Int J Burn Trauma 2017;7(2):17-26
www.IJBT.org /ISSN:2160-2026/IJBT0050499

Review Article

Mortality outcomes in trauma patients undergoing prehospital red blood cell transfusion: a systematic literature review

Gregory S Huang, C Michael Dunham

Trauma/Surgical Critical Care, St. Elizabeth Youngstown Hospital, 1044 Belmont Ave., Youngstown 44501, OH, USA

Received February 9, 2017; Accepted March 29, 2017; Epub April 15, 2017; Published April 30, 2017

Abstract: The value of prehospital red blood cell (RBC) transfusion for trauma patients is controversial. The purposes of this literature review were to determine the mortality rate of trauma patients with hemodynamic instability and the benefit of prehospital RBC transfusion. A 30-year systematic literature review was performed in 2016. Eligible studies were combined for meta-analysis when tests for heterogeneity were insignificant. The synthesized mortality was 35.6% for systolic blood pressure ≤ 90 mmHg; 51.1% for ≤ 80 mmHg; and 63.9% for ≤ 70 mmHg. For patients with either hypotension or emergency trauma center transfused RBCs, the synthesized Injury Severity Score (ISS) was 27.0 and mortality was 36.2%; the ISS and mortality correlation was r = 0.766 ($P = 0.0096$). For civilian patients receiving prehospital RBC transfusions, the synthesized ISS was 27.5 and mortality was 39.5%. One civilian study suggested a decrement in mortality with prehospital RBC transfusion; however, patient recruitment was only one per center per year and mortality was < 10% despite an ISS of 37. The same study created a matched control subset and indicated that mortality decreased using multivariate analysis; however, neither the assessed factors nor raw mortality was presented. Civilian studies with patients undergoing prehospital RBC transfusion and a matched control subset showed that the synthesized mortality was similar for those transfused (37.5%) and not transfused (38.7%; $P = 0.8933$). A study of civilian helicopter patients demonstrated a similar 30-day mortality for those with and without prehospital blood product availability (22% versus 21%; $P = 0.626$). Mortality in a study of matched military patients was better for those receiving prehospital blood or plasma (8%) than the controls (20%; $P = 0.013$). However, transfused patients had a shorter prehospital time, more advanced airway procedures, and higher hospital RBC transfusion ($P < 0.05$). A subset with an ISS > 16 showed similar mortality with and without prehospital RBC availability (27.6% versus 32.0%; $P = 0.343$). Trauma patient mortality increases with the magnitude of hemodynamic instability and anatomic injury. Some literature evidence indicates no survival advantage with prehospital RBC availability. However, other data suggesting a potential benefit is confounded or likely to be biased.

Keywords: Air ambulances, blood transfusion, emergency medical services, hemorrhage, hypotension, injury severity score, military medicine, mortality, trauma centers, wounds and injuries

Introduction

Hemorrhage is a main cause of mortality in trauma patients [1, 2]. Previous literature has commonly focused on trauma center resuscitation by minimizing crystalloids and using massive transfusion protocols with fixed ratios of packed red blood cells (PRBC), fresh frozen plasma, and platelet transfusions [2]. With combat in Israel and Afghanistan, the military has described its use of prehospital blood transfusion [3-5]. The use of prehospital blood transfusion has also been portrayed in civilian populations [6-9].

The most contemporary studies on trauma efficacy were published by Brown et al. in 2015. In their multicenter trial, Brown et al. suggested a mortality benefit with prehospital red blood cell (RBC) transfusion [7]. However, the same first author also published single center data that showed no improvement in mortality with prehospital RBC administration [6]. Despite conflicting literature, emergency medical services

Table 1. PRISMA 2009 flow table

Records identified through PubMed	464
Records after duplicates removed	314
Abstracts screened	314
Full-text articles assessed for eligibility	61
Full-text articles excluded	50
Useful articles	11
Useful articles from 61 bibliographies	18
Studies used in the quantitative analysis	29

have adopted prehospital blood administration [4, 6, 8]. With the short shelf life and strict storage conditions of blood, there are many logistical concerns for managing prehospital blood as described by Bodnar et al. [10] and Soudry and Stein [11].

Our group performed a systematic literature review of trauma patient to determine the mortality rate and magnitude of anatomic injury for those with hemodynamic instability and if prehospital RBC transfusion provides a survival benefit.

Materials and methods

We performed a literature review and analysis to determine if prehospital blood transfusion is associated with an improvement in mortality. The literature search included a 30 year period (1986-2016) using the following PubMed selection criteria. The word "transfusion" was required to be in the title of all manuscripts. The following medical subject headings were sequentially combined with "transfusion" to select potentially relevant manuscripts: 1) trauma centers, 2) multiple trauma, 3) air ambulances, 4) emergency medical services, and 5) military medicine.

Manuscript titles and abstracts were reviewed to determine if data existed for trauma patients. A manuscript was determined to be of potential value, if it included information regarding mortality outcomes in trauma patients with 1) hypotension, 2) a need for emergency RBC transfusion, or 3) blood product availability before trauma center arrival. Using the system by Sauaia et al., we assessed each article included in the review and assigned a level of evidence from I (highest quality) to V (very low quality) [12].

To address our study aims, we examined the following relationships in trauma patients: (1) mortality and hypotension, (2) mortality and Injury Severity Score (ISS) in hypotensive patients, (3) mortality and ISS for civilian patients receiving prehospital blood, (4) mortality for trauma center patients undergoing emergency RBC transfusion, (5) mortality for military patients undergoing prehospital RBC transfusion, (6) mortality in prehospital and hospital patients undergoing transfusion, and (7) mortality and availability of prehospital blood by helicopter transport crews. Sherren and Burns article was not included in the 29 articles used in the analysis because of incomplete data [13]. Despite including 147 patients, only scene mortality was described; hospital mortality was not described.

Statistical analysis

Data were entered in a Microsoft Excel 2010 (Redmond, WA, USA) worksheet and imported into the SAS System for Windows, release 9.2 (SAS Institute Inc., Cary, NC, USA) to perform statistical analysis. Inter-study testing of heterogeneity for mortality outcomes was performed, using the chi square or I^2 and Q statistic. Correlation coefficient analysis was performed using the Pearson method (for ISS and mortality). Most data and statistical analyses presented in this review emanates from the published manuscripts. Epi Info™ 7.0.9.7 (Centers for Disease Control and Prevention, 2012) was used to perform intergroup event proportion statistical analyses. The level of significance was considered $P < 0.05$.

Results

Of 29 studies included, the level of evidence was V in 2 investigations (6.9%) [3, 14], III in 8 investigations (27.6%) [2, 6, 15-20], and IV in the other 19 investigations (65.5%). The literature search process is summarized in **Table 1**.

Mortality in trauma patients with hemodynamic instability

The relationship between mortality and systolic blood pressure (BP) for trauma patients is described in **Table 2**. Mortality increased from 35% to more than 60% as hypotension worsened. The test for mortality heterogeneity was insignificant for systolic BP ≤ 90 mmHg (P =

Table 2. Mortality by degree of systolic hypotension

Study	Systolic BP ≤ 90			Systolic BP ≤ 80			Systolic BP ≤ 70		
	No.	Died	%	No.	Died	%	No.	Died	%
Arbabi, 2004 [22]	2043	980	48.0	1684	849	50.4	981	700	72.4
Bruns, 2008 [23]	1781	623	35.0	2551	1479	58.0	1344	925	68.8
Hasler, 2012 [24]	1863	433	23.2	826	257	31.1	499	189	37.9
Talving, 2005 [25]	-	-	-	71	35	49.3	71	35	49.3
Martin, 1992 [16]	316	118	37.3	-	-	-	-	-	-
Tinkoff, 2002 [20]	302	111	36.8	-	-	-	-	-	-
Yaghoubian, 2007 [26]	194	49	25.3	-	-	-	-	-	-
	6499	2314	35.6	5132	2620	51.1	2895	1849	63.9

BP, Blood pressure; Systolic BP, Units in mmHg; -, Data not available; %, Percent.

Table 3. Injury Severity Score and mortality in hypotensive trauma patients

Study	Criteria	ISS	Total	Deaths	%	
Yaghoubian, 2007 [26]	PreH sBP ≤ 90	17	194	49	25.3	
Bruns, 2008 [23]	PreH sBP ≤ 90	19	1781	623	35.0	
Martin, 1992 [16]	PreH sBP ≤ 90	25	316	118	37.3	
Inaba, 2008 [15]	Un-X RBC	26	1236	489	39.6	
Schwab, 1986 [19]	Un-X RBC	27	99	37	37.4	
Nunez, 2010 [2]	Un-X RBC	27	485	136	28.0	
Ball, 2011 [1]	Un-X RBC	28	153	69	45.1	
Miraflor, 2012 [17]	Un-X RBC	28	132	45	34.1	
Dutton, 2005 [27]	Un-X RBC	34	161	71	44.1	
Ruchholtz, 2006 [18]	Un-X RBC	39	116	56	48.3	
		27.0	4673	1693	36.2	95% CI 35-38%

PreH, Prehospital; sBP, Systolic blood pressure; ISS, Injury severity score; Un-X RBC, Un-crossmatched red blood cells; %, Percent; CI, Confidence interval.

Table 4. Mortality of civilian patients undergoing prehospital RBC transfusion

Study	Scene	ISS	Total	Deaths	%	
Berns, 1998 [28]	T	-	45	23	51.1	
Bodnar, 2014 [10]	S	32	71	32	45.1	
Brown, 2015 [6]	B	18	240	74	30.8	
Dalton, 1993 [29]	S	32	112	51	45.5	
Higgins, 2012 [30]	B	-	32	10	31.3	
Sumida, 2000 [9]	B	28	17	7	41.1	
Sunde, 2015 [14]	S	-	3	2	66.7	
Weaver, 2013 [31]	S	-	50	26	52.0	
		27.5	570	225	39.5	95% CI 36-44%

RBC, Red blood cell; ISS, Injury severity score; T, Interhospital transfer; S, From scene; B, From both the scene and interhospital transfers; -, Data not available; %, Percent; CI, Confidence interval.

0.1025), systolic BP ≤ 80 mmHg (P = 0.3173), and systolic BP ≤ 70 mmHg (P = 0.7788).

ISS and mortality in trauma patients, who were either hypotensive or received emergency RBC transfusion, are presented in **Table 3**. This analysis of 10 studies showed that these trauma patients had an average ISS of 27.0 and mortality of 36.2%, with a narrow confidence interval. The test for mortality heterogeneity was insignificant (P = 0.2059). Correlation analysis demonstrated a significant relationship between ISS and mortality (r = 0.766; P = 0.0096).

The mortality and ISS of civilian trauma patients who received prehospital RBC transfusions are detailed in **Table 4**. The test for study mortality heterogeneity was insignificant (P = 0.1969). Results of the meta-analysis showed an average ISS of 27.5 (range, 18-32), and mortality approached 40% (range, 31-67%) with a narrow confidence interval.

Table 5. Mortality of trauma center patients undergoing emergency RBC transfusion

Study	ISS	Total	Deaths	%	
Baker, 2001 [32]	-	81	29	35.8	
Ball, 2011 [1]	28	153	69	45.1	
Ruchholtz, 2006 [18]	39	116	56	47.5	
Dutton, 2005 [27]	34	161	71	44.1	
Schwab, 1986 [19]	27	99	37	37.4	
Inaba, 2008 [15]	26	1236	489	39.6	
Como, 2004 [33]	-	161	72	44.7	
Miraflor, 2012 [17]	28	132	45	34.1	
Nunez, 2010 [2]	27	485	136	28.0	
	29.9	2624	1004	38.3	95% CI 36-40%

RBC, Red blood cell; ISS, Injury severity score; -, Data not available; %, Percent; CI, Confidence interval.

Table 6. Twenty-four-hour mortality of military patients undergoing prehospital RBC transfusion

Study	Scene	ISS	Total	Deaths	%	
Barkana, 1999 [3]	S	19	32	3	9.4	
Powell-Dunford, 2014 [5]	S	-	31	8	25.8	
			63	11	17.5	95% CI 8-27%

RBC, Red blood cell; ISS, Injury severity score; -, Data not available; %, Percent; CI, Confidence interval.

Table 7. Non-matched mortality of trauma patients receiving prehospital RBC transfusion

	RBC yes	RBC no	*p*-value
Number of patients	50	1365	
From the scene	52%	96%	< 0.01
Injury severity score	37	33	0.18
Base deficit	10	8	< 0.01
Admission hypotension	74%	73%	0.86
PTC crystalloids (L)	2.6	1.0	< 0.01
24-hour trauma center RBC (units)	15.5	6.6	< 0.01
Survival curve of 30-day mortality	4%	12%	0.11

RBC, Red blood cell; RBC yes, RBC transfusion given prehospital; RBC no, RBC transfusion not given prehospital; PTC, Pretrauma center.

The mortality rate for patients receiving emergency RBC transfusion at a trauma center is presented in **Table 5**. The test for study mortality heterogeneity was insignificant ($P = 0.7389$). Results of the meta-analysis showed an average ISS of 30 and a mortality approaching 40%, with a narrow confidence interval. The trauma center emergency RBC transfusion group (**Table 5**) and prehospital RBC transfusion group (**Table 4**) had similar meta-analytic ISS and mortality. The 24-hour mortality of military patients undergoing RBC transfusions at the scene is described in **Table 6**. Mortality approached 20%.

Mortality analysis of prehospital RBC transfusion

A study by Brown et al. [7] described 50 patients from 9 trauma centers over an 8 year period, who received prehospital RBC transfusions. The comparison of trauma patients who received prehospital RBCs to those without prehospital RBCs is shown in **Table 7.** No raw mortality data were presented. We extrapolated mortality rates from survival curves presented in the Brown et al. manuscript. The average ISS for those receiving prehospital RBCs was 37. The mortality rate between the prehospital RBC transfused group and group that received no transfusion was insignificantly lower ($P = 0.11$). Compared to patients without prehospital RBC transfusion, those who received a prehospital RBC transfusion had a greater amount of pretrauma center crystalloids and 24-hour trauma center RBC transfusions. The transfused-patient mortality rate of only 4% was inconsistent with the results from our analysis of prehospital transfusion mortality of 40% (**Table 4**). The 12% mortality for patients without prehospital RBC transfusion seemed low, especially considering that the ISS of was 33. The analyses in **Tables 4** and **5** show an expected mortality of at least 35% with a similar ISS. Half of the trauma patients who received prehospital RBC were interhospital transfers, whereas virtually all trauma patients who did not receive prehospital RBC were from the scene.

Table 8. Matched mortality of trauma patients receiving prehospital red blood cell transfusions

	PTC RBC transfusion	No PTC RBC transfusion	*p*-value
Number of patients	35	78	
From the scene	71%	76%	0.64
Injury severity score	34	30	0.81
Base deficit	10	9	0.88
Admission hypotension	60%	74%	0.02
24-hour trauma center RBC (units)	14.0	8.3	< 0.01

PTC, Pretrauma center; RBC, Red blood cell.

Table 9. Mortality of matched civilian patients undergoing prehospital RBC transfusions

Study	RBC yes				RBC no				RR	*p-value*
	ISS	No.	Died	%	ISS	No.	Died	%		
Brown, 2015 [6]	22	71	26	36.6	22	142	48	33.8	1.1	0.7605
Sumida, 2000 [9]	28	17	7	41.2	28	31	19	61.3	0.7	0.2323
		88	33	37.5		173	67	38.7	1.0	0.8933

RBC, Red blood cell; ISS, Injury severity score; RR, Risk ratio; RBC yes, RBC transfusion given prehospital; RBC no, RBC transfusion not given prehospital; %, Percent; Brown study, all from scene; Sumida study, some interhospital transfers.

Table 10. Mortality of matched civilian patients transported by helicopter with prehospital blood available

	Life flight service	Other air service	*p*-value
	PHTX available	PHTX not available	
Number of patients	716	169	
Scene hypotension	14%	15%	0.855
Injury severity score	22	22	0.998
Prehospital transfusion	137 (19%)	0 (0%)	< 0.0001
30-day mortality	22%	21%	0.626
24-hour mortality	14%	13%	0.529
Massive transfusion	8%	12%	0.133

PHTX, Prehospital blood products transfusion.

Brown et al. [7] used propensity scoring analysis to match civilian trauma patients who received prehospital RBC to those who did not receive prehospital RBC, and the findings are shown in **Table 8**. Compared to those who did not receive prehospital RBC, the prehospital transfusion group was given substantially more blood after trauma center arrival. Prehospital RBC transfusion was independently associated with an 88% reduction in the risk of 30-day mortality ($P = 0.01$); however, the raw mortality was not stated. Additionally, the variables included in the multivariate regression analysis were not described.

The mortality of matched civilian patients undergoing prehospital RBC transfusion compared to those without prehospital transfusion is described by other investigators and presented in **Table 9**. The prehospital transfusion group and no prehospital transfusion group both had a combined mortality approaching 40%, with no statistical significance. The test for interstudy mortality heterogeneity was insignificant (I^2 46.7% and Q statistic 1.8750; $P = 0.1709$).

Holcomb et al. [8] studied adult civilian trauma patients transported by helicopter from the scene who received blood products (plasma and/or RBC), either prehospital or early in their hospital course. The Life Flight helicopter service was capable of providing RBC and/or plasma prehospital. The other air helicopter service had no provision for providing RBC and/or plasma prehospital. A comparison of patient outcomes is described in **Table 10**. The 24-hour and 30-day mortality rates and for patients transported by the Life Flight helicopter service were statistically similar to those of the control group.

O'Reilly et al. matched military trauma patients who received prehospital blood and/or plasma to controls, and they reported a significant improvement in mortality as seen in **Table 11** [4]. However, these two groups were different, since the prehospital transfused patients had a shorter prehospital time, more advanced airway procedures, a lower heart rate at admission, and higher in-hospital RBC transfusion rate. O'Reilly et al. also provided data for military patients with an ISS > 16 and compared

Table 11. Mortality of matched military patients receiving prehospital blood products

	PHTX yes	PHTX no	*p*-value
Time period	> June 2008	< July 2008	
Number of patients	97	97	
Injury severity score	22	21	
Prehospital time (min)	68	109.5	0.008
Advanced airway	19 (20%)	9 (9%)	0.041
Admission systolic blood pressure	132	131	0.145
Admission heart rate	92	105	0.041
Any in-hospital PRBC transfusion	75 (77%)	38 (39%)	< 0.001
Prehospital + in-hospital PRBC (units)	4	0	< 0.001
Prehospital + in-hospital FFP (units)	2	0	< 0.001
Massive transfusion	12 (12%)	8 (8%)	0.388
Afghanistan patients	21 (22%)	14 (14%)	0.2624
Mortality	8 (8%)	19 (20%)	0.013

PHTX, Prehospital red blood cell and/or plasma transfusion; PRBC, Packed red blood cells; FFP, Fresh frozen plasma. The mortality of Afghanistan patients was limited to hospital stay, i.e., not 30-days.

Table 12. Mortality of matched military patients (ISS ≥ 16) with and without prehospital RBC availability

	PHRBC available	PHRBC not available	*p*-value
Time period	> June 2008	< July 2008	
Number of patients	485	122	
Mortality	134 (27.6%)	39 (32.0%)	0.343

PHRBC, Prehospital red blood cells.

mortality for those with and without prehospital RBC availability (**Table 12**) [4]. Having prehospital RBC available did not improve mortality.

Discussion

This review included both civilian and military studies, and no study had a level I or II evidence. When we performed our data analysis, the tests for heterogeneity were typically not significant and indicated that combining study mortality results were appropriate for ascertaining a more accurate point estimate.

Mortality in trauma patients with hemodynamic instability

For patients with prehospital or trauma center hypotension, mortality was nearly 40% (systolic BP ≤ 90 mmHg) (**Table 2**). Mortality progressively worsened as the magnitude of hypotension increased. For patients who had either prehospital hypotension or received uncrossmatched RBCs upon trauma center arrival, mortality approached 40% (**Table 3**). The synthesized mortality was nearly identical to the mortality rate of those with prehospital or trauma center hypotension (**Table 2**), suggesting that this mortality point estimate is reliable. The narrow confidence interval also indicates that this mortality rate is an accurate point estimate. Patients with prehospital hypotension or those who received uncrossmatched RBCs upon trauma center arrival had substantial bodily injury (mean ISS, 27.0). The result of the correlation analysis (r = 0.8) suggests a strong positive relationship between anatomic injury severity (ISS) and mortality in trauma patients with hemodynamic instability.

For civilian patients undergoing prehospital RBC transfusion, the mean mortality was nearly 40% and the 95% CI was narrow (**Table 4**). The mean mortality was similar to that for other relevant populations (**Tables 2** and **3**). These findings further support that the mortality rate point estimate for civilian patients undergoing prehospital RBC transfusion is accurate. Only half of the studies provided an ISS, and the mean ISS (27.5) is virtually identical to that for patients with prehospital hypotension or those who needed urgent RBC transfusion upon trauma center arrival (**Table 3**). This finding suggests that substantial anatomic injuries are typically found.

Civilian patients undergoing emergency RBC transfusion at a trauma center had a significant amount of anatomic injury (mean, ISS 29.9) and high mortality rate (38%) with a narrow 95% CI (**Table 5**). Further, the mean mortality rate is not different from that for other similar populations (**Tables 2**-**4**). These findings indicate that the mortality rate point estimate for civilian populations undergoing trauma center emergency RBC transfusion is accurate. The mean ISS is also similar to that for other relevant trauma patients (**Tables 3** and **4**), suggesting that substantial anatomic injuries are typically found.

For military patients undergoing prehospital RBC transfusion, the 24-hour mortality was 50% (**Table 6**) of the hospital rate for civilian patients undergoing prehospital transfusion (**Table 4**). However, the accuracy of the mortality rate point estimate is uncertain, because the 95% CI is substantial. This discrepancy in mortality could be due to three potential causes. First, few patients and observations were included. Second, the military mortality rate represents the 24-hour mortality, whereas the civilian mortality rate is derived from the 30-day mortality or the hospitalization mortality. Finally, compared to civilian patients (**Table 4**), military patients had a lower magnitude of anatomic injuries (ISS), which may have also affected mortality.

Mortality analysis for prehospital RBC transfusion

In a multicenter trial, Brown et al. [7] described 50 civilian trauma patients who received prehospital RBC transfusion (**Table 7**). These patients emanated from 9 trauma centers over an 8-year period, which represents one patient per trauma center per year. Such a low yield certainly presents the distinct possibility for bias, i.e., these 50 patients may not represent the characteristics of a larger parent cohort. Mortality rates were extrapolated from the manuscript's survival curves, and they were found to be ≤ 10%, despite an ISS > 30. These findings are at odds with that of the literature review, which found that with a mean ISS of nearly 30, mortality rates were typically close to 40%. These observations strongly suggest that the 50 patients in the multicenter trial are likely not representative of a typical trauma population that needs prehospital RBC transfusion. Furthermore, the raw trauma mortality rates for the prehospital transfusion and non-transfusion groups were not significantly different.

Additionally, the two cohorts were different in that the patients receiving prehospital RBC transfusion were managed more aggressively, receiving a greater amount of pretrauma center crystalloids and 24-hour trauma center RBC transfusions, factors that might influence mortality outcomes. Furthermore, half of the trauma patients who received prehospital RBC were interhospital transfers, whereas virtually all of the trauma patients who did not receive prehospital RBC were from the scene, which introduces selection bias. All of these factors may have contributed to the mortality rate being discordant with our meta-analysis results. Because of this potential bias, this study was excluded from the meta-analysis of the prehospital RBC transfusion mortality (**Table 4**).

The investigators [7] tried to eliminate the data noise by performing a comparison of matched patients using propensity scoring analysis (**Table 8**). Of concern is the failure to report the 30-day mortality; however, it was reported that the prehospital RBC transfusion was independently associated with a substantial reduction in the risk of mortality. Two other concerns are that the prehospital transfusion group was given substantially more blood after trauma center arrival and the variables included in the multivariate regression analysis were not described. Thus, it is difficult to be confident that prehospital RBC administration provides a mortality advantage for trauma patients.

A synthesis of two matched civilian cohort studies by Brown et al. [6] and Sumida et al. [9] (**Table 9**) strongly suggests that prehospital RBC transfusion is not associated with a survival advantage. This study by Brown et al. [6] was a single institution study at the University of Pittsburg Medical Center, which had more patient encounters than their multicenter trial [7]. Brown et al. matched both groups, and all patients included were transported from the scene with no interfacility transfers included. The number of PRBCs transfused during the first 24-hours in both groups was not significantly different. Although the number of patient encounters was limited in the Sumida et al. study [9] compared to the Brown et al. study [6], the Sumida et al. data were included for the purpose of completeness. The synthetic mortality between the prehospital RBC transfusion group and no prehospital RBC group was not statistically different. This mortality rate was consistent with our synthetic mortality of civilian patients undergoing prehospital and trauma center RBC transfusion (**Tables 4** and **5**). It is also important to note that the mortality rate was inconsistent with that of the Brown et al. multicenter trial [7].

The study by Holcomb et al. [8] investigated adult civilian trauma patients transported by helicopter from the scene who received blood products (plasma and/or RBCs), either prehospital or early in their hospital course. The 24-hour and 30-day mortality rates were the same for patients transported by a helicopter service capable of administering blood products, when compared to a helicopter service without that capability (**Table 10**). These data imply that the availability of prehospital blood products for trauma patients does not provide a survival benefit.

The study by O'Reilly et al. [4], which matched military trauma patients receiving prehospital blood and/or plasma to controls from an earlier time without prehospital transfusion capability, demonstrated a significant improvement in mortality (**Table 11**). Although the ISS was similar, these two groups represented entirely different cohorts in regard to the prehospital time, percent of advanced airway procedures, heart rate at admission, and hospital RBC transfusion rate. As each of these factors potentially favored increased survival for the prehospital transfusion group, the mortality difference in favor of prehospital transfusion is confounded. Although it is possible that multivariate logistic regression analysis might have clarified this concern, such an interrogation was not provided in the manuscript The O'Reilly et al. investigation presented mortality data in the subset of patients with an ISS > 16 (**Table 12**) [4]. Since mortality was similar for the groups with and without prehospital RBC transfusion capabilities, there seems little value in routinely providing prehospital RBC transfusion.

Meta-analysis of prehospital blood products

After completing of our meta-analysis, we performed another literature review and discovered a meta-analysis by Smith et al. published in 2016 [21]. Smith et al. investigated prehospital blood products (platelets, plasma, or RBCs) administration in trauma patients and the effect on mortality [21]. Similar to our results, Smith et al. did not note improvements in outcomes. Our study is different in that our primary focus was on prehospital RBC transfusions. Smith et al. computed an unadjusted risk of mortality in prehospital blood products administration and included three studies that we excluded. A study by Kim focused on the use of prehospital plasma, which was not the focus of our study. We did not include the studies by Price and Smith because they were not published as peer-reviewed manuscripts. The test for heterogeneity in the Smith et al. meta-analysis was substantial (I^2 = 63%), suggesting that the data should not have been combined.

Study strengths and limitations

Our meta-analysis is the only review to date that has investigated the mortality of trauma patients undergoing prehospital RBC transfusions. The literature search was extensive so that it is highly unlikely that any studies in peer-reviewed journals were excluded. The most significant limitation of this review is the low quality of evidence of the publications reviewed, despite being published in peer reviewed journals. Our review considered both military and civilian studies. The military studies were mostly case series with incomplete data likely due to the difficulty in collecting all variables in a combat situation. The military data needed to be included because the O'Reilly et al. study illustrates the paradigm shift after 2008, at which time prehospital blood products administration became the norm during war [4].

Conclusions

Trauma patient mortality increases as the intensity of the hemodynamic instability and level of anatomic injury progress. According to the literature review, some evidence demonstrates no survival improvement with prehospital RBC availability. However, other information suggesting a potential benefit is either confounded or likely to be biased. Since the quality of the existing literature evidence is poor, we recommend that additional studies be performed, such as prospective or randomized controlled trials.

Acknowledgements

The authors would like to thank Marina C. Hanes, ELS for copyediting the manuscript.

Disclosure of conflict of interest

None.

Address correspondence to: C Michael Dunham, Trauma/Surgical Critical Care, St. Elizabeth Youngstown Hospital, 1044 Belmont Ave., Youngstown 44501, OH, USA. E-mail: dunham.michael@sbcglobal.net

References

[1] Ball CG, Salomone JP, Shaz B, Dente CJ, Tallah C, Anderson K, Rozycki GS and Feliciano DV. Uncrossmatched blood transfusions for trauma patients in the emergency department: incidence, outcomes and recommendations. Can J Surg 2011; 54: 111-115.

[2] Nunez TC, Dutton WD, May AK, Holcomb JB, Young PP and Cotton BA. Emergency department blood transfusion predicts early massive transfusion and early blood component requirement. Transfusion 2010; 50: 1914-1920.

[3] Barkana Y, Stein M, Maor R, Lynn M and Eldad A. Prehospital blood transfusion in prolonged evacuation. J Trauma 1999; 46: 176-180.

[4] O'Reilly DJ, Morrison JJ, Jansen JO, Apodaca AN, Rasmussen TE and Midwinter MJ. Prehospital blood transfusion in the en route management of severe combat trauma: a matched cohort study. J Trauma Acute Care Surg 2014; 77: S114-120.

[5] Powell-Dunford N, Quesada JF, Malsby RF, Chou V, Gerhardt RT, Gross KR and Shackelford SA. Risk management analysis of air ambulance blood product administration in combat operations. Aviat Space Environ Med 2014; 85: 1130-1135.

[6] Brown JB, Sperry JL, Fombona A, Billiar TR, Peitzman AB and Guyette FX. Pre-trauma center red blood cell transfusion is associated with improved early outcomes in air medical trauma patients. J Am Coll Surg 2015; 220: 797-808.

[7] Brown JB, Cohen MJ, Minei JP, Maier RV, West MA, Billiar TR, Peitzman AB, Moore EE, Cuschieri J and Sperry JL. Pretrauma center red blood cell transfusion is associated with reduced mortality and coagulopathy in severely injured patients with blunt trauma. Ann Surg 2015; 261: 997-1005.

[8] Holcomb JB, Donathan DP, Cotton BA, Del Junco DJ, Brown G, Wenckstern TV, Podbielski JM, Camp EA, Hobbs R, Bai Y, Brito M, Hartwell E, Duke JR and Wade CE. Prehospital transfusion of plasma and red blood cells in trauma patients. Prehosp Emerg Care 2015; 19: 1-9.

[9] Sumida MP, Quinn K, Lewis PL, Jones Y, Barker DE, Ciraulo DL, Cowell V, Luk S, Murphy D and Jacobs L. Prehospital blood transfusion versus crystalloid alone in the air medical transport of trauma patients. Air Med J 2000; 19: 140-143.

[10] Bodnar D, Rashford S, Hurn C, Quinn J, Parker L, Isoardi K and Williams S. Characteristics and outcomes of patients administered blood in the prehospital environment by a road based trauma response team. Emerg Med J 2014; 31: 583-588.

[11] Soudry E and Stein M. Prehospital management of uncontrolled bleeding in trauma patients: nearing the light at the end of the tunnel. Isr Med Assoc J 2004; 6: 485-489.

[12] Sauaia A, Moore EE, Crebs JL, Maier RV, Hoyt DB and Shackford SR. Evidence level of individual studies: a proposed framework for surgical research. J Trauma Acute Care Surg 2012; 72: 1484-1490.

[13] Sherren PB and Burns B. Prehospital blood transfusion: 5-year experience of an Australian helicopter emergency medical service. Critical Care 2013; 17 Suppl 2: S112.

[14] Sunde GA, Vikenes B, Strandenes G, Flo KC, Hervig TA, Kristoffersen EK and Heltne JK. Freeze dried plasma and fresh red blood cells for civilian prehospital hemorrhagic shock resuscitation. J Trauma Acute Care Surg 2015; 78: S26-30.

[15] Inaba K, Teixeira PG, Shulman I, Nelson J, Lee J, Salim A, Brown C, Demetriades D and Rhee P. The impact of uncross-matched blood transfusion on the need for massive transfusion and mortality: analysis of 5,166 uncross-matched units. J Trauma 2008; 65: 1222-1226.

[16] Martin RR, Bickell WH, Pepe PE, Burch JM and Mattox KL. Prospective evaluation of preoperative fluid resuscitation in hypotensive patients with penetrating truncal injury: a preliminary report. J Trauma 1992; 33: 354-361; discussion 361-352.

[17] Miraflor E, Yeung L, Strumwasser A, Liu TH and Victorino GP. Emergency uncrossmatched transfusion effect on blood type alloantibodies. J Trauma Acute Care Surg 2012; 72: 48-52; discussion 52-43.

[18] Ruchholtz S, Pehle B, Lewan U, Lefering R, Muller N, Oberbeck R and Waydhas C. The emergency room transfusion score (ETS): prediction of blood transfusion requirement in initial resuscitation after severe trauma. Transfus Med 2006; 16: 49-56.

[19] Schwab CW, Civil I and Shayne JP. Saline-expanded group O uncrossmatched packed red blood cells as an initial resuscitation fluid in severe shock. Ann Emerg Med 1986; 15: 1282-1287.

[20] Tinkoff GH and O'Connor RE. Validation of new trauma triage rules for trauma attending response to the emergency department. J Trauma 2002; 52: 1153-1158; discussion 1158-1159.

[21] Smith IM, James RH, Dretzke J and Midwinter MJ. Prehospital blood product resuscitation for trauma: a systematic review. Shock 2016; 46: 3-16.
[22] Arbabi S, Jurkovich GJ, Wahl WL, Franklin GA, Hemmila MR, Taheri PA and Maier RV. A comparison of prehospital and hospital data in trauma patients. J Trauma 2004; 56: 1029-1032.
[23] Bruns B, Gentilello L, Elliott A and Shafi S. Prehospital hypotension redefined. J Trauma 2008; 65: 1217-1221.
[24] Hasler RM, Nuesch E, Juni P, Bouamra O, Exadaktylos AK and Lecky F. Systolic blood pressure below 110 mmHg is associated with increased mortality in penetrating major trauma patients: multicentre cohort study. Resuscitation 2012; 83: 476-481.
[25] Talving P, Palstedt J and Riddez L. Prehospital management and fluid resuscitation in hypotensive trauma patients admitted to Karolinska University Hospital in Stockholm. Prehosp Disaster Med 2005; 20: 228-234.
[26] Yaghoubian A, Lewis RJ, Putnam B and De Virgilio C. Reanalysis of prehospital intravenous fluid administration in patients with penetrating truncal injury and field hypotension. Am Surg 2007; 73: 1027-1030.
[27] Dutton RP, Shih D, Edelman BB, Hess J and Scalea TM. Safety of uncrossmatched type-O red cells for resuscitation from hemorrhagic shock. J Trauma 2005; 59: 1445-1449.
[28] Berns KS and Zietlow SP. Blood usage in rotor-wing transport. Air Med J 1998; 17: 105-108.
[29] Dalton AM. Use of blood transfusions by helicopter emergency medical services: is it safe? Injury 1993; 24: 509-510.
[30] Higgins GL 3rd, Baumann MR, Kendall KM, Watts MA and Strout TD. Red blood cell transfusion: experience in a rural aeromedical transport service. Prehosp Disaster Med 2012; 27: 231-234.
[31] Weaver EA, Eshelby S, Norton J and Lockey DJ. The introduction of on-scene blood transfusion in a civilian physician-led pre-hospital trauma service. Scand J Trauma Resusc Emerg Med 2013; 21 Suppl 1: S27.
[32] Baker JB, Korn CS, Robinson K, Chan L and Henderson SO. Type and crossmatch of the trauma patient. J Trauma 2001; 50: 878-881.
[33] Como JJ, Dutton RP, Scalea TM, Edelman BB and Hess JR. Blood transfusion rates in the care of acute trauma. Transfusion 2004; 44: 809-813.