Improved survival in critically injured combat casualties treated with fresh whole blood by forward surgical teams in Afghanistan

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BACKGROUND: The objective of this study was to assess transfusion strategies and outcomes, stratified by the combat mortality index, of casualties treated by small surgical teams in Afghanistan. Resuscitation that included warm fresh whole blood (FWB) was compared to blood component resuscitation.

STUDY DESIGN AND METHODS: Casualties treated by a Role 2 surgical team in Afghanistan from 2008 to 2014 who received 1 or more units of red blood cells (RBCs) or FWB were included. Patients were excluded if they had incomplete data or length of stay less than 30 minutes. Patients were separated into two groups: 1) received FWB and 2) did not receive FWB; moreover, both groups potentially received plasma, RBCs, and platelets. The analysis was stratified by critically versus noncritically injured patients using the prehospital combat mortality index. Kaplan-Meier plot, log-rank test, and multivariable Cox regression were performed to compare survival.

RESULTS: In FWB patients, median units of FWB and total blood product were 4.0 (interquartile range [IQR], 2.0-7.0) and 16.0 (IQR, 10.0-28.0), respectively. The Kaplan-Meier plot demonstrated that survival was similar between FWB (79.1%) and no-FWB (74.5%) groups (p = 0.46); after stratifying patients by the combat mortality index, the risk of mortality was increased in the no-FWB group (hazard ratio, 2.8; 95% confidence interval, 1.2-6.4) compared to the FWB cohort.

CONCLUSION: In forward-deployed environments, where component products are limited, FWB has logistical advantages and was associated with reduced mortality in casualties with a critical combat mortality index. Additional analysis is needed to determine if these effects of FWB are appreciable in all trauma patients or just in those with severe physiologic derangement.

Whole blood transfusion was standard therapy for hemorrhage during both world wars and the Korean and Vietnam conflicts.[1,2] Then, for the 3 decades after the Vietnam conflict, component therapy and crystalloid resuscitation became the standard of care without comparative efficacy studies demonstrating improved outcomes.[1–3] Recent conflicts involving US military forces over the past 2 decades saw a resurgence in the use of whole blood on the battlefield, initially using warm fresh whole blood (FWB) from "walking blood banks," and since 2016 adding cold-stored, fully tested whole blood. The

ABBREVIATIONS: CMI-PH = prehospital combat mortality index; DODTR = Department of Defense Trauma Registry; FWB = fresh whole blood; ISS = injury severity score; MTFs = medical treatment facilities.

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use of FWB has been associated with improved outcomes for combat wounded.[4,5] Over the past 2 decades, damage control resuscitation has evolved, and deployed trauma teams transfuse blood components in ratios recapitulating whole blood, while collecting warm FWB for the exsanguinating casualty.[6] The Armed Services Blood Program data indicate that over 10,700 units of warm FWB have been transfused by US military teams during the recent conflicts in Iraq and Afghanistan.[7]

In the current battlefield system of care, casualties move from point of injury through increasing levels of care on the battlefield. Damage control resuscitation is initiated at the point of injury (Role 1 care) with aggressive control of external hemorrhage using tourniquets and hemostatic dressings, avoidance of crystalloids, early administration of tranexamic acid, and resuscitation using whole blood.[8–12] Role 2 medical treatment facilities (MTFs) provide forward resuscitative care and damage control surgery, with limited resources and 8 to 20 personnel. A Role 3 MTF is the highest level of care in the combat zone and has the capability to store and transfuse blood components, including apheresis platelets collected on site, and provide specialty surgical care and extended intensive care. Role 4 MTFs are outside the combat zone and are comprehensive health care facilities. Since Role 2 MTFs are meant to bridge the time/space gap from wounding to definitive hemorrhage control by using damage control principles, they are designed to be mobile and have minimal resources and a limited blood supply. Care at Role 2 MTFs is intrinsic to the damage control battlefield paradigm in that these small surgical teams provide rapid surgical hemorrhage control and then transfer patients to Role 3 MTFs. Since the initial descriptions of damage control resuscitation, battlefield resuscitation practices have dramatically changed to incorporate these principles based on focused empiricism and supporting data.[4,5,8,13–15]

Indications for a walking blood bank and FWB transfusion in the far-forward combat environment include an inadequate supply of fully tested cold-stored whole blood or component therapy or when component therapy is deemed to be ineffective.[16] Surgical teams in austere environments collect FWB from prescreened donors and transfuse it shortly after collection. Having a robust and well-rehearsed walking blood bank is a necessity for forward-deployed surgical teams. The existing literature regarding whole blood outcomes is limited but suggests improved survival when FWB is administered to combat casualties.[4,5] Previous studies of FWB use may have been biased, even though they had the advantage of the injury severity score (ISS) to assess anatomic injury burden, they did not assess outcomes based on the severity of physiologic burden; additionally, survivor bias is difficult to overcome in retrospective studies assessing transfusion outcomes.[4,5,15] The objective of this study was to assess outcomes of critically injured patients who received FWB as compared to those who received no FWB and partial (i.e., no platelets) or complete (i.e., with platelets) component therapy by Role 2 surgical teams.

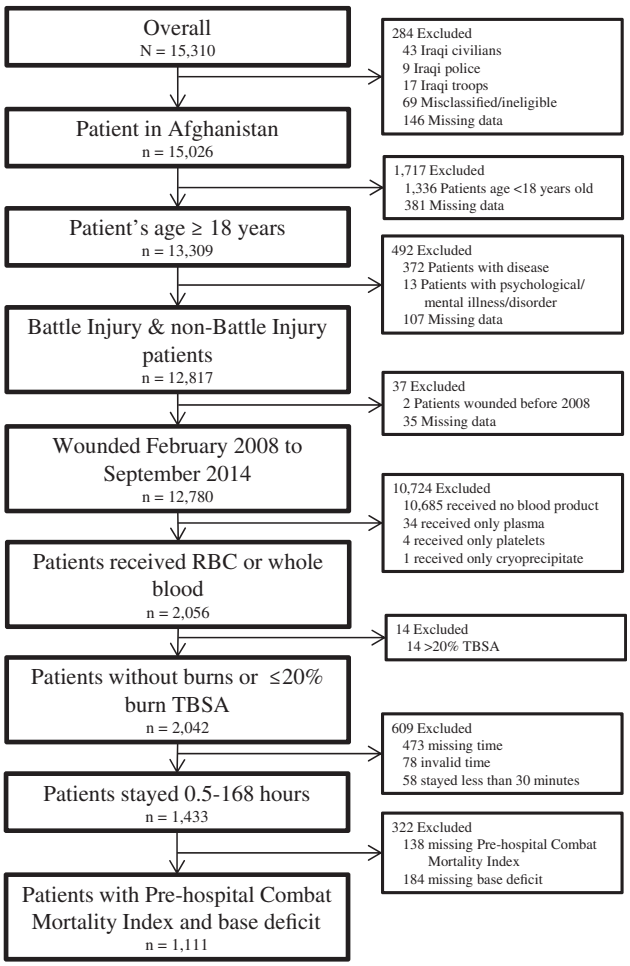

Fig. 1. Flow diagram of patients (n = 1111) in Role 2 Database by inclusion and exclusion criteria, October 2009 to September 2014. TBSA = total burn surface area.

STUDY DESIGN AND METHODS

This study was reviewed and approved by the US Army Institute of Surgical Research regulatory department and was

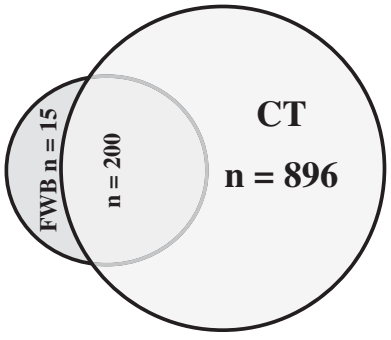

Fig. 2. Venn diagram of study patients (n=1111) treated at Role 2 facilities in the Afghanistan combat theater, October 2009 to September 2014. CT = partial or complete component therapy.

TABLE 1. Demographics and patient characteristics of study patients (n = 1111) treated at Role 2 facilities in the Afghanistan combat theater by FWB use, October 2009 to September 2014

	FWB (n = 215)		No FWB (n = 896)		
Variable	n	%	n	%	p value
Male	212	98.6	862	96.2	0.0962
Age, median (IQR)	25.0	22.0 to 30.0	25.0	22.0 to 30.0	
Battle-injured	199	92.6	811	90.5	0.3490
Affiliation					<0.0001
Military, US	83	38.6	151	16.9	
Military, non-US	77	35.8	451	50.3	
Other	55	25.6	294	32.8	
Injury mechanism					0.3698
Explosion	113	52.6	423	47.2	
Gunshot wound	81	37.7	372	41.5	
Mortality at discharge	17	7.9	54	6.0	0.3114
Base deficit, median (IQR)	−7.0	−12.0 to 4.0	−5.0	−8.0 to −2.0	<0.0001
Blood product, units, median (IQR)	16.0	10.0 to 28.0	6.0	4.0 to 12.0	<0.0001
FWB	4.0	2.0 to 7.0	N/A	N/A	
RBC	6.0	3.0 to 10.0	4.0	2.0 to 6.0	<0.0001
FFP	5.0	2.0 to 8.0	3.0	1.0 to 5.0	<0.0001
Platelets	0.0	0.0 to 0.0	0.0	0.0 to 0.0	0.1825
Crystalloid, L, median (IQR)	3.7	2.1 to 5.6	3.0	2.0 to 4.1	<0.0001
CMI					0.0008
Mild	41	19.1	277	30.9	
Moderate	74	34.4	323	36.0	
Severe	57	26.5	159	17.7	
Critical	43	20.0	137	15.3	

CMI = combat mortality index; FFP = fresh frozen plasma; FWB = fresh whole blood; IQR = interquartile range; N/A = not applicable.

determined to be exempt. This was a secondary analysis that used data from adult trauma patients that required transfusion and included both battle and nonbattle injuries occuring in Afghanistan from February 2008 to September 2014. Data were obtained from the Joint Trauma System Role 2 Database. The Role 2 Database was initiated in 2008 and is a database into which Role 2 personnel enter trauma patient data from the clinical records; 24 Role 2 locations were included in this analysis. The strength of this database is that it includes a significantly large amount of patients which did not get captured by the Department of Defense Trauma Registry (DODTR); up until 2014, a patient had to be admitted to a Role 3 MTF to be captured by, and entered into, the DODTR.

Patients eligible for inclusion in this analysis received at least 1 unit of red blood cells (RBCs) or FWB. Patients were excluded on the basis of 1) incomplete data; 2) more than 20% total body surface area burn; or 3) died of wounds in less than 30 minutes after MTF arrival to compare as equal groups as possible, given that FWB requires approximately 30 minutes to collect and process prior to initiation of transfusion.[15]

Patients were divided into two groups: 1) received FWB and 2) did not receive FWB. Both groups potentially received plasma, RBCs, or platelets. The primary outcome was survival to Role 2 discharge. Blood products (FWB, RBCs, platelets, and plasma) and volume of crystalloid delivered prehospital and in the first 24 hours after admission were included in the analysis. The plasma-to-RBC ratio was calculated as number of plasma units plus FWB units divided by RBC units plus FWB units.[17] Platelet ratios were not analyzed because only a small number of Role 2 surgical teams had access to platelets during the study time frame.

Potential confounders determined a priori included physiologic injury severity defined by prehospital combat mortality index (CMI-PH) (critical, less critical), admission base deficit, battle or nonbattle injury, and patient affiliation (US military, non-US military, other). The CMI-PH was developed by researchers at the US Army Institute of Surgical Research to quantify injury severity with use of physiologic parameters, prehospital heart rate, Glasgow Coma Scale, and systolic blood pressure.[18] CMI-PH is classified as mild

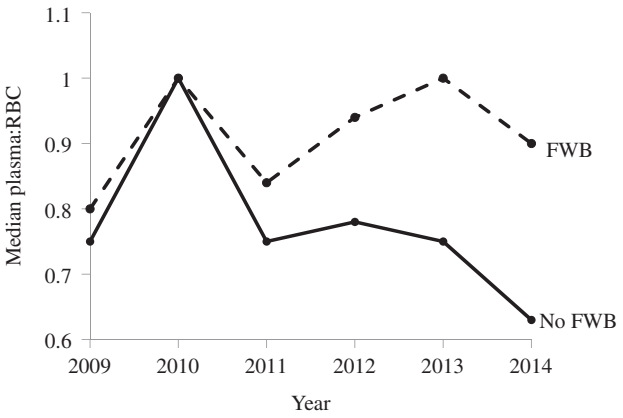

Fig. 3. Median plasma: RBC ratio by FWB use over time for study patients (n=1111) treated at Role 2 facilities in the Afghanistan combat theater, October 2009 to September 2014.

(CMI = 0), moderate (CMI = 1), severe (CMI = 2), or critical (CMI ≥ 3). The CMI score was developed and used in this analysis because ISS and the Abbreviated Injury Scale was not available in the Role 2 Database.

When prehospital vital signs were not available, admission vital signs were substituted for the calculation of CMI-PH. Injury severity was stratified as less critical CMI-PH less than 3 and critical CMI-PH of 3 or greater. To account for differences in injury location and pattern of injury, we adjusted for battle injury, which includes all injuries that occurred during a hostile action or battle compared to traumatic injury form nonbattle injuries such as accidental gunshot wounds, falls, or vehicle injuries. Patient affiliation was included as a covariate to adjust for variation in baseline health status and use of protective gear. Patient affiliation included US military, non-US military (i.e., NATO,

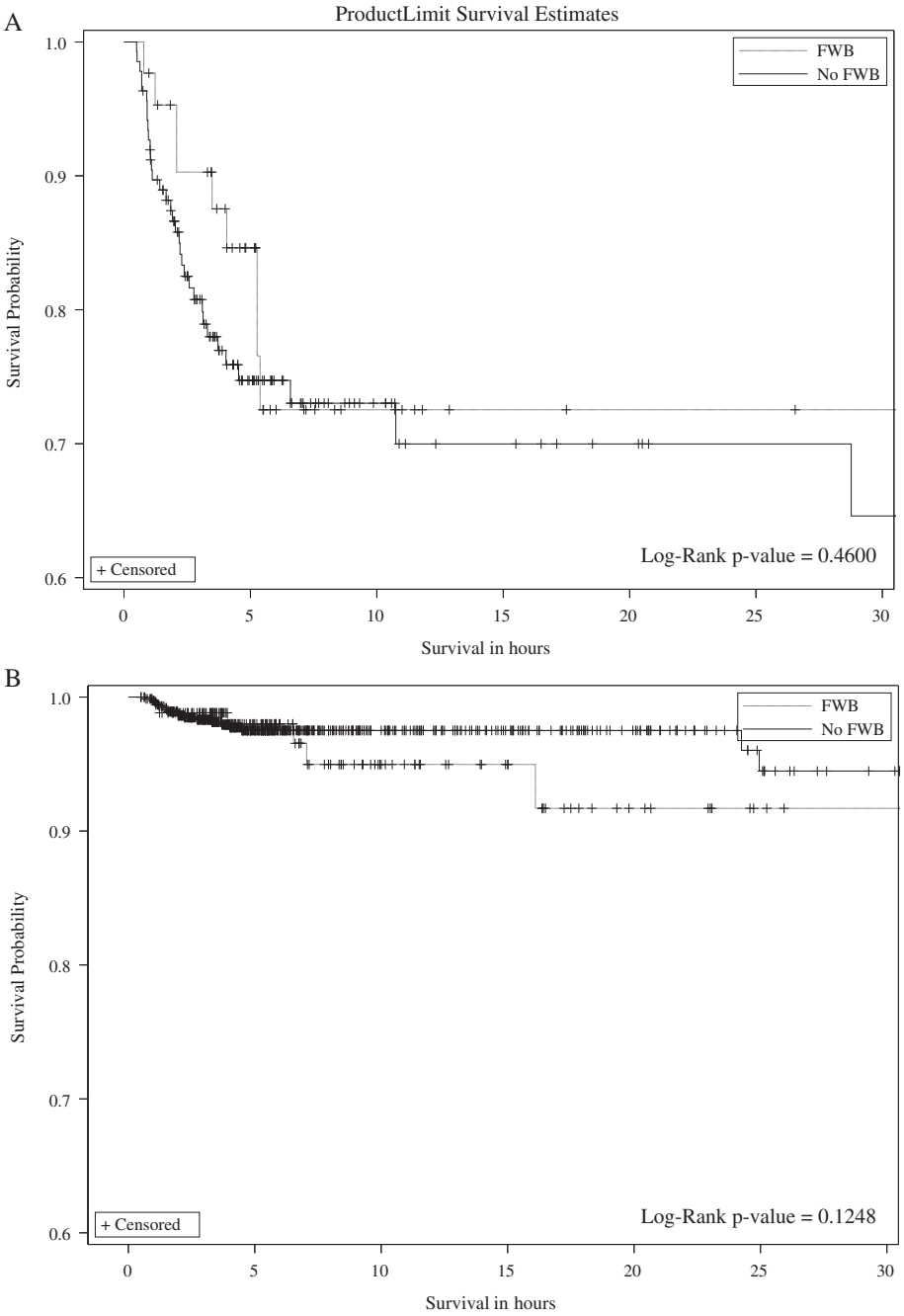

Fig. 4. Kaplan-Meier curve for survival to Role 2 discharge by fresh whole blood (FWB) use in A) critically (n=180) and B) noncritically (n=931) injured study patients treated at Role 2 facilities in the Afghanistan combat theater, October 2009 to September 2014.

TABLE 2. Multivariate Cox regression of mortality for critical* patients (n = 180) and noncritical patients (n = 931) treated at Role 2 facilities in the Afghanistan combat theater, October 2009 to September 2014

	HR (95% CI)			
	Critical patients		Noncritical patients	
Variable	Unadjusted	Adjusted	Unadjusted	Adjusted
No FWB versus FWB	1.3 (0.6-2.8)	**2.8 (1.2-6.4)**	0.5 (0.2-1.2)	0.9 (0.4-2.0)
Base deficit	**0.9 (0.9-1.0)**	**0.9 (0.9-1.0)**	**0.8 (0.8-0.9)**	**0.8 (0.8-0.9)**
Battle-injured	0.9 (0.4-2.1)	0.8 (0.3-2.0)	**0.3 (0.1-0.6)**	**0.2 (0.1-0.6)**
Affiliation				
Military, non-US	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Military, US	**2.3 (1.1-4.9)**	**3.1 (1.4-7.2)**	0.2 (<0.1-1.2)	0.2 (<0.1-1.4)
Other	1.1 (0.6-2.3)	0.9 (0.4-1.8)	0.7 (0.3-1.5)	0.6 (0.2-1.3)

CI = confidence interval; FWB = fresh whole blood; HR = hazard ratio.
* Critical patients were defined by Combat Mortality Index (CMI), where critical patients had a CMI≥3 and non-critical patients had a CMI < 3.

Afghanistan National Security Force, Afghanistan police), and other (local national civilians, Department of Defense civilians, enemy combatants, and unspecified patients).

Demographic characteristics, CMI-PH, vital signs, blood product, and crystalloid transfusion were compared between study groups. Continuous variables were presented as median (interquartile range [IQR]), while categorical variables were presented as counts and proportions. The chi-square and Mann-Whitney U test were used to test for differences between study groups. Kaplan-Meier log-rank was used to compare unadjusted Role 2 survival between FWB and no-FWB study groups. Multivariable Cox regression was used to adjust for confounding effects on survival to Role 2 discharge. The final Cox regression models had the lowest Akaike information criterion, which indicated the best quality of the final statistical models relative to the other tested models. The Kolmogorov-Type Supremum Tests indicated the final Cox regression models met the proportional hazards assumption.

Statistical significance was determined at the $p < 0.05$ level (two-sided). All analyses were conducted with computer software (SAS version 9.4, SAS Institute, Inc).

RESULTS

Of the 15,310 available patient records, 12,780 patients were eligible based on patient age, injury type, location, and date. From the eligible study population, there were 2056 patients who received RBCs or whole blood. Excluded were 14 patients who had more than 20% total burn surface area, 609 patients were excluded because they were dead on arrival or died within 30 minutes of arrival, and 322 patients with missing covariate data. The final study population included 1111 patients (Fig. 1). Of the study population, 215 (19.4%) patients received FWB, while 896 (80.6%) patients received component therapy only (Fig. 2). Among the 896 patients in the no-FWB group, 101 (11.3%) received platelets.

The two groups were similarly made up of young adult males injured in battle (Table 1). Study groups varied by patient affiliation. The FWB group had more US military members (38.6% vs. 16.9%) compared to the no-FWB group. Compared to no-FWB group, more FWB patients had a critical (20.0% vs. 15.3%) or severe (26.5% vs. 17.7%) CMI-PH. FWB patients received median 4.0 (IQR, 2.0-7.0) units of FWB and more total component therapy (RBC, fresh frozen plasma, platelets) products (16.0; IQR, 10.0-28.0) compared to the no-FWB group (6.0; IQR, 4.0-12.0). The median length of stay at Role 2 was 5.0 (IQR, 3.1-9.3) hours with a 90th percentile of 21.0 hours.

During the study period, the median plasma-to-RBC ratio was 1:1 (range, 0.8-1.0) for the FWB group as compared to 0.8:1 (range, 0.6-1.0) for the no-FWB group ($p < 0.0001$) (Fig. 3). Survival was similar between critical (79.1% vs. 74.5%; $p = 0.4600$) and less critically (95.4% vs. 97.5%; $p = 0.1248$) injured FWB and no-FWB groups, respectively (Fig. 4). In the critically injured patient group (CMI-PH ≥ 3), the median number total blood products transfused was 21.0 (IQR, 14.0-33.0) units for those who received FWB and 9.0 (IQR, 4.0-16.0) for those who did not receive FWB ($p < 0.0001$). The median (IQR) ratio of FWB given (i.e., FWB/(FWB + platelets + cryoprecipitate + plasma + RBC)) was 0.29 (0.18-0.47) among FWB patients. In the less critically injured patient group (CMI-PH < 3), the median number of blood products transfused was 15.0 (IQR, 9.0-25.0) units for those who received FWB and 6.0 (IQR, 3.0-11.0) units for those who did not receive FWB ($p < 0.0001$).

In adjusted analyses, there was no significant difference in mortality of less critical patients who received no FWB versus FWB (hazard ratio [HR], 0.9; 95% CI, 0.4-2.0; $p = 0.74$). After adjusting for admission base deficit, battle injury, and patient affiliation in the Cox regression, the risk of mortality at Role 2 discharge was elevated in critically injured patients who received no FWB (HR = 2.8; 95% CI, 1.2-6.4; $p = 0.0166$) compared to patients who received FWB (Table 2).

DISCUSSION

Among critically injured patients treated by Role 2 surgical teams, FWB transfusion was associated with an optimal hemostatic resuscitation ratio of plasma to RBC transfusion; a higher average CMI-PH score; and improved survival to Role 2 discharge compared to those casualties who did not

receive FWB in a setting where platelets were usually not available to support component therapy. This project captures data from Role 2 forward surgical teams and includes data not included in the DODTR. Until 2014, a casualty had to arrive at a Role 3 MTF to be captured in the DODTR; casualties who died prior to arriving at the Role 3 or host nation casualties whose highest level of care was at the Role 2 before being transferred to the host nation hospitals were not included. This analysis is also unique in that we used the CMI-PH to differentiate patient response to FWB transfusion since the data from the Role 2 Database did not have validated ISS data; the CMI was developed by researchers at the ISR to overcome this limitation.[18] This analysis demonstrates lower survival in patients with a higher CMI-PH who received a balanced component transfusion strategy compared to transfusion with FWB.

Outcomes evaluated survival to Role 2 discharge as the chosen outcome for this analysis given that data from this population could not always be captured beyond the Role 2 MTFs during the study dates. Also, given that data from civilian trauma centers demonstrates that hemorrhagic deaths occur rapidly, with the median time to death being 2.0 to 2.6 hours from admission and that 85% of hemorrhagic deaths occur within 6 hours; patients who survived to discharge from the Role 2 MTFs would have a low probability of subsequent death from hemorrhage.[19]

The plasma-to-RBC ratio was similar between the study groups at the beginning of the study period, but the median ratios of the groups started to diverge in 2011. Patients who received FWB had a median plasma-to-RBC ratio of 1:1, while patients who did not receive FWB had a plasma-to-RBC ratio of 0.8:1; both of these ratios would be considered "balanced" given that the definitive ratio has not been precisely demarcated—the overall consensus remains that the closer to 1:1 the better. One possibility for this observation is that those units that used more FWB recognized the importance of use of hemostatic transfusion rations. In addition, the FWB group received more blood product and included a larger proportion of patients with a critical or severe CMI-PH as compared to those who did not receive FWB. Patients who received FWB had worse physiological derangement based on the CMI-PH scare compared to those who did not receive FWB. In critically injured patients, we found the adjusted risk of mortality to be almost three times greater in the no-FWB group as compared to the FWB group. This may be due in part to the fact that only 11.3% of the no-FWB group received platelets, whereas the FWB group received platelets in the whole blood.

Our results are in concordance with the two previously published studies of whole blood use in combat casualties. Spinella et al.[5] analyzed 100 combat casualties from 2004 to 2007 who received FWB in addition to RBCs and plasma versus 254 casualties who received RBCs, plasma, and apheresis platelets; they reported an association between whole blood transfusion and 30 day survival. In addition, Nessen et al.[4] reported nonregistry data collected from six Role 2 Forward Surgical Teams from 2005 to 2010 in which 94 casualties treated with FWB plus partial (no platelets) component therapy had improved survival to discharge as compared to 394 patients who received partial component therapy. These studies are suggestive that FWB may contribute to improved survival.

Contrary to our results, Perkins et al.[15] analyzed combat casualties who received a massive transfusion (defined as >10 units transfused in 24 hr) and reported no difference in 30-day survival for 85 patients who received whole blood use versus 284 patients who received a transfusion strategy including platelets. In the Perkins analysis, less FWB was transfused (proportional to total blood products in the Spinella analysis), and survival at 24 hours approached significance. The interpretation of their results may mean: 1) FWB and component therapy including platelets have the same effect on outcomes in patients who received a massive transfusion, or 2) stratifying patients by massive transfusion may impart a dual selection bias. First, the authors may have excluded patients who died before meeting massive transfusion criteria. Second, the need for massive transfusion may be determined not only by severity of the injury but also by initial blood product intervention such that the initial transfusion intervention could reduce total blood product requirements and preferentially exclude patients from the analysis.

Given that it takes approximately 30 minutes to request, collect, and process FWB, patients who died within 30 minutes of arrival at a Role 2 MTF were not eligible for this study; however, that may be the patient cohort who would have the most clinically impressive response to WB if it could have been transfused immediately.[15] Recently, Shackelford et al.[14] demonstrated the importance of including early deaths in the analysis because it was this group of patients who had the potential to benefit the most from early transfusion. By excluding the early deaths, this study has the potential for selection bias. We tried to overcome this selection bias by excluding all early death in both the FWB and no-FWB cohorts to minimize this bias; however, by overcoming the selection bias, we introduced a survival bias and also potentially excluded the most significantly hemorrhaging patients who may have benefited from the FWB intervention. The intent of excluding all early deaths is that we analyzed casualties who survived long enough to actually receive either product and therefore could observe the effect of the intervention even though the early deaths may actually be the ones who are hemorrhaging rapidly and would therefore benefit most from FWB transfusion. Retrospective transfusion studies assessing outcomes have inherent biases, but considering that FWB is not a Food and Drug Administration–approved product and that these data were from far-forward austere surgical teams in the combat zone, these data are extremely important, despite the limitations; however, the potential survival bias needs to be further investigated.

In this study, all whole blood was collected from a walking blood bank and used immediately as a warm product.

Research has demonstrated warm FWB may be better than cold-stored whole blood as the storage process may decrease the function of components.[20–23] Currently, in the military operations in Iraq, Afghanistan, and Syria, many of the Role 2 surgical teams are equipped with low Group O titer whole blood stored at 4°C, allowing them to transfuse whole blood at the point of injury, en route to a Role 2 facility, or within minutes of arrival. The association of survival and low Group O titer whole blood is currently lacking; however, it has been anecdotally embraced, not just because of the logistical advantages of whole blood but because of feedback from the continuum of care of observed improved clinical outcomes. Further studies examining all patients, and not excluding the early deaths, can be conducted in patients who receive low Group O titer whole blood and will help further elucidate the potential benefit of early whole blood transfusion in trauma, although these potential study groups will differ from the current study, given that our study included only FWB transfusions. Research has demonstrated there are in vitro differences in the efficacy of cold-stored blood versus warm FWB; these differences also require further clinical investigation.[15,16,20,22,23]

Although the group that did not receive FWB had a ratio below 1:1, both study groups received a plasma to RBC ratio close to 1:1, and current evidence suggests that this is optimal.[8] Another possibility for significant difference in the outcomes, even more so than the plasma:RBC ratio accounting for the differential outcomes observed in this study is the fact that the FWB group received fresh, functional platelets, compared to only 11.3% (101/896) of the no-FWB group that received platelets. The importance of platelet transfusion for hemostasis in life-threatening traumatic hemorrhage has been demonstrated, most recently in a large randomized controlled trial.[8] Additional consideration in the outcomes may be attributed to differential capabilities of the surgical teams; it is possible that teams that were better able to initiate damage control resuscitation in a 1:1 manner, were also more likely to transfuse FWB, and were overall more prepared to care for hemorrhaging combat casualties. Role 2 surgical teams are usually split into two teams to provide surgical coverage for a larger area, especially in Afghanistan, where the topography precludes easy evacuation; because of this, most Role 2 MTFs are minimally manned (8-10 people) and are not augmented by extra personnel to assist with resuscitation. Therefore, the simpler process of hanging 1 unit of whole blood versus 3 units of blood components may facilitate a quicker response to meet transfusion requirements. And while there are challenges to run a walking blood bank during casualty resuscitations, Role 2 MTFs usually rely on training other medical elements on the forward-deployed bases to assist with walking blood banks. These issues are specific to forward-deployed military surgical teams but may also impact rural civilian hospitals, where platelets and additional manpower are not readily available.

Several limitations of the study must be taken into consideration when interpreting these results. No anatomic injury severity data were available in the Role 2 Database; this is a huge limitation when performing any analysis on the patient population cared for by far-forward surgical teams before 2014 when the DODTR started to include Role 2 patients. To overcome this significant hindrance, we used the CMI-PH to adjust for physiologic injury severity. The CMI-PH was developed as a surrogate for injury severity and includes physiologic scoring; in austere military health care settings, CMI-PH is a better predictor of mortality when compared to other scoring systems, such as revised trauma score, shock index, and field triage score.[18] Another benefit to using CMI-PH was that these data were collected before the intervention and outcome, which is not always the case for ISS. Oftentimes, ISS is assessed by providers after intervention and outcomes, which may present a source of collider bias, given that patients who die immediately at the point of injury have limited documentation of injuries that can be viewed externally, while patients receiving extensive medical care will be assessed using documentation of both external and internal injuries, and the US military patients will also undergo a full autopsy i.e., computed tomography scans).[24] Therefore, while not published currently, the CMI-PH appears to be a better predictor of mortality than other scoring systems in the military population.[18] In addition to no anatomic injury severity data, the Role 2 Database does not include information on time to transfusion. We did include prehospital administration of blood in the calculation of total blood product the patient received, but this data set was limited by a lack of information about the amount of time between point of injury and initiation of blood transfusion. Furthermore, the Role 2 Database does not include follow-up information on these patients, and we are able to assess only survival to Role 2 discharge. In trauma that results in a hemorrhage injury, the risk of bleeding to death is associated with time to resuscitation and hemorrhage control and earlier end points are needed to better understand death from hemorrhage.[19] Thus, we believe this limitation to our analysis is minimal as we are assessing patients during their greatest risk of death. Other limitations of the Role 2 Database include the following: It is not validated against medical records; the proportion of Role 2 patients captured in this database are unknown, given that data were voluntarily collected by health care providers; and the data lack entry standardization. Despite the limitations of the Role 2 Database, it is the largest source of Role 2 forward surgical team data during this time period, which is especially important given the impact of time on trauma outcomes.[14,25]

Despite the limitations in this analysis and given the challenges of obtaining clinical data from far forward, austere and resource-constrained environments, this study has unique and compelling features that lay the foundation for future military and civilian investigations. This analysis represents the largest analysis of far forward whole blood transfusion at Role 2 surgical facilities. Not only do these results support the feasibility of using FWB in the forward combat environment with a limited blood supply, but the results

suggest that FWB transfusion, especially in patients who presented with significant physiologic derangement, may improve early survival. This analysis of FWB use spans the longest period of time in which WB transfusion practices have been in our trauma system and used a novel physiologic scoring system to stratify patients. These results may not only be generalizable to hemorrhaging adult trauma patients being treated in austere environments with a limited blood supply, but they also warrant further investigation in robust stateside Level 1 trauma centers.

These results corroborate previous studies demonstrating lower mortality in patients who received FWB. In addition, over time, the plasma-to-RBC ratio in the FWB patients was closer to 1:1 as compared to patients who did not receive FWB. FWB was the only source of platelets in these patients, which may have impacted survival. Despite limitations of this study, whole blood transfusion in the combat wounded may confer a survival advantage to those who are critically injured. Further investigation is warranted in both military and civilian populations to determine if there is a threshold or ratio at which whole blood transfusion confers a survival advantage; if there are differential effects of whole blood transfusion among patient populations; and if the timing of whole blood transfusion effects survival. Robust multicenter trials are needed to compare the potential benefits of whole blood to component therapy for patients with traumatic hemorrhage.

CONCLUSIONS

Whole blood transfusion of traumatically injured combat casualties at Role 2 MTFs is associated with transfusion of optimized component ratios, a critical CMI-PH, and improved survival to discharge from forward surgical teams compared to component therapy often lacking platelets. FWB confers a clear logistic advantage in the austere environment given that each unit transfused contains a full complement of components given simultaneously and may confer a survival advantage in critically injured patients. As further data emerge regarding the benefits of whole blood, small surgical teams could be optimized with cold-stored, universal-donor whole blood for resuscitation while awaiting FWB. Further research is needed to compare the potential benefits of whole blood to optimal component therapy for patients with traumatic hemorrhage.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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