RT. This technique serves as a method of temporary hemorrhage control as a bridge to definitive treatment. It has seen application in both military and civilian trauma care.[70] The procedure uses common femoral artery catheter access to inflate an occlusive balloon at different zones of the aorta. The aorta can be divided into 3 zones: zone 1 is from the left subclavian artery to the celiac trunk, zone 2 is below the celiac and suprarenal, and zone 3 is infrarenal to the aortic bifurcation. REBOA is deployed in zone 1 for severe intra-abdominal or retroperitoneal hemorrhage, whereas zone 3 is used for pelvic hemorrhage.[71]

In the early observational evaluation of REBOA in trauma, its use was associated with improved mortality.[69,72-86] However, these studies' design and execution commonly suffered survival bias and bias by indication, as the patients undergoing RT typically had cardiac arrest in these cohorts.[70] These studies often also included penetrating and patients with blunt trauma, making the determination of value suspect in patients with blunt trauma specifically. Due to these confounders, it is unclear whether these nonrandomized, observational studies compared 2 similar populations and were ultimately graded X in our evaluation.

We performed a comprehensive review of the medical literature comparing REBOA to RT in arrested and peri-arrest patients with blunt trauma. The literature review yielded 800 publications. Articles were excluded due to poor study design, incorrect population, incorrect intervention, or incorrect outcomes. Of the 32 remaining publications, 30 were excluded using our systematic grading criteria, and 2 level III studies are included in this policy.[67,68]

In the first study by Aso et al[68] in 2017, the investigators performed a retrospective review of the National Inpatient Database in Japan from 2010 to 2014. Two hundred and fifty-nine patients with trauma, aged older than 15 years,

with uncontrolled hemorrhagic shock were included in their analysis. Penetrating thoracic patients with trauma were excluded. Importantly, the authors used propensity scoring to address the potential biases of prior observational studies. The primary outcome was mortality and secondary outcomes included ventilator-free days, total hospitalization costs, total amount of fluid resuscitation, and total transfusion within day 1. Using the propensity score-adjusted analysis, this study found no benefit with REBOA versus RT in the primary outcome (HR 0.94, 95% CI 0.60 to 1.48) or in the secondary outcomes. The authors concluded that inhospital outcomes were not significantly different between REBOA and RT in patients with trauma with uncontrolled hemorrhage.[68]

The second study graded level III, by Joseph et al[68] (2019) was conducted in the United States. The authors performed a case-control retrospective analysis of the 2015 to 2016 American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) dataset using an advanced propensity score matching process. This larger study evaluated 420 total patients, of which 140 REBOA patients (cases) were matched 1:2 with 280 non-REBOA patients (controls). The outcome measures were rates of mortality and complications. The mortality was higher in the REBOA group (35.7% versus 18.9%, P=.01), and specific complications, including acute kidney injury and lower extremity amputation, were also higher (10.7% versus 3.2%, P=.02 and 3.6% versus 0.7%, P=.04, respectively). Application of this study is limited by the fact that it included penetrating trauma, albeit 92.1% were patients with blunt trauma. The authors concluded that REBOA was associated with higher mortality and acute kidney injury and lower leg amputation rates.[68]

In addition to the level III evidence that does not show a benefit from REBOA in this patient population, REBOA requires a multidisciplinary team with structured protocols, policies, education, and quality assessments. The vast majority of trauma centers in the United States do not have REBOA capabilities, much less the majority of EDs.[70] Given that there is no demonstrated benefit and may be harmful, it is unlikely to be cost-effective to stand up these programs for use in this broadly defined blunt trauma population of patients. There are existing REBOA programs that will continue to refine a potential patient population that benefits from this intervention. Our recommendations do not apply to a military setting or to penetrating patients with trauma.

Summary

There are limitations, such as the inclusion of some penetrating patients with trauma, to the highest quality literature available to determine if there is benefit of REBOA versus RT. The best available evidence concludes that REBOA is associated with no benefit and potential harm.[67,68] Consequently, we do not recommend its routine use in arrested and periarrest adult patients with blunt trauma.

Future Research

At the time of this writing, there are ongoing trials of REBOA in other disease states, including postpartum hemorrhage and nontraumatic out-of-hospital cardiac arrest. These studies combined with further insights from subgroups of patients with blunt trauma may give insight into a blunt trauma population that may benefit. A randomized clinical trial of REBOA in a subpopulation of arrested and periarrest adult blunt trauma patients would be necessary to recommend its routine use.

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members for this topic.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

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Appendix E1. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix E2. Approach to downgrading strength of evidence.

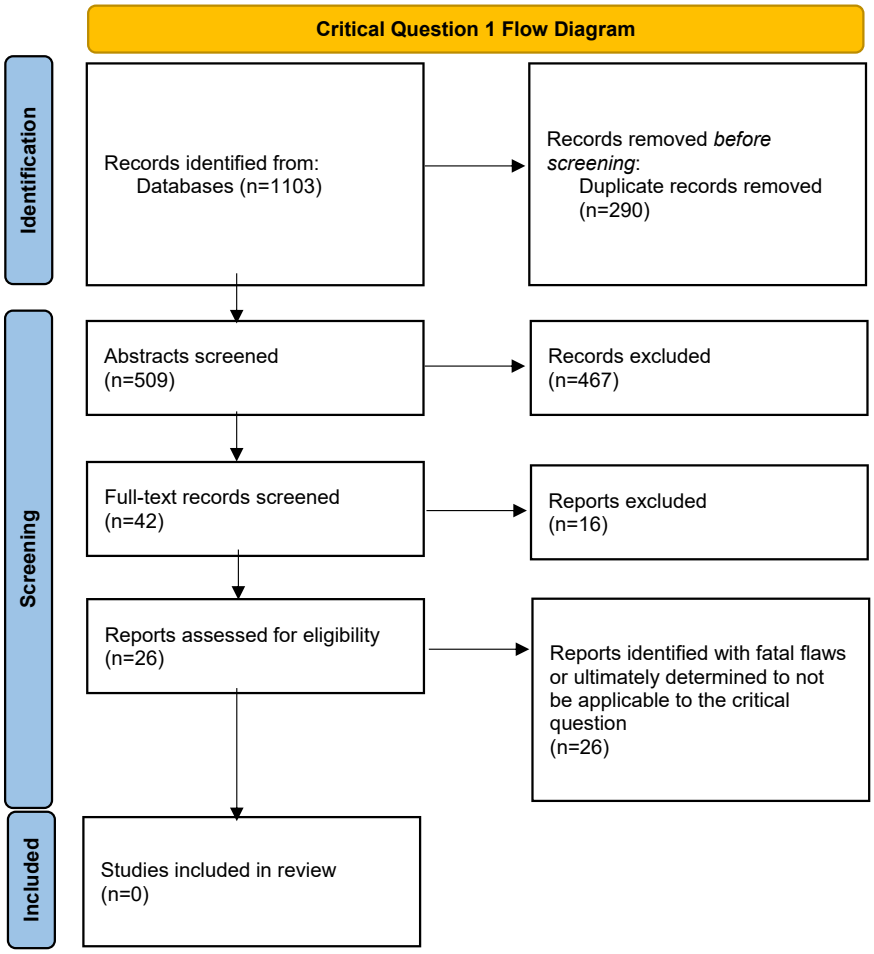
	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

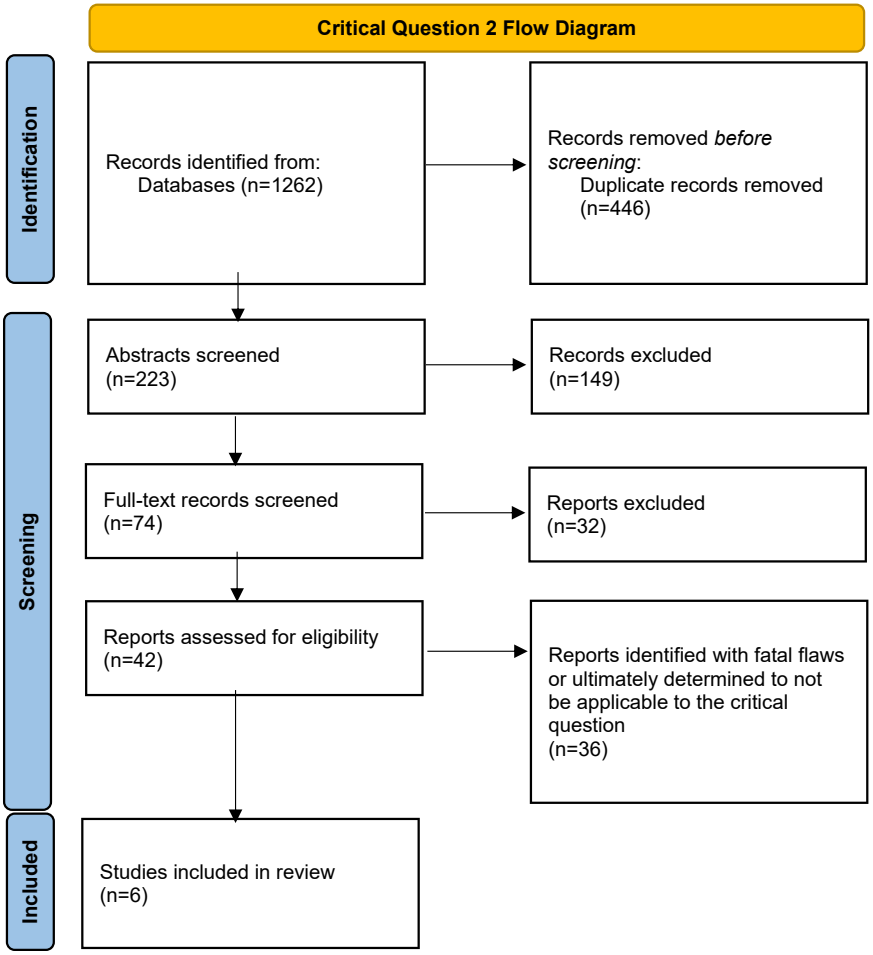
Appendix E3. Likelihood ratios and number needed to treat.*

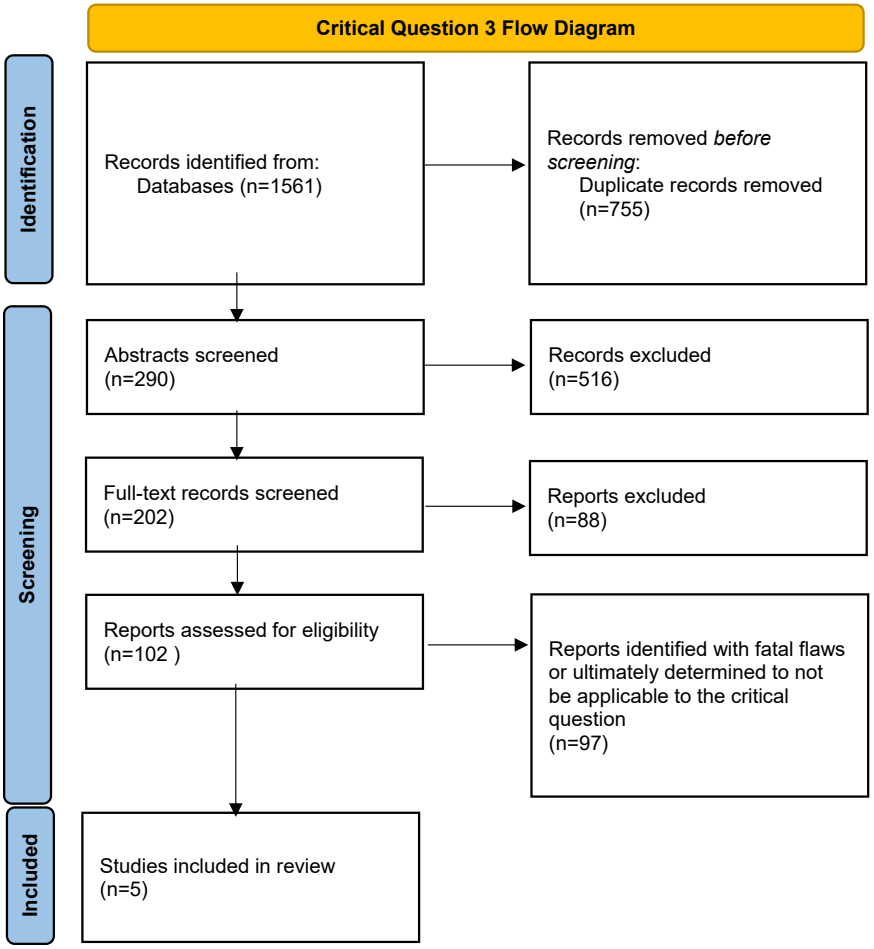
LR (+)	LR (–)	
1.0	1.0	Does not change pretest probability
1–5	0.5–1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

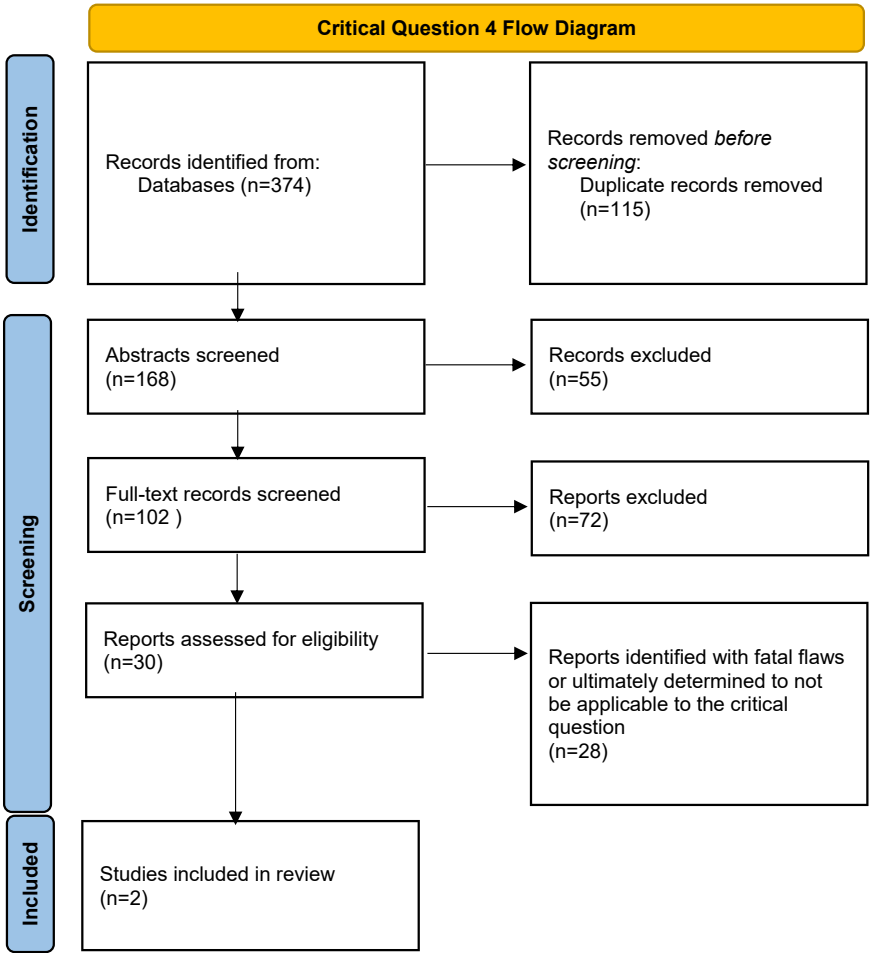
LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).

APPENDIX E4. PREFERRED REPORTING ITEMS FOR SYSTEMATIC REVIEWS AND META-ANALYSES (PRISMA) FLOW DIAGRAMS.[7]




Critical Question 2 Flow Diagram
Identification
Screening
Included
Records identified from:
Databases (n=1262)
Records removed *before screening*:
Duplicate records removed
(n=446)
Abstracts screened
(n=223)
Records excluded
(n=149)
Full-text records screened
(n=74)
Reports excluded
(n=32)
Reports assessed for eligibility
(n=42)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n=36)
Studies included in review
(n=6)


Critical Question 3 Flow Diagram
Identification
Records identified from:
Databases (n=1561)
Records removed *before screening*:
Duplicate records removed
(n=755)
Screening
Abstracts screened
(n=290)
Records excluded
(n=516)
Full-text records screened
(n=202)
Reports excluded
(n=88)
Reports assessed for eligibility
(n=102)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n=97)
Included
Studies included in review
(n=5)


Critical Question 4 Flow Diagram
Identification
Records identified from:
Databases (n=374)
Records removed *before screening*:
Duplicate records removed
(n=115)
Screening
Abstracts screened
(n=168)
Records excluded
(n=55)
Full-text records screened
(n=102)
Reports excluded
(n=72)
Reports assessed for eligibility
(n=30)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n=28)
Included
Studies included in review
(n=2)

Evidentiary Table.

Author & Y Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Ahmed et al[16] (2020)	III for Q 2	Retrospective review of National Trauma Database (NTDB). Also - multivariate logistic regression model on clinical variables related to patient mortality - Receiver-operating characteristic (ROC) curve was fit and area under the curve (AUC) with sensitivity analysis	Pts- ground level from home, 65 y + with normal systolic blood pressure (SBP) [Ref 90 –160 mmHg], PR [Ref: 60-100, GCS 15 Other variables: sex, race and ethnicity, respiratory rate (RR), ISS, existing comorbidities including: smoking, chronic kidney disease (CKD), cerebrovascular accident/neurologic deficit (CVA), diabetes mellitus (DM), hypertension (HTN) Objective: to determine incidence of inhospital mortality and develop validated risk model to identify high risk	-40,800 pts-938 (2.3%) pts died in the hospital; 39,862 (97.7%) survived – Sig dif based on: Age (median [IQR]) (82.0 [77.0, 86.0], vs. 80.0 [73.0, 85.0],p.001 sex (male: 49.8% vs. 30.6%,P.001). ISS (median [IQR]: 9.0 [9.0, 14.0] vs 9.0 [4.0, 9.0], *P*<.001 Sensitivity analysis showed higher rate of comorbidities, including CKD and HTN, (7.5% vs 2.8%, and 67.3% vs 62.5%, all *P*<.05),. Tested model for Higher level of care (LOC) (trauma center designation I & II) vs lower level and impact on mortality - none found	Brain injury-most frequent injury found (21.86% vs 21.48% -higher brain Hemorrhage and cervical spine injury in group that died Femoral neck or intertrochanteric Fractures - no difference between groups **Normal physiological measures at the scene do not eliminate the risk of inhospital mortality in geriatric patients who fell from a ground level height at home - 2.3% incidence of inhospital mortality- older age, male gender, lower SBP, higher HR, and RR, ISS, and a history of CKD, DM, and HTN requiring medications were associated with a higher risk of inhospital mortality

Anantha et al[30] (2021)	III for Q 2	Single-center retrospective Also- multivariable logistic regression analysis done to identify predictors of appropriate triage Also multivariable logistic regression analysis to evaluate variables independently associated with appropriate triage	Included all (ISS >15), ≥65 y (between 1/14 and 9/17. Undertriage- lack of trauma team activation (TTA) despite presence of severe injuries. Primary outcome- inhospital mortality; secondary outcomes - mortality within 48 h of admission and urgent hemorrhage control or shock (need for transfusion) or lactate being ≥4.0 mmol/L.	1,039 pts, 628 (61%) did not undergo TTA. Undertriaged pts were older, had more comorbidities (stroke, dementia and bleeding disorders Inhospital mortality was 5% vs 31% (P<.0001). 1% of undertriaged pts needed urgent hemorrhage control, vs to 6% appropriately triaged group (P<.0001). 1% undertriaged patients died within 48 hours vs 19% appropriately triaged group (P<.0001). Predictors of appropriate triage: GCS, pulse rate, SBP, lactic acid, ISS, shock, and absence of dementia, stroke, or alcoholism	utility of ISS - a retrospectively collected variable may - not useful for triage
Brown et al[29] (2015)	III for Q 2	Retrospective review- Data extraction National trauma data bank	Used SBP of 110 mmHg instead of 90 mmHg to determine if geriatric pts (>65) have mortality rates similar to those with lower BP Used physiologic (out-of-hospital vital signs (VS), GCS and anatomic criteria (from International Classification of Diseases-9th Rev.	438,828 geriatric pts Geriatric pts newly triaged with SBP 90 to 109 mmHg odds of mortality same as those with SBP <90 mmHg (Adjusted OR 1.03; 95% CI) Also had similar discrimination and better goodness of fit using SBP <110 and those with SBP range (90-109) had odds of mortality similar to those with SBP <90 (Adjusted OR1.02; 95% CI) Using SBP of <110 mmHg for trauma	Majority of pts were adults not geriatric however still large number of geriatric pts. Conclusion that older people with BP of 109-90 have same mortality as those with BP of 90 mmHg suggests they warrant trauma center care

			(ICD-9 codes) to determine placement into trauma center Trauma center need based on ISS >15, ICU admission, urgent surgery and death as 1 outcome. Mortality was secondary outcome	center improves undertriage in geriatric pts but not in adults. It improves sensitivity at the expense of specificity. Characteristics of the Geriatric and Adult Cohorts **Geriatric Cohort n=438,828** / **Adult Cohort n=1,117,116** / ***P*** Age, median (IQR), y: 80 (73-86) / 37 (25-50) / <.01 Sex, male, %: 39 / 71 / <.01 Blunt injury, %: 99 / 85 / <.01 Out-of-hospital time, median (IQR): 48 (37-70) / 44 (32-67) / <.01 Out-of-hospital SBP, median (IQR): 144 (128-164) / 131 (118-146) / <.01 Out-of-hospital SBP < 90 mmHg, %: 2.7 / 5.3 / <.01 Out-of-hospital SBP <110 mmHg, %: 9.0 / 15.5 / <.01 ISS, median (IQR): 9 (4-10) / 6 (4-13) / <.01 TCN, %: 32 / 40 / <.01 Mortality, %: 4.4 / 3.8 / <.01	
Hung et al[31]	III	10 y single-	Patients aged ≥55 y in	2,218 patients 30-d mortality was 7.5%	TTA is tiered. First tier 2

(2018)		center cohort study – retrospective review trauma registry in Hong Kong 2006-2015	trauma registry Separated ages 55-70, and >70 y. Outcomes: death within 30 d; the need for surgery; or the need for ICU care	for aged 55-70 y and 17.7% for >70 y. The undertriage rate was 59% for age 55 y –70 y, and 69.1% for those aged >70 y.	emergency medicine physicians. Second tier -2 general surgeons, an orthopedic surgeon, and an ICU physician. Sensitivity of TTA criteria decreases as age increases- Justifies need for specific criteria for pts aged ≥70 y.
Ichwan et al[28] (2015)	III for Q 2	Retrospective review of Ohio trauma registry	Used >70 y of age to define geriatrics Triage criteria predicted need for trauma care	Geriatric triage criteria applied increased sensitivity but not specificity Mortality was similar between 2 groups 6.8 (adult) vs 9.3 (geriatric) Appeared geriatric patients were less severely injured (lower ISS and lower ICU care) but mortality rate 6.8 in geriatrics vs 9.3 in adults Increased geriatric trauma from 42%-57% Sensitivity increased (61%-93%) but specificity decreased (61%-49%) have CI	Use of geriatric trauma criteria improved sensitivity of identifying need for trauma center
Lim et al[27] (2020)	III	Retrospective cohort from 1/2016 to 12/2017	All patients aged >18 y with ISS ≥16) Goal was to validate Korean Trauma Acti-vation (KTAS) Score which has 4 levels and to analyze the prognostic performances of KTAS in	827 patients, 30-d mortality observed in 14.9% (n=123). Patients in the survivor group were younger and had higher values of both ISS and shock index. Survivors (n=704) Age (y) 59.1 (46.1-72.0) Nonsurvivors (n=123) Age (y) 69.1 (57.0-76.1)	Mortality of older adult was increased by 2.7 % for each year of life

			30-d		
Brown et al[29] (2012)	III for Q 3	Multicenter prospective cohort study of adults, 7 institutions during a 8-y period (2003-2010)	Inclusion criteria: blunt trauma, presence of out-of-hospital or ED hypotension (SBP] <90 mmHg) or an elevated base deficit (BD) (>6 mEq/L), blood transfusion requirement within the first 12 h, and any body region exclusive of the brain with an abbreviated injury score (AIS) of 2 or higher, allowing exclusion of patients with isolated traumatic brain injury. Patients aged <18 y >90 years and those with cervical spinal cord injury were also excluded from enrolment. High FFP/PRBC (≥1:1.5) and PLT/PRBC (≥1:9) ratios at 6, 12, and 24 hours were compared with low ratio groups. Multiple-organ failure (MOF) was outcome	Of the 1,961 subjects in the cohort, 604 met massive transfusion (MT) inclusion criteria and constituted the study cohort. For the entire cohort, the 6-, 12-, and 24-h mortality was 8.6%, 12.1%, and 13.1%, respectively. These subjects required a median of 16.3 U (IQR, 12.5±25.7) of packed red blood cells (PRBC), 8.3 U (4.3±13.4) of fresh frozen plasma FFP, and 1.5 U (0.67±2.5) of platelets (PLT) during the first 24 hours. Overall, 55.3% developed multiorgan failure (MOF), 48.2% developed NI, and 29.8% developed ARDS. A high FFP/PRBC ratio at 6 h was associated with an independent mortality reduction at 6, 12, and 24 h. Similarly, a high FFP/PRBC ratio at 12 h was associated with an independent mortality reduction at 12 h and 24 h, and a high ratio at 24 h was associated with a mortality benefit at 24 h When FFP/PRBC ratio was analyzed as a time-dependent covariate, a higher ratio was associated with an independent reduction in mortality (Table 3). Similarly, when PLT/PRBC ratio was analyzed as a time-dependent covariate, a higher ratio was associated with an independent reduction in mort A high ratio of FFP/PRBC or PLT/PRBC at 6 h was not independently associated	Despite similar degrees of early shock and coagulopathy, high FFP/PRBC and PLT/PRBC ratios are associated with a survival benefit as early as 6 h and throughout the first 24 h. Moreover, this held true at all time points at which ratio groups were determined. Most importantly, when FFP and PLT to PRBC ratios were analyzed as time-dependent variables, an increasing ratio was independently associated with a mortality reduction during the first 24 h from injury. Early resuscitation using high FFP/PRBC and PLT/PRBC ratios results in reduced mortality at 6 h and throughout the first 24 h from injury. When time-dependent effects of early component transfusion are accounted for, an increasing FFP/PRBC and PLT/PRBC ratio remains protective against early

				with the risk of developing MOF, NI, or ARDS during admission. Similarly, a high FFP/PRBC or PLT/PRBC ratio at 12 h or 24 hours was not associated with any complication outcome studied ($P<.05$)	death from hemorrhage.
Reynolds et al[61] (2012)	III for Q 3	Multicenter prospective cohort study of adults with blunt injury with hemorrhagic shock 7 institutions during a 6-y period (December 2003-January 2010)	Inclusion criteria: blunt trauma, presence of out-of-hospital or ED systolic hypotension (<90 mmHg) or an elevated base deficit (<6 mEq/L), blood transfusion requirement within the first 12 h, and any region of the body excluding the brain with an Abbreviated Injury Scale score of 2 or higher, allowing the exclusion of patients with isolated traumatic brain injury. Patients <16 y or >90 years and those with cervical spinal cord injury were also excluded from enrolment. For the current secondary data analysis, only patients	Of the 1,961 patients with blunt injury enrolled during the study period, 604 (31%) required 10 U or more of PRBCs in the first 24 h after injury and constituted the primary study population. Regression analysis revealed that temperature in an MT cohort (lowest 24-h measurement as a continuous variable) was associated with a significantly greater independent risk of mortality after controlling for differences in demographics, injury severity, shock parameters, and transfusion and resuscitation confounders (OR 0.82; 95% CI 0.7Y0.9; $P=.013$). An interpretation of this OR suggests that a greater independent risk of mortality of more than 18% is associated with every decrease in the temperature level (-C) of a patient requiring MT in the first 24 h after injury. When stratified by the period of enrolment, a temperature lower than 34-C remained a significant independent predictor of mortality with more than a	This analysis verifies that hypothermia, nadir temperatures lower than 34-C in the first 24 hours, is common and independently associated with a greater independent risk of mortality of more than 85% on patients requiring MT. These associations were most robust on patients who received a low FFP/PRBC transfusion ratio and were negated in the recent enrolment period (2007-2010) in which a more aggressive blood component resuscitation strategy has been previously documented. These data suggest that the clinical significance of hypothermia may be affected by the way a patient is resuscitated and may be as important as

			requiring MT, defined as 10 U or more of PRBCs in the first 24 h after injury, were selected for analysis. Our primary outcomes for the analysis were inhospital mortality, MOF development, and nosocomial infection (NI).	twofold higher risk of mortality in the early period (OR 2.24; 95% CI 1.2Y4.1; *P*=.012) When stratified by the attainment of a high FFP/PRBC transfusion ratio (>1:2) in the first 24 hours versus a low FFP/PRBC transfusion ratio (<1:2), a temperature lower than 34-C remained a significant independent predictor of mortality in the low FFP/PRBC ratio group with more than a twofold higher risk of mortality (OR 2.2; 95% CI 1.1±4.2; *P*=.021). In those patients requiring MT who received a high FFP/PRBC transfusion ratio, a temperature lower than 34-C was no longer a significant independent risk factor for mortality (OR 1.8; 95% CI 0.933.5; *P*=.100).	addressing the early coagulopathy in these patients
Hagiwara et al[62] (2016)	III for Q 3	retrospective observational study, 15 medical institutions participated from Japan, subgroup study from the Japanese	189 blunt trauma patients ≥18 y with an ISS ≥16 requiring RBC transfusions within the first 24 h. cutoff values of the FFP/RBC ratio for outcome.	A total of 139 blunt trauma patients survived and were discharged alive, and 62 blunt trauma patients died FFP/RBC ratio at 6 h for survivor 1.0 [0.5, 1.3] vs 0.8[0.6, 1.0], *P* value .066 FFP/RBC ratio at 24 h for survivor 1.0 [0.6, 1.3] vs 0.83[0.6, 1.1], *P* value .177	Blunt trauma patients transfused with an FFP/RBC ratio ≥ 1 within the first 6 h after admission had a hazard ratio of about 0.4. In other words, their risk of death was reduced by about 60%. Transfusion of an FFP/RBC ratio ≥ 1 within

		Observational Study for Coagulation and Thrombolysis in Early Trauma (J-OCTET) January and December 2012	cutoff values of the FFP/RBC ratio for outcome.	Cox proportional hazards analysis of time to death FFP/RBC ratio ≥1 within 6 h 0.29 (0.14-0.62) *P*=.001 FFP/RBC ratio ≥1 within 24 h 1.27 (0.59-2.74) *P*=.540 PSM was performed to compare the 2 groups (FFP/RBC ratio ≥1 within the first 6 h and FFP/RBC ratio <1 within the first 6 h). The propensity score was created from the following 13 covariates: age, fluid therapy before admission, use of anticoagulant/antiplatelet drugs, ISS, use of tranexamic acid, PR, SBP, RR, white blood cells (WBC), Hb, PLT, creatine phosphokinase (CPK), and base excess (BE). Patients with an FFP/RBC ratio ≥1 within the first 6 h had significantly better survival, with an unadjusted hazard ratio of 0.44 and an adjusted hazard ratio of 0.29 (adjusted by all variables in Table 2).	the first 6 h was associated with the outcome of severe blunt trauma patients with ISS ≥ 16 and needed a transfusion within 24 h. The present results suggest that early aggressive administration of FFP may be crucial for resuscitation in patients with severe blunt trauma requiring blood transfusion

Holcomb et al[63] (2015)	III for Q 3	Pragmatic, phase 3, multisite, randomized clinical trial at 12 level I trauma centers in North America August 2012 and December 2013	Inclusion criteria: patient having at least 1 U of any blood component transfused prior to hospital arrival or within 1 hour of admission and prediction by an Assessment of Blood Consumption score of 2 or greater or by physician judgment of the need for a massive transfusion (defined as =10 U of RBCs within 24 h).	No significant differences in mortality were detected at 24 h (12.7% in the 1:1:1 group vs 17.0% in the 1:1:2 group; difference, −4.2% [95% CI, −9.6% to 1.1%) or at 30 d (22.4% vs 26.1%, respectively; difference, −3.7% [95% CI, −10.2% to 2.7%) range of intent-to-treat P values computed for all possible combinations of 30-d outcomes for the 4 patients with missing values did not change these results. Exsanguination, the predominant cause of death within the first 24 h, was decreased in the 1:1:1 group (9.2%) vs the 1:1:2 group (14.6%) (difference, −5.4% [95%	Transfusing patients based on an empirical ratio rather than guided solely by laboratory data (goal-directed) is considered controversial by some researchers. This trial was not designed to study this question. However, after the controlled, ratio-driven intervention was completed, clinicians treated patients based on local laboratory-guided standard-of-care practice. It appears that laboratory-

			Exclusion: Received a lifesaving intervention from an outside hospital or health care facility, had devastating injuries and expected to die within 1 hour of admission (eg, lethal traumatic brain injury), directly admitted from a correctional facility, required a thoracotomy prior to receiving randomized blood products in the ED, <15 years or weighed <50 kg if age unknown, known pregnancy in the ED, had burns covering >20% total body surface area Suspected inhalation injury, Received >5 consecutive minutes of cardiopulmonary resuscitation (with chest compressions) prior to arriving at the hospital or within the ED, known do-not-resuscitate order prior to randomization, Enrolled in a	CI, −10.4% to −0.5%], *P*=.03); the median time to death due to exsanguination was 106 min (interquartile range [IQR], 54-198 min) and 96 minutes (IQR, 43-194 min), respectively. From 24 h through 30 d, the numbers of additional all-cause deaths were similar (32 for the 1:1:1 group vs 31 for the 1:1:2 group). Over 30 d, deaths due to exsanguination occurred in 10.7% of patients in the 1:1:1 group vs 14.7% in the 1:1:2 group, whereas deaths due to traumatic brain injury were 8.1% vs 10.3%, respectively. Additional causes of death were infrequent More patients achieved anatomic hemostasis in the 1:1:1 group (86.1% vs 78.1% in the 1:1:2 group, *P*=.006) with a median time of 105 minutes (IQR 64-179 min) vs 100 minutes (IQR 56-181 min), respectively (*P*=.44) in those who achieved anatomic hemostasis During the intervention, patients received median ratios of plasma to RBCs of 1.0 in the 1:1:1 group and 0.5 in the 1:1:2 group. The median ratios of platelets to RBCs during the intervention were 1.5 for the 1:1:1 group and 0.4 for the 1:1:2 group.	directed catching up occurred in the 1:1:2 group with plasma and platelets approaching a cumulative ratio of 1:1:1. Other studies have shown similar results with laboratory-directed resuscitation. This catching up after the completion of randomized blood product transfusion may have decreased the ability to detect differences in mortality at 24 h and 30 d or in the prespecified ancillary outcomes Limitations include power to detect differences smaller than the effect size we considered to be both clinically meaningful and affordable to study when we designed the trial.

			concurrent, ongoing, interventional, randomized clinical trial, Activated the opt-out process for the PROPPR trial (usually by wearing a bracelet given out at a community consent presentation), More than 3 U of red blood cells given before randomization primary outcome: 24 h and 30-d mortality		
Sperry et al[64] (2008)	III for Q 3	Multicenter prospective cohort study evaluating clinical outcomes in blunt injured adults with hemorrhagic shock 7 US institutions, during a 3.5-year period (November 2003-March	Included: blunt mechanism of injury, presence of prehospital or ED systolic hypotension (<90 mmHg) or an elevated base deficit (≥6 meq/L), blood transfusion requirement within the first 12 h, and any body region exclusive of the brain with an AIS ≥2, allowing exclusion of patients with isolated traumatic brain injury.	high F:P ratio, n-102, low F:P ratio, n=313. Of the 1,036 blunt injured patients enrolled during the study period, 415 patients had a blood transfusion requirement of ≥8 units within the initial 12 h after injury, and constituted the study population. In this cohort, 39 patients received no FFP within the first 12 h from injury (FFP: PRBC ratio = 0) despite having a ≥8 unit blood transfusion requirement. The overall mortality for the study population was 33.5%, whereas the overall complication rates for MOF, NI, and ARDS were 56.4%, 46.5%, and 29.6%, respectively.	patients who received an FFP:PRBC transfusion ratio ≥1:1.5, relative to patients who received <1:1.51 FFP:PRBC ratio, had a significant lower risk of inhospital mortality following massive transfusion after controlling for important confounders. This protective effect was most pertinent for mortality within the first 48 h after injury and was independent of the blood transfusion requirement each individual patient

		2007)	Patients aged <16 y or >90 y and those with cervical spinal cord injury were excluded. For the current study, only patients who required ≥8 units of PRBCs within the first 12 hours from injury were included in the analysis. The FFP:PRBC variable, specifically the low F:P group, was then categorized as 1:2 (1:1.51-1:2.50, n=105), 1:3 to 4 (1:2.51-1:4:50, n=111), and ≤1:5 (≤1:4.51, n=97) groups, MOF and mortality were outcomes	Those who received a high F:P ratio had higher ISS score and extremity AIS scores, higher APACHE II scores, lower GCS scores, and had lower nadir core body temperature measurements in the first 24 h postinjury. They also had greater length of stay, ICU, and ventilator requirements; however, these comparisons would be inaccurate if an early mortality difference existed between the 2 groups. Hospital-free days, ICU-free days, and ventilator-free days were compared with adjust for any such difference and confirmed that high F:P ratio patients had fewer hospital-ICU, and ventilator-free days. Although the survival curves overall were not statistically different (log- rank: P=0.119), the mortality rate at day 1 postinjury was significantly lower in the high F:P group (3.9% vs. 12.8%, P=0.012). Although underpowered to be statistically different, when the FFP:PRBC variable was stratified into groups (high F:P, 1:2, 1:3–4, and ≤1:5), similar findings with early separation of the survival curves are apparent at day 1 postinjury, with a dose response being demonstrated, based on the transfused FFP:PRBC ratio	received. Although crude mortality differences between the high F:P and low F:P groups did not reach statistical significance, the significant difference in early (24 h) mortality was likely responsible for this overall mortality risk reduction. As the FFP:PRBC ratio became smaller (less FFP relative to PRBCs) a dose-response relationship was demonstrated for mortality, with those patients who received minimal or no FFP having the highest early mortality.

				high F:P ratio, relative to patients who received a low F:P ratio, was independently associated with a 52% lower risk of mortality (HR 0.48, *P*=.002, 95% CI 0.3-0.8), after controlling for important confounders. The hazard retion for high F:P ratio patients remained significant with the protective effect for mortality being unaltered (HR 0.57, *P*=.026, 95% CI 0.35-0.93). However, a high F:P ratio was associated with almost a twofold higher risk of ARDS, after controlling for important confounders. Study is a secondary analysis of a prospective cohort study looking at the genomic and proteomic response after severe injury and hemorrhagic shock.	
Aso et al[68] (2017)	III for Q 4	Retrospective Cohort of	Trauma patients with uncontrolled	259 patients total • 191 REBOA, 68 RT	Retrospective Registry Study. But propensity

		national Inpatient Database (Japan) 2010-2014.	hemorrhagic shock. Excluded penetrating thoracic trauma. > 15 y old. Propensity score adjusted Outcome: Mortality 2ndary ventilator-free days, total amount of fluid within 1 d, total transfusion within 1 d, total hospitalization costs.	Propensity score-adjusted Cox Regression: Hazards ratio = 0.94 (95% CI 0.60-1.48) No difference in secondary outcomes	score adjusted.
Joseph et al[67] (2019)	III for Q 4	Case Control US single center	Case-control Study using ACS-TQIP	420 REBOA cases matched 280 controls 50/240=35.7% 53/180=18.9%	

BE, base excess; *BP,* blood pressure; *CPK,* creatine phosphokinase; *DM,* diabetes mellitus; *GCS,* Glasgow Coma Scale; *HTN,* hypertension; *ICD,* International Classification of Diseases; *NTDB,* National Trauma Database; *LOC,* level of care; *MOF,* multiorgan failure; *MT,* massive transfusion; *PLT,* platelets; *PRBC,* packed red blood cells; *RBC*, red blood cell; *ROC*, receiver operating characteristic; *TCN*, trauma center need; *TTA*, trauma team activation; *VS*, vital signs; *WBC*, white blood cells.