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Studies of Patients with Trauma-Related Hemorrhage: What Patient Outcomes are Examined and When? A Systematic Review

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Aim: To determine outcomes measured following blood transfusion for the resuscitation of adult patients who experienced trauma-related hemorrhage and compare them based on the timeframe in which they occurred: short-, intermediate-, and long-term.

Design: Systematic Review.

Review methods: We included articles that met the following criteria: published in English between January 1, 2014 and December 31, 2023; with full text available; peer-reviewed; and adult population (≥19 years). Two authors reviewed each title, abstract, and full text for inclusion using the online review tool, Covidence; a third author adjudicated conflicts. A similar method was used for data extraction. Outcomes were categorized as those that occurred in the short-term (day of injury to < 30 days post-injury), intermediate-term (30 days to six months post-injury), and long-term (> six months to one year post-injury). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was used to rate the quality and strength of the reviewed evidence.

Data Sources: PubMED, CINAHL, Scopus, and Embase.

Results: The final analysis included 50 articles. Outcomes were categorized as those related to mortality, pathophysiologic outcomes, indices of coagulopathy, and duration of treatment. All four outcome categories were reported in at least one study during the short-term timeframe. Mortality was reported in 12 articles, the duration of treatment was reported in four articles, and pathophysiologic outcomes were reported in one article during the intermediate-term timeframe. Two articles reported mortality during the long-term timeframe.

Conclusion: Short-term outcomes of patients resuscitated with blood products following a trauma-related hemorrhage have been well studied. Future studies are needed to assess the intermediate- and long-term outcomes of patients following a trauma-related hemorrhage.

Impact: Understanding patient outcomes following trauma-related hemorrhage may help guide clinicians in the provision of care beyond the initial resuscitation period, and ultimately improve patient recovery and rehabilitation.

Keywords: blood transfusion, wounds and injuries, trauma, hemorrhage, patient outcomes

Trauma is a leading cause of death and disability in the United States.[1,2] From 2001 through 2020, the rate of trauma patients who required hospitalization in the United States has increased from 460 to 876 hospitalizations per 100,000 trauma victims.[2] The mortality rate following a traumatic injury was 12.3%, with a survival rate of approximately 88%,[3] resulting in over 2.8 million American trauma survivors annually.[4] With advances in care for trauma patients and high survival rates, patients must adjust to post-injury life. Trauma survivors reported limitations in mobility, self-care, and daily activities.[5] In addition, they reported higher levels of pain compared to the general population.[5] As such, investigators suggest expanding research efforts beyond short-term outcomes such as mortality and including a more holistic approach to trauma survivors' outcomes.[6]

Among those critically injured, uncontrolled trauma-related hemorrhage (TRH) remains the primary preventable cause of death.[7] Therefore, rapid surgical control, ie, finding and stopping the source of hemorrhage, remains the only definitive treatment. However, until the source of bleeding is found, standard emergency treatment for TRH includes transfusion of blood products using one of two initial approaches: whole blood or a combination of blood components

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(packed red blood cells, fresh frozen plasma, platelets) in a ratio that mimics the composition of whole blood. Recent research has not shown a difference in mortality at 48 hours after injury[8–10] up to 30 days following the injury[11,12] of patients who received whole blood versus blood component transfusions. Currently, studies that examine the relationship between transfusion strategy and mortality beyond 30 days post-injury are limited.

Furthermore, the identification of long-term sequelae to trauma and its treatment is essential in optimizing the outcomes of trauma survivors. For example, Choi et al[13] identified that minimizing readmissions of trauma patients is a major goal of a trauma system and that understanding physiologic interventions is vital to preventing readmissions and optimizing a patient's health-related quality of life. With the increase in the rate of patient survival after trauma, a thorough understanding of outcomes beyond 30 days post-injury is paramount. Thus, this systematic review aims to identify the short-, intermediate-, and long-term outcomes of adult patients who received blood transfusions for the treatment of TRH. Therefore, we included articles in our review that used either or both transfusion strategies to create a comprehensive review of outcomes being measured in the current literature.

Methods

Literature Search Method

PubMED, CINAHL, Scopus, and Embase were searched for peer-reviewed research-based studies published between January 1, 2014, to December 31, 2023 using inclusion criteria of adult (19 years old and older) and English-language. The rationale for limiting the search to the last 10 years was threefold. First, the research question for this systematic review was: What patient outcomes are being measured in the TRH literature of patients who are treated for TRH with blood transfusions? We were not searching for evidence of any of the other treatments for TRH. We were simply focusing on the outcomes that were being measured in the blood transfusion research that was conducted in the past 10 years. Second, we wanted the most current literature on these outcomes. Although many patient outcome measures have undergone advancement in the 150 years since Florence Nightingale created her mortality charts,[14] in-hospital mortality was and still is the most common patient outcome measure. Yet, we know that in the last two decades at least, there has been more emphasis on patient-reported outcomes (PROMs) such as quality of life and other longer term measures.[15] We wanted to look beyond in-hospital mortality for intermediate and longer term measures.

Finally, as Booth (2010) claims, in any systematic review there is a trade-off between rigor and relevance.[16] This trade-off depends upon the amount of resources one has to conduct the review versus the information yield from the review and the critical nature of the review results. As this review was concerned with identifying patient outcome measures used in studies and was not aimed at changing a practice based upon evidence, a narrower timeframe is justified. In addition, extending our review by 5 years (doubling the review period), yielded an additional 9 articles, demonstrating the diminishing return for extending this review given the research question.

The PubMed and CINAHL searches were conducted using the MeSH terms: "blood transfusion", "hemorrhage", "treatment outcomes", and "wounds and injuries". The search strategy was "(((("Blood Transfusion"[Mesh]) AND "Hemorrhage"[Mesh]) AND "Treatment Outcome"[Mesh]) AND "Wounds and Injuries"[Mesh]" with the filters for "Adults", "English", and Scopus does not use MeSH terms, therefore, the following search strategy was used: "Blood Transfusion" AND "Hemorrhage" AND "Treatment outcomes" AND "Wounds and Injuries" AND (LIMIT-TO (PUBYEAR, 2023) OR LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019) OR LIMIT-TO (PUBYEAR, 2018) OR LIMIT-TO (PUBYEAR, 2017) OR LIMIT-TO (PUBYEAR, 2016) OR LIMIT-TO (PUBYEAR, 2015) OR LIMIT-TO (PUBYEAR, 2014)) AND (LIMIT-TO (EXACTKEYWORD, "Adult")) AND (LIMIT-TO (LANGUAGE, "English")). Additionally, Embase uses Emtree terminology, and the following search strategy was used: "blood transfusion"/exp OR "blood transfusion" AND "injury" AND "treatment outcome" and "bleeding" AND [English]/lim AND ([adult]/lim OR [aged]/lim OR [very elderly]/lim) AND [2014–2023]/py.

A total of 455 studies were returned, and 112 duplicate studies were removed, leaving 343 studies for title and abstract review. Following the removal of 241 studies during the title and abstract review, we performed a full-text review of the remaining 102 studies; 50 studies remained for data extraction. See Figure 1, PRISMA Diagram, for a summary of the review process. See Table 1 for a list of included studies.

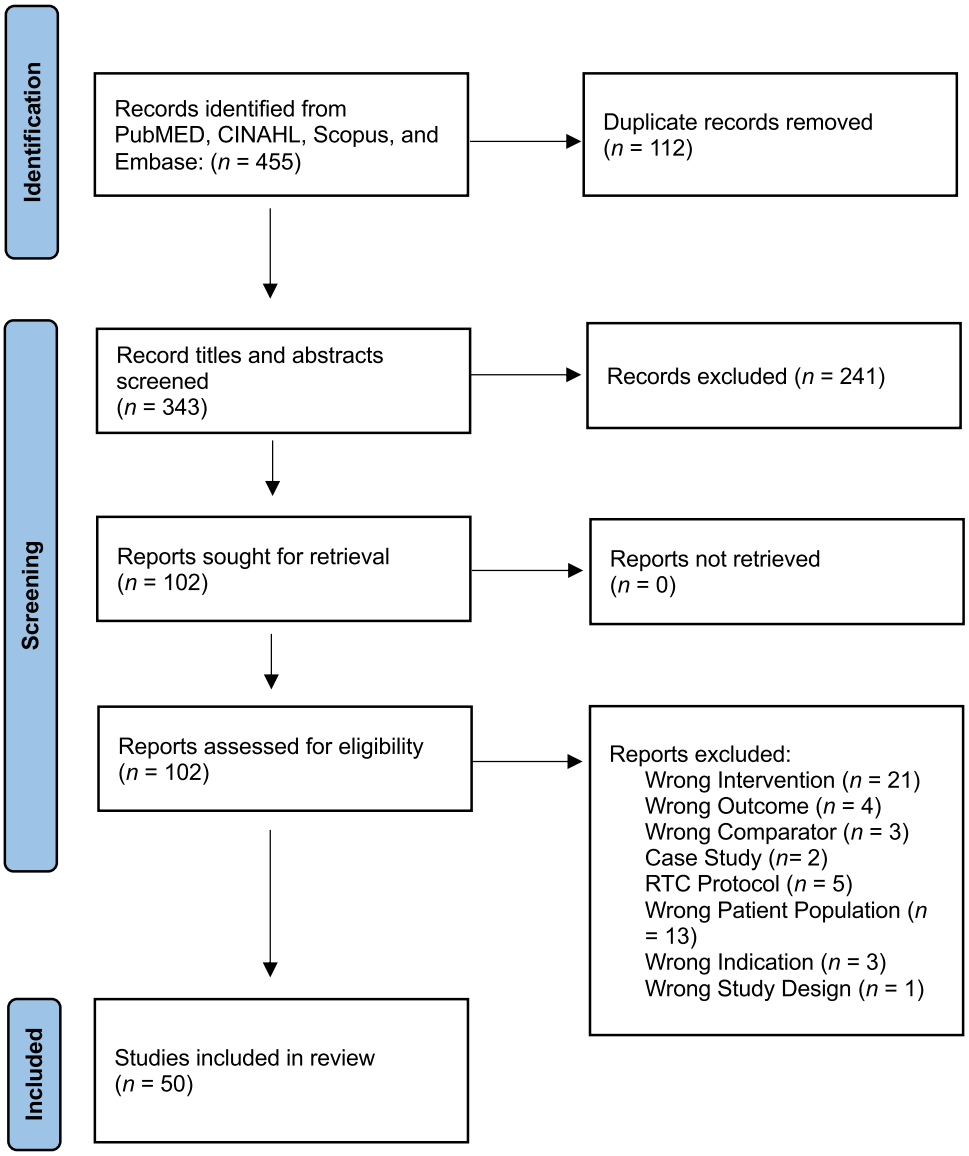

Figure 1 PRISMA Diagram.
Note: Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. Creative Commons.

Management and Analysis of Included Studies

We used the online systematic review tool, Covidence (Veritas Health Innovation, Melbourne, Australia), to complete this analysis. A data extraction tool was developed within Covidence. The timeframes were defined a priori: the short-term timeframe included from the time of injury until 30 days post-injury, the intermediate-term timeframe was from 30 days to six months post-injury, and the long-term was from six months to one year post-injury. The individual timeframes were included as data collection categories in Covidence. The outcomes of blood transfusions from the reviewed articles were directly transcribed into the corresponding timeframe within Covidence. Two authors reviewed each title, abstract, and full text for inclusion and conflicts were adjudicated by a third author. Meta-analysis of these data was not completed due to the heterogeneity of the interventions and outcomes measured.

Quality Assessment of Included Studies

The quality of the reviewed studies was completed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework.[67] The GRADE framework uses four quality of evidence rating categories: very

Table 1 Patient Outcomes and Quality of Evidence

Lead Author (Date)	Study Sample	Study Design	Short-Term Outcome	Intermediate-Term Outcome	Long-Term Outcomes	Country
Allon, R. (2020)[17]	n = 1	Case Report	• ICU LOS	• Hospital LOS	• "Return to normal life"	Israel
Anto, V. (2019)[18]	n = 501	Secondary Data Analysis	• None reported	• MT 30-day survival	• None reported	United States
Balvers, K. (2017)[19]	n = 385	Observational	• 24-hour survivability, Administration of TXA • The proportion of patients with normalized coagulopathy (within 24 hours)	• None reported	• None reported	England, Norway, Denmark, Germany, and Netherlands
Barmparas, G. (2018)[20]	n = 120	Cross Sectional	• Mortality (measured up to 7 days post injury)	• None reported	• None reported	United States
Brinck, T. (2016)[21]	n = 354	Secondary Data Analysis	• None Reported	• 30-Day mortality	• None reported	Finland
Brown, J.B. (2015)[22]	n = 720	Cohort Study	• Morbidity at hospital discharge • Mortality • Venous Thrombosis	• None reported	• None reported	United States
Cole, E. (2021)[23]	n =1169	Cohort Study	• All-Cause Mortality o <3 hours o 3–24 hours o >24 hours • TBI Mortality • Blood and Component use • Hospital LOS • Discharge destination	• None reported	• None reported	United Kingdom
Cornelius, B. (2019)[24]	n = 95	Case Control Study	• Morbidity • Mortality • Venous Thrombosis	• None reported	• None reported	United States
Dorken- Gallastegi, A. (2022)[25]	n = 5135	Cohort Study	• 24-hour mortality • In hospital mortality	• None reported	• None reported	United States
Duchesne, J. (2021)[26]	n = 253	Observational	• Mortality • Transfusion volume in the first 24-hours after ED admission • In-hospital outcomes and complications	• None reported	• None reported	United States
Fan, Y. (2023)[27]	n = 434	Randomized-Control Study	• Volume of blood transfused in first 24 hours • Coagulation function and blood routine after transfusion • Organ function injury score (SOFA) • ICU LOS • Hospital LOS	• None reported	• None reported	China
Giancarelli, A. (2016)[28]	n = 156	Secondary Data Analysis	• Hypocalcemia • Coagulopathy	• None reported	• None reported	United States
Haltmeier, T. (2018)[29]	n = 335	Secondary Data Analysis	• Mortality	• None reported	• None reported	United States

Hamidi, M. (2018)[30]	n = 2776	Secondary Analysis	• Mortality • Hospital LOS • ICU-free days • Ventilator-free days • Blood products received • Complications o ARDS o AKI o Sepsis o DVT o PE o Unplanned return to the OR o Unplanned intubation o Unplanned return to the ICU	• Hospital LOS, ICU-free days, ventilator-free days, complications (ARDS, AKI, sepsis, VTE)	• None reported	United States
Hanna, K. (2020)[31]	n = 8494	Cohort Study	• 24-hour mortality • In-hospital mortality • Complication o AKI o ARDS o DVT o PE	• None Reported	• None Reported	United States
Harris, C.T. (2018)[32]	n = 760	Secondary Analysis	• Count of patient who received pRBCs	• None reported	• None reported	United States
Hazelton, J.P. (2019)[33]	n = 91	Case Control Study	• Trauma bay Mortality • 24-hour Mortality • 4-hour posttransfusion laboratory values o HGB o HCT o PLT o INR o PTT • 24-hour posttransfusion Laboratory Values o HGB o HCT o PLT o INR o PTT • Overall blood product utilization • 24-hour blood product use	• 30-day Mortality	• None reported	United States
Holcomb, J.B. (2015)[34]	*n* = 680	Randomized Control Trial	• 24-hour mortality • Exsanguination • Anatomic Hemostasis	• 30-day mortality	• None reported	United States and Canada
Hwang, K. (2018)[35]	*n* = 180	Secondary Analysis	• FFP:pRBC ratio	• 90-day Survival Rate	• Non reported	Korea

(*Continued*)

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Table 1 (Continued).

Lead Author (Date)	Study Sample	Study Design	Short-Term Outcome	Intermediate-Term Outcome	Long-Term Outcomes	Country
Kang, B.H. (2017)[36]	*n* = 252	Secondary Analysis	• 24-hour mortality • ICU LOS • Transfusion time	• None reported	• None reported	Korea
Kemp Bohan, P.M. (2021)[37]	n = 216	Cohort Study	• ICU LOS • Hospital LOS • Unplanned ICU transfers • Unplanned intubations • DVT • PE • 24-hour mortality • Mortality during hospital stay	• 30-day mortality	• None Reported	United States
Khurrum, M. (2021)[38]	n = 252	Cohort Study	• Transfusion requirements at 24-after ED admission • In-hospital mortality • Hospital LOS • ICU LOS • AKI • ARDS • VTE	• None reported	• None reported	United States
Kornblith, L. (2019)[39]	n = 248	Cohort Study	• Platelet Count • Platelet Aggregation	• None reported	• None reported	United States
Lim, G. (2018)[40]	n = 58	Case Control Study	• In hospital mortality • ICU LOS • Hospital LOS	• None reported	• None reported	United States
Meizoso, J. (2018)[41]	n = 218	Non-randomized experimental study	• Massive Transfusions • Shutdown Fibrinolysis • Physiologic Fibrinolysis • Hyperfibrinolysis • DVT • PE • VTE • Vasoactive Drug • ALI • AKI • Hyperbilirubinemia • ICU-free days • Hospital LOS • Mortality	• None reported	• None reported	United States
Moore, H. (2018)[42]	n = 125	Randomized Control Trial	• 28-day Mortality • 24-hour mortality • MOF within 28 days of injury • Time from injury to first red blood cell transfusion • TEG • Vent-free days • ICU free Days • ALI within 28 days	• None reported	• None reported	United States
Morris, M. (2020)[43]	n = 508,463	Secondary Analysis	• In-hospital mortality • Hospital LOS	• None reported	• None reported	United States
Muradov, J. (2019)[44]	n = 130	Secondary Analysis	• Survival	• None reported	• None-reported	United States

Nederpelt, C.J. (2020)[45]	n = 4427	Cohort Study	• 24-hour mortality • In-hospital mortality • Unplanned return to the OR • Infection complications • VAP • ARDS • Sepsis • Extremity compartment syndrome • ICU LOS • Discharge disposition	• None reported	• None reported	United States
Nussbaumer, W. (2017)[46]	n = 306	Secondary Analysis	• Count pRBC units transfused • Count of platelet units transfused • Count of plasma units transfused • Mean pRBC: Platelet: Plasma Ratio • In hospital mortality • Time to discharge of patients	• In hospital mortality	• None reported	Austria
Olaussen, A. (2016)[47]	n = 156	Secondary Analysis	• Mortality at hospital discharge	• None reported	• None reported	Australia
Prat, N. (2017)[48]	n = 219	Secondary Analysis	• Hospital LOS • ICU LOS • Ventilator Free Days • Overall mortality • Blunt injury mortality • Penetrating injury mortality • Count of transfusions within 24 hours after admission • Count of FFP units • Count of Apheresis platelet units • Count of Cryoprecipitate units • Crystalloid volume • Colloid volume	• None reported	• None reported	United States
Rehn, M. (2019)[49]	n = 539	Non-randomized experimental study	• Survival to hospital • Overall survival	• None reported	• None reported	United Kingdom
Reitz, K. (2020)[50]	n = 626	Secondary Analysis	• 28-day mortality • 24-hour mortality	• None reported	• None reported	United States
Roquet, F. (2019)[51]	*n* = 897	Cohort Study	• 24-hour mortality • Count of pRBCs transfused during first 24 hours • ICU LOS • Hospital LOS • Ventilator days	• 30-day survival	• None reported	France
Savage, S. (2016)[52]	n = 316	Cohort Study	• Mortality • Hospital LOS • ICU LOS • Damage control laparotomy • Count of CAT+ occurrences per patient • Time of transfusions	• None reported	• None reported	United States

(*Continued*)

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Table 1 (Continued).

Lead Author (Date)	Study Sample	Study Design	Short-Term Outcome	Intermediate-Term Outcome	Long-Term Outcomes	Country
Schreiber, M. (2015)[53]	n = 256	Randomized Control Trial	• In-hospital mortality • ARDS • ARF • Sepsis • VAP • BSI • Surgical site infections • UTI • DVT • PE	• None reported	• None reported	United States
Seheult, J. (2018)[54]	n = 270	Secondary Analysis	• 24-hour mortality Blood use • Hospital LOS • ICU LOS	• None reported	• None reported	United States
Siletz, A.E. (2021)[55]	n = 70	Cohort Study	• 4-hour blood transfusion volume • Total blood transfusion volume • Morbidity • Hospital free days • ICU free days • TEG measurements	• 30-day mortality	• None reported	United States
Söderlund, T. (2017)[56]	n = 102	Secondary Analysis	• Observed mortality • Expected mortality • ICU LOS • Ventilator days	• None reported	• None reported	Finland
Sperry, J.L. (2018)[57]	n = 501	Randomized Control Trial	• 24-hour mortality • In-hospital mortality • Number of blood components transfused in the first 24 hours post injury • MSOF • ALI/ARDS • TRALI • Nosocomial infections • PTT • TEG • Volume of prehospital crystalloid solution • Count of patients who received prehospital pRBC transfusions	• 30-day mortality •	• None reported	United States
Stanworth, S.J. (2016)[58]	n = 442	Cross Sectional Study	• 24-hour mortality • Critical care during hospital stay • Ventilator days	• 30-day mortality	• 1-year mortality	United Kingdom
Stevens, W.T. (2017)[59]	n = 1536	Secondary Analysis	• Morbidity • TRALI • ARDS • Thromboembolic events • Pneumonia • Sepsis • AKF • Mortality	• None reported	• None reported	United States

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Taylor, J.R. (2018)[60]	*n* = 547	Secondary Analysis	• Adjusted 24-hour mortality • Unadjusted 24-hour mortality • ICU free days • Ventilator free days • Hospital free days • Venous thrombosis • MSOF • Sepsis • Infection • AKI • ALI	• Adjusted 30-day mortality • 30-day mortality	• None reported	United States
Tran, A. (2019)[61]	n = 890	Secondary Analysis	• 24-hour hemorrhage-related mortality • Count of patient who required hemostasis within 24-hours post injury	• 30-day all-cause mortality	• None reported	Canada
Undurraga Perl, V. J. (2016)[62]	n = 346	Secondary Analysis	• Surgical procedures performed within 90 minutes of arrival • Survival at 3, 6, 12, 24, and 72 hours • Death due to exsanguination or hemorrhagic shock • Units of blood products received during the randomized treatment period • Units of blood products received in the first 24 hours from arrival • Hospital-free days • ICU-free days • Ventilator-free days • AKF • MSOF • ARDS	• 30-day survival • Disposition at 30 days (discharged to home, remained hospitalized, discharged to morgue, or other)	• None reported	United States
Wafaisade, A. (2016)[63]	n = 516	Cohort Study	• ICU LOS • Hospital LOS • Thrombolytic events • Sepsis • MSOF • Time to death (days) • Mortality (6h, 12h, 24h in-hospital overall) • TXA administration	• 30-day mortality	• None reported	Germany
Wijaya, R. (2016)[64]	n = 46	Cohort Study	• 24-hour mortality	• None reported	• None reported	Singapore
Williams, J. (2020)[65]	n = 350	Secondary Analysis	• Hemolytic reactions at 3, 24, and 48 hours post injury • Transfusion reaction	• None reported	• None reported	United States
Yu, A. (2018)[66]	n = 178	Cohort Study	• ICU LOS • Hospital mortality • Hospital LOS	• None reported	• None reported	United States

Abbreviations: ABC, Assessment of Blood Consumption; AIS, Abbreviated Injury Score; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; ARF, acute renal failure; ALI, acute lung injury; AIS, abbreviated injury score; BE, base excess; BMI, body mass index; BSI, blood stream infection; CAT+, critical administration threshold; DVT, deep vein thromboembolism; ED, emergency department; FAST, Focus Assessment with Sonography for Trauma; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; HCT, hematocrit; HGB, hemoglobin; HR, heart rate; ICU, Intensive Care Unit; INR, International Normalized Ratio; ISS, injury severity score; LOS, length of stay; MOI, mechanism of injury; MSOF, multisystem organ failure; MT, massive transfusion; NISS, New Injury Severity Score; OR, operating room; PE, pulmonary embolism; PLT, platelets; pRBC, packed red blood cells; PT, prothrombin time; PTT, Partial thromboplastin time; RR, respiratory rate; RTS, Revised Trauma Score; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment; TBI, traumatic brain injury; TEG, Thromboelastography; TRALI, Transfusion Related Acute Lung Injury; TRISS, Trauma and Injury Severity Score; TXA, tranexamic acid; UTI, urinary tract infection; VAP, ventilator associated pneumonia; VS, vital signs; VTE, venous thromboembolism.

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low, low, moderate, and high. The randomized trials begin the rating process as highly rated evidence and observational studies begin at the low quality level. The quality rating was decreased for risks of bias, inconsistency, indirectness, imprecision, and publication bias.[68–70] The quality rating was increased for large effects, dose-response, and if all residual confounders increased the confidence of the estimated effect.[67,71] Two authors independently assessed each of the included studies for the following quality indicators: study design, risk of bias, consistency, directness, precision, and publication bias per the GRADE framework. The third author refereed disagreements regarding quality indicator categories. Full results of the GRADE analysis are presented in Table 2.

Results

A total of 50 studies were included in the final analysis (Table 1). Sample sizes varied widely, from 1 to 34,421 individuals.[17,43] The Injury Severity Score (ISS) was included in all but six of the studies.[40,46,49,51,64] In the studies that did include ISS, the mean score ranged from 10–33, indicating moderately to severely injured samples. Outcomes were categorized as short-term outcomes (day of injury to less than 30 days post-injury), intermediate-term outcomes (30 days to six months post-injury), and long-term outcomes (greater than six months post-injury). Roughly half (51%) of the studies are secondary data analyses.[18,21,23,28–30,32,35–37,43,44,46–48,50,54,56,59–62,65] Fifteen are cohort studies (30%),[22,28,31,38,39,43,45–47,51,52,55,63,64,66] nine quasi-experimental (18%),[23,26,30,35,37,41,49,60,61] seven are observational studies (14%),[19,21,25,29,32,48,65] six are randomized control trials (12%),[27,34,42,53,57,72] five are case-control (10%),[24,33,36,40,54] four are cross-sectional (8%),[20,56,58,59] three are survival analyses (6%),[18,44,50] and one is a case report (2%).[17]

Short-Term Outcomes (<30 Days Post-Injury)

Mortality

All studies reported short-term outcomes. Mortality was the most reported outcome in 41 (82%) of the studies.[19,20,22–27,29–31,33,34,36–38,40–54,56–64,66] In studies where mortality was the primary outcome of interest, it was evaluated at standard timeframes of 24-hours,[19,23,25,31,33,34,36,37,42,45,50,51,54,57–64,73] 28-days,[42,50] or identified as "in-hospital" mortality.[20,22–27,29–31,33,37,38,40,41,43,45,47–49,52,53,56,57,59,62,63] One study reported mortality "between six hours and 58 days after admission".[44]

Pathophysiologic Outcomes

Of the 50 studies reviewed, 15 (30%) reported pathophysiologic outcomes aside from mortality. The most commonly reported outcomes were: acute respiratory distress syndrome, reported in eight (15.6%) studies;[22,30,31,45,53,57,59,62] acute kidney injury,[30,31,38,41,59,60,62] and sepsis,[30,31,38,53,59,60,63] each reported in seven (14%) studies; pulmonary embolisms[18,30,31,37,41,53] in six studies (12%), and multiorgan failure[42,57,60,62] was reported in four (8%) studies; and deep vein thrombosis,[30,41,53] reported in three (6%) studies. Finally, pulmonary emboli and deep vein thrombosis were combined and reported as "thrombolytic events" in one study,[63] and transfusion-associated cardiac overload in another.[65]

Four (8%) of the studies used infections as an outcome with variable definitions.[53,57,60] Taylor et al[60] and Nederpelt et al[45] defined infections in general, whereas Schreiber et al[53] specifically identified bloodstream infections, surgical site infections, and urinary tract infections, and Sperry et al[57] grouped these into a broad category of nosocomial infections. Acute lung injuries,[42,60] transfusion-related acute lung injury,[59,65] hemolytic reactions,[22,65] and pneumonia[53,59] were each identified in two studies.

Table 2 Grading of Recommendations, Assessment, Development, and Evaluations Guideline (GRADE) Rating of Outcome Categories by Timeframe

	Short-Term	Intermediate-Term	Long-Term
Mortality	Low	Low	Very Low
Pathologic Outcomes	Very Low	Very Low	Very Low
Indices of Coagulopathy	Very Low	Very Low	Very Low
Duration of Treatment	Very Low	Very Low	Very Low

Notes: Short-Term = Time of injury to 30 days post injury, Intermediate-Term = 30 to 180 days after injury, Long-Term = 180 to 365 days after injury.

Indices of Coagulopathy

Of the reviewed studies, 10 (20%) reported indices of coagulopathy, including hypocalcemia,[28] partial thromboplastin time,[27,33,57] international normalized ratio,[33] thromboelastography,[42,57] post-transfusion platelet count,[33,39,46] platelet aggregation,[39] trauma-induced coagulopathy,[22] shutdown fibrinolysis,[41] physiologic fibrinolysis,[41] and hyperfibrinolysis.[41,60]

Duration of Treatment (Length of Stay and Length of Ventilator Therapy)

Seventeen studies (34%) reported intensive care unit (ICU) length of stay,[27,30,31,36–38,40–42,45,47,48,51,52,55,56,60,66] whereas 12 studies (24%) reported hospital length of stay.[27,30,37,40,41,46,48,51,52,55,60,66] Seven (14%) investigators reported duration of mechanical ventilator support.[30,42,47,48,51,56,60] One article reported 'mechanically ventilated hours',[47] four reported ventilator-free days,[30,42,48,60] and two reported the "duration of mechanical ventilation in days".[51,56]

Intermediate-Term Outcomes (30 Days to Six Months Post-Injury)

Mortality

If mortality occurred or not was reported in 14 (28%) of the reviewed studies.[33–35,37,46,51,55,57,58,60–63,65] Eleven (22%) of the reviewed studies reported a primary outcome of 30-day mortality.[29,33,34,37,46,51,55,56,62,63,65] The outcome of 90-day survival was reported in only one study.[35]

Pathophysiologic Outcomes

The concept of complications was reported in only one study (2%),[30] and encompassed all occurrences of acute respiratory distress syndrome, acute kidney injury, sepsis, and venous thromboembolism as a composite outcome.

Duration of Treatment (Length of Stay and Length of Ventilator Therapy)

Allon et al, in a case study, reported a single patient's length of hospital stay of 78 days.[17] Disposition at 30-days post-injury,[62] time to discharge,[46] and ICU-free and ventilator-free days[30] were each reported in separate studies.

Long-Term Outcomes (Greater Than Six Months Post-Injury)

Mortality

Only two investigator groups reported findings of a single long-term outcome, mortality at one year.[17,58] Stanworth et al compared mortality 12 months post-traumatic injury.[47] While not specified as a mortality outcome, Allon et al reported that a trauma survivor "returned to work and to her normal life"[17] at 12 months post-injury in a single patient case study.

Quality of Evidence

The GRADE framework was used to assess the quality of the evidence for the of outcome subcategories during the short-, intermediate-, and long-term timeframes. The mortality evidence was rated as low during the short- and intermediate-term timeframes. The evidence rating for mortality during the long-term timeframe was very low. Pathologic outcomes, indices of coagulopathy, and duration of treatment quality of evidence were rated as very low during all timeframes. See Table 2.

Discussion

In the current review, we categorized outcomes following resuscitation after TRH from 50 studies into those that occurred in the short-, intermediate-, and long-term. The outcomes were classified as those related to mortality, pathophysiologic outcomes, indices of coagulopathy, and length of stay and length of ventilator therapy. Within the short-term timeframe, all four of the outcome categories were reported in at least one study. The intermediate-term outcome categories reported were mortality, pathophysiologic outcomes, and length of stay. The only outcome category reported in the long-term timeframe was mortality, indicating a severe lack of knowledge surrounding sequelae of major trauma and resuscitation.

Currently, the long-term outcomes of patients experiencing trauma are not well understood. Recent evidence suggests that pre-existing patient characteristics may influence the long-term outcomes.[13,74] For example, Haider et al found that a trauma patient's low education level was highly correlated with functional limitations and not returning to work;[33] however, the authors did not report how a patient's quality of life was related to interventions made during the immediate

time following a traumatic injury. Poor outcomes within the trauma patient population have been attributed to the patient's low levels of resilience, low education level, and low socioeconomic status.[75] None of the studies reviewed in our analysis reported outcomes beyond those that occurred within the clinical setting. Further investigation is warranted on the influence of sociodemographic and psychosocial factors on outcomes following major trauma (ie, quality of life, mental and emotional health, return to work).

As demonstrated in this review, the short-term outcomes of patients who were resuscitated with either whole blood or blood components after experiencing a TRH have been well studied; however, the quality of evidence for all recommendations were rated as very low quality except mortality during the short- and long-term timeframe. Importantly, the preponderance of low to very low-quality evidence for outcomes reported across all timeframes suggests a need for high-quality studies, and further inquiry as to outcomes in the intermediate- and long-term timeframes.

In the current review, we categorized outcomes into defined timeframes that align closely with the stages of trauma care, which range from the pre-hospital setting (eg, bystander intervention and prehospital Emergency Medical Services Care), to definitive hospital care, to rehabilitation, recovery, and reentry to society.[76] As advances in medical care improve patient survival and promote optimal recovery following TRH, attention to more intermediate- and long-term outcomes is warranted. Indeed, current recommendations emphasize the need for early assessment of the trauma patient's rehabilitation needs to facilitate optimal recovery.[77] A better understanding of intermediate- and long-term outcomes may assist clinicians in developing interventions and preparing patients for their rehabilitation trajectory, both mentally and physically.

Current literature supports similar survival benefits when comparing the transfusion of whole blood versus blood components for the resuscitation of patients experiencing a TRH. Perkins et al[78] found no difference in mortality when they compared use of fresh whole blood versus blood components. Similarly, Yazer et al compared low titer O whole blood transfusions to component transfusions and found no difference in mortality at six- or 24-hours, or at 30-days. Furthermore, they found no difference in the frequency of acute kidney injury, thromboembolisms, or sepsis by transfusion strategy.[79] Further, Cotton et al,[80] found no difference in 24-hour or 30-day mortality, or acute respiratory distress syndrome, infections complications, sepsis, acute kidney failure, length of hospital or ICU stay, or ventilator days in a randomized control study comparing whole blood and blood component transfusions. Importantly, however, limited data exist on both intermediate- and long-term outcomes across all transfusion modalities. Future studies utilizing a longitudinal study methodology may further elucidate the extent to which transfusion modality (whole blood versus component therapy) influences patient outcomes beyond 30 days post-injury. Additionally, other aspects of recovery, such as psychological outcomes, self-care abilities, performance of daily activities, and return to work must also be considered when coordinating care for patients who have experienced a TRH.[81]

This review has limitations. The reviewed articles were limited to English and between the years of 2014 through 2023. There is a possibility that even though multiple databases were searched there is a chance that relevant articles were missed. Meta-analysis was not conducted due to the narrative nature of this review. Additionally, publication bias may have limited studies available for this review.

Conclusion

Collectively, the findings of this review demonstrate the need for high-quality studies validating current knowledge of short-term outcomes among patients resuscitated after TRH. In addition, future studies are needed to assess intermediate- and long-term outcomes for these patients, as they may support the implementation of interventions or policies to promote optimal recovery among this patient population.

Disclosure

The authors report no conflict of interest in this work.

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