The prehospital use of younger age whole blood is associated with an improved arrival coagulation profile

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INTRODUCTION: Recent in vitro data have shown that the hemostatic profile of whole blood (WB) degrades significantly after 14 days, yet the optimal storage remains debated. We hypothesized that arrival coagulation studies would be improved in patients receiving younger WB in the prehospital setting.

METHODS: This study was approved by our institutional institutional review board. We evaluated all trauma patients who received prehospital blood products by our helicopter service between July 2017 and July 2019. "Young" WB was defined as 14 days or less. Patients who received at least 1 U of young WB were classified as YOUNG, while the remainder was classified as OLD. Continuous data are presented as medians (25th–75th interquartile range) with comparisons performed using Wilcoxon rank sum. Assessments of clinical hemostatic potential included arrival platelet cell count and rapid thrombelastography. Multivariate regression analysis was also performed (Stata 12.1; College Station, TX).

RESULTS: A total of 220 patients received prehospital WB during the study period. Of these, 153 patients received YOUNG WB, while 67 were transfused only OLD WB units. There were no differences in demographics, prehospital or arrival physiology, or Injury Severity Score among the two groups. The measures of clot initiation (activated clotting time) and kinetics (k time) were improved, as were the measures of clot acceleration/fibrinogen function (angle) and platelet function (maximum amplitude). As well, arrival platelet count was higher in the YOUNG cohort. No significant differences in postarrival transfusion were noted ($p = 0.220$). Multivariate analysis showed the greatest differences in maximum amplitude and α angle but failed to reach significance.

CONCLUSION: Previous in vitro data have suggested deterioration of platelet function in cold-stored WB after 14 days. The current study demonstrated decreased global hemostasis by clinically available laboratory tests, especially related to fibrinogen and platelet interactions on univariate, but not multivariate analysis. This did not translate into increased transfusion requirements. Further studies are needed to determine the optimal storage duration for cold-stored WB for transfusion in the bleeding trauma patient, as well as rule out the presence of confounding variables. (*J Trauma Acute Care Surg.* 2021;90: 607–614. Copyright © 2021 American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Therapeutic, level IV.

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Like many aspects of surgical care, the history of the resuscitation of critically injured patients has been cyclical in nature. While whole blood (WB) was recognized as early as World War I as an optimal resuscitation medium, logistical and economic pressure in later conflicts led to the implementation of crystalloid fluids.[1–3] As the complications of massive crystalloid resuscitation became more and more prevalent,[1,3,4] packed red cells and, later, component therapy were studied, vastly improving outcomes.[5,6] Recognition of coagulopathy as a significant predictor of poor outcome led to the study of optimal component ratios, again improving outcomes.[5–7] Despite these improved clinical outcomes, recent in vitro and clinical studies have elucidated the poor coagulation profile of even optimal component therapy,[3,8] ironically driving renewed interest in WB therapy.

Recent guidelines have emphasized the potential role of WB in both prehospital and hospital settings.[9,10] The use of WB has been shown to decrease the need for further blood products, and improve survival.[11,12] Logistical barriers, however, still prevent the widespread adoption of WB resuscitation. Safe storage and timely administration of WB have been a major concern in its adoption. The hemostatic profile of WB has recently been shown to degrade significantly after 14 days of cold storage in the in vitro setting.[13] Currently, the recommended shelf life of cold-stored WB is 21 days, which can be expanded to 35 days with the use of citrate-based preservatives.[14,15] These guidelines are based almost entirely on effects on red blood cells, without consideration of hemostatic potential.[14] The downstream clinical effect of aged WB on the coagulation pattern of severely injured patients has yet to be studied. Understanding the sequelae of using aged WB on traumatic coagulopathy would help guide the maximum storage times for this product.

To date, there are no data comparing clinical endpoints for WB as it ages in storage. The following study demonstrates the effect of aging WB on the presenting rapid thromboelastography (r-TEG) profiles, platelet effects, and clinical outcomes of severely injured patients. We hypothesize that the prehospital transfusion of "young" WB will lead to improvements in the presenting hemostatic profiles of hemorrhaging patients over transfused "old" blood. Showing clinical changes in the biochemical hemostatic profile of trauma patients with young WB would serve to guide the storage and use of product as its use becomes more widespread in those patients who require the most hemostatic support.

PATIENTS AND METHODS

Study Setting

The University of Texas Health Science Center—Houston and the Memorial Hermann Hospital Institutional Review Boards approved this study. The Red Duke Trauma Institute at Memorial Hermann Hospital is an American College of Surgeons–verified level I trauma center and the primary teaching hospital for the McGovern Medical School, University of Texas Health Science Center. Memorial Hermann is one of only two level 1 trauma centers in Houston, Texas, the fourth largest city in the United States. The hospital is a 1,082-bed facility within Texas Medical City and is home to the John S. Dunn Helistop, the busiest heliport in the United States for its size. The trauma center admits more than 8,000 trauma patients

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annually with the most severely injured cared for in the 20-bed shock-trauma intensive care unit (ICU).

The hospital operates a hospital-based helicopter program, Life Flight (LF), which provides aeromedical support within a 150-mile radius. Accredited by the Commission on Accreditation of Medical Transport Systems, LF is Houston's only hospital-based air medical service. Each of the six helicopters is staffed by highly skilled personnel and equipped with advanced emergency equipment and necessary medications, and it can transport up to two patients simultaneously.

Blood Product Implementation and Timelines

In November 2017, we added 2 U of low-titer (<1:256) nonleukoreduced group O whole blood to each of our helicopters, alongside two existing units of RBCs and 2 U of plasma. Blood is supplied exclusively from Gulf Coast Regional Blood Center, which provides accurate records of blood collection and distribution dates. All blood products on LF helicopters are then dispensed directly to the air ambulance from Memorial Hermann Hospital. The exact dates of collection, processing, distribution, and administration are therefore readily and accurately available. Assessment of Blood Consumption scores ≥2 are used as transfusion triggers by LF care providers, with type of blood product and volume being determined at the discretion of the care providers present on LF. Each level 1 trauma activation patient has blood collected and sent for r-TEG as part of standard resuscitation. Rapid thromboelastography (TEG) curves and values are collected prospectively and are available for every patient. The r-TEG values are available in real time in the trauma bay and are used by the attending physicians to guide resuscitations and the transfusion of blood products in hospital.

Study Population

All level 1 trauma patients (16 years or older) being transported to Memorial-Hermann hospital via LF from November 2017 to November 2019 who received prehospital blood products were evaluated. Demographics, mechanism of injury, injury and transport times, Injury Severity Score (ISS), and prehospital vitals were retrospectively reviewed. In addition, TEG data (activated clotting time [ACT], *k* time, α angle, maximum amplitude (MA), clot lysis at 30 minutes values) and platelet counts were reviewed. Further transfusion and management decisions once the patient had arrived to the Red Duke Trauma Center were done at the discretion of the trauma care providers. Patients who died before having initial laboratory specimens drawn and those patients who received only component therapy (red blood cells, plasma) before arrival were excluded.

WB Data and Definitions

Data collection was performed using the prospectively maintained blood product transfusion databases for both LF and the RDTC. Data on the age of WB was collected using records from Gulf Coast Regional Blood Center, the sole provider of blood products for LF and RDTC. Based on recent data from our institution, WB was defined as *young* if the product was transfused with 14 days or less of cold-storage time.[13] Blood transfused with greater than 14 days of cold-storage time was defined as *old*. Therefore, for analysis purposes, patients receiving at least 1 U of young blood were defined as YOUNG, while all others were defined as OLD.

The primary outcome of interest was coagulation profile on arrival, with secondary outcomes including mortality, initial resuscitation volumes, acute renal failure, sepsis, respiratory failure, venous thromboembolic events, overall hospital-free days, ICU-free days, ventilator-free days, and daily hemolysis panels (creatinine, potassium, lactate dehydrogenase, total bilirubin, and haptoglobin). *Emergency department (ED) blood products* were defined as postarrival products while the patient remained in the ED. For those patients who were transferred directly from helipad to operating room, this was defined as those products received within the first 20 minutes of arrival. *Post-ED blood products* were defined as those products transfused after leaving the ED through the first 24 hours postarrival.

All r-TEG specimens were performed according to previously published guidelines.[16] The r-TEG values consisted of the following: ACT, which is increased with factor deficiency or severe hemodilution; *k* time, generally increased with hypofibrinogenemia or platelet deficiency; α angle, decreased with hypofibrinogenemia or platelet deficiency; MA, which reflects platelet contribution to clot strength and is decreased with platelet dysfunction or severe hypofibrinogenemia; and clot lysis at 30 minutes, the percent amplitude reduction at 30 minutes after MA, which when elevated reflects a state of hyperfibrinolysis.

Data Analysis

Continuous data are presented as median with 25th and 75th interquartile range or as mean with SD, and comparisons between groups were performed using the Wilcoxon rank sum (Mann-Whitney *U* test) or Student's *t* test, respectively. Categorical data are reported as proportions and, where appropriate, tested for significance using χ^2 or Fisher's exact tests. Multivariate logistic regression was also performed for presenting clinical parameters. All statistical tests were two tailed with $p < 0.05$ set as significant. Stata statistical software (version 12.1; College Station, TX) was used for analysis.

TABLE 1. Demographics and Baseline Data for Patients Presenting After Receiving at Least 1 U of Prehospital WB

	YOUNG (n = 153)	OLD (n = 67)	*p*	Standardized Mean Difference
Age, y	37 (26–57)	35 (26–48)	0.207	0.101
Male sex	112 (73)	55 (83)	0.112	0.188
White race	76 (50)	32 (48)	0.809	0.040
Blunt mechanism	110 (72)	46 (69)	0.655	0.090
Head AIS	3 (0–4)	3 (0–4)	0.715	0.199
Chest AIS	3 (2–4)	3 (0–4)	0.259	0.237
Abdomen AIS	3 (0–4)	3 (0–3)	0.351	0.236
ISS	27 (14–38)	27 (19–41)	0.238	0.053

Age, AIS, and ISS scores are presented as median (interquartile range). Sex, race, and mechanism variables are presented as n (%). YOUNG, at least 1 U of LTO-WB transfused within 14 days or less of cold-storage time. OLD, all LTO-WB transfused after 14 days of cold-storage time.

AIS, Abbreviated Injury Scale; LTO-WB, nonleukoreduced group O whole blood.

RESULTS

During the study period, 443 patients received prehospital blood products by LF. Of these, 220 received at least 1 U of prehospital WB and had initial laboratory specimens obtained. A total of 153 patients received YOUNG WB, while 67 were transfused only OLD WB units.

There were no differences in demographics, mechanism, or injury severity between the two groups (Table 1). With respect initial scene vitals, there were no differences between the two groups (Table 2). There were also no differences in prehospital fluid and transfusion volumes. There was no difference between YOUNG WB and OLD WB groups in terms of the number of patients receiving additional prehospital units of packed red blood cell (pRBC) (7 [4.6%] vs. 4 [6.0%], $p = 0.66$), plasma (1 [0.6%] vs. 2 [3.0%], $p = 0.17$), or platelets (7 [4.6%] vs. 6 [9.0%], $p = 0.20$). There was no difference between YOUNG WB and OLD WB in the number of patients with Abbreviated Injury Scale scores ≥3 of the abdomen (25 [16.4%] vs. 11 [17.6%], $p = 0.82$) or chest (34 [22.4%] vs. 15 [22.9%], $p = 0.94$).

Arrival heart rate and Glasgow Coma Scale were similar between the groups (Table 3). While median arrival systolic and diastolic blood pressures were higher in the young WB group, these differences were nonsignificant. The YOUNG WB group presented with higher lactate and worse base deficit yet had higher median arrival platelet count and more hemostatic r-TEG parameters (Table 3).

With respect to initial ED and post-ED blood products, there was no statistically significant difference in units transfused between the two groups (Table 4).

There was no difference in mortality between the YOUNG and OLD WB groups (21% vs. 26%, $p = 0.420$). There were also no differences in rates of acute renal failure, sepsis, respiratory failure, or venous thromboembolic events. Overall hospital-free days, ICU-free days, and ventilator-free days were similar between YOUNG and OLD WB groups. Daily hemolysis panels (creatinine, potassium, lactate dehydrogenase, total bilirubin, and haptoglobin) were not statistically different between groups.

Patients were dichotomized into "abnormal" versus "normal" r-TEG values using our institutions cut points. Patients receiving YOUNG WB less often presented with abnormal MA (<55 mm) values compared with patients receiving OLD WB (12% vs. 43%, $p = 0.038$). Patients receiving YOUNG WB had similar rates of derangement in ACT (>128 seconds) (39% vs. 44%, $p = 0.322$), k time (≥2.5 minutes) (42% vs. 52% group, $p = 0.124$), and α angles (<60°) (5% vs. 12%, $p = 0.064$) compared with patients receiving OLD WB. There were no differences in number of patients receiving additional packed red cells, plasma, or platelets in each group.

Because of their correlation to disturbed fibrinogen and platelet function in vitro,[13] MA and α angle values were selected for multivariate analysis. Controlling for variables of age, sex, scene systolic blood pressure, and ISS, YOUNG WB was associated with an odds ratio of 0.37 (95% confidence interval, 0.12–1.04) for demonstrating an α angle of <60° on arrival

TABLE 2. Prehospital Scene Vitals and Field Resuscitation Volumes for Patients Receiving Young (≤14 Days of Cold-Storage Time) and Old (>14 Days of Cold-Storage Time) Units of WB

	YOUNG (n = 153)	OLD (n = 67)	p	Standardized Mean Difference
Heart rate, bpm	114 (93–134)	109 (92–125)	0.276	0.014
Systolic blood pressure, mm Hg	100 (84–126)	90 (73–117)	0.130	0.189
Diastolic blood pressure, mm Hg	65 (49–82)	62 (47–71)	0.211	0.192
Glascow Coma Scale	8 (3–14)	10 (3–15)	0.178	0.077
Positive field focused assessment with sonography in trauma	66%	76%	0.146	0.074
Crystalloid, mL	275 (50–610)	400 (0–1,000)	0.753	0.240
Red blood cells, U	0 (0–0)	0 (0–0)	0.633	0.115
Plasma, U	0 (0–0)	0 (0–0)	0.860	0.161
WB, U	1 (1–1)	1 (1–1)	0.245	0.082

All data are presented as median (interquartile range).

TABLE 3. Arrival Vital Signs and Laboratory Values of Patients Receiving Young (≤14 Days of Cold-Storage Time) and Old (>14 Days of Cold-Storage Time) Units of WB

	YOUNG (n = 153)	OLD (n = 67)	p
Heart rate, bpm	113 (92–133)	110 (90–122)	0.453
Systolic blood pressure, mm Hg	102 (82–130)	97 (75–124)	0.151
Diastolic blood pressure, mm Hg	64 (50–80)	59 (40–78)	0.053
Glascow Coma Scale	3 (3–15)	3 (3–15)	0.267
Hemoglobin, g/dL	12.4 (10.6–13.7)	12.8 (10.4–14.2)	0.429
Platelet count, ×1,000	198 (137–255)	170 (131–229)	0.050
Lactate, mmol/L	4.7 (3.4–6.8)	3.8 (2.4–6.5)	0.034
Base excess	−7 (−10 to −3)	−4 (−8 to −1)	0.052
r-TEG ACT, s (<128 s)	113 (105–121)	113 (105–128)	0.080
r-TEG k time, min (<2.5 min)	1.5 (1.1–1.8)	1.8 (1.2–2.1)	0.024
r-TEG α angle, ° (>60°)	73 (70–76)	71 (66–75)	0.014
r-TEG MA, mm (>55 mm)	63 (58–68)	60 (55–65)	0.063
r-TEG LY-30, % (<3%)	0.6 (0.0–2.7)	0.6 (0.0–1.8)	0.612

All data are presented as median with interquartile range in parenthesis. Normal r-TEG values for our institution are found in parenthesis alongside the associated variable.
LY-30, clot lysis at 30 minutes.

TABLE 4. ED and Post-ED Blood Products Administered to Patients Receiving Young (≤14 Days of Cold-Storage Time) and Old (>14 Days of Cold-Storage Time) Units of WB

	YOUNG (n = 153)	OLD (n = 67)	p
ED RBC, units	1 (0–5)	1 (0–5)	0.287
ED plasma, units	1 (0–5)	2 (0–6)	0.220
ED platelet, units	0 (0–1)	0 (0–1)	0.936
ED WB, units	0 (0–0)	0 (0–0)	0.593
post-ED RBC, units	1 (0–4)	0 (0–5)	0.506
post-ED plasma, units	0 (0–2)	0 (0–2)	0.713
post-ED platelet, units	0 (0–1)	0 (0–2)	0.301

Data are presented as median number of units transfused with associated interquartile ranges in parenthesis.
RBC, red blood cell.

TABLE 5. Multivariate Regression Analysis Predicting Abnormal Arrival α Angle and Maximum Amplitude on Presenting r-TEG Parameters Corrected for Differences in Age, Sex, Scene Systolic Blood Pressure, and ISS

	OR	95% CI	*p*
α angle <60°			
Young WB	0.37	0.12–1.04	0.058
Age, y	0.96	0.93–0.99	0.050
Male sex	0.67	0. 18–2.35	0.529
ISS	1.04	1.01–1.07	0.003
SBP	0.99	0.98–1.01	0.801
MA <55 mm			
Young WB	0.49	0.25–1.03	0.053
Age, y	0.98	0.96–1.01	0.091
Male sex	0.65	0.27–1.56	0.332
ISS	1.04	1.02–1.07	0.002
SBP	0.99	0.99–1.01	0.833

Data are presented as ORs, with 95% CI. $R^2 = 0.466$.
95% CI, 95% confidence interval; OR, odds ratio.

($p = 0.058$). Controlling for the same variables, YOUNG WB was also associated with an odds ratio of 0.49 (95% confidence interval, 0.25–1.03) for arrival MA of <55 mm ($p = 0.053$). Younger age was associated with improved α angle, while high ISS predicted worsening α angle and maximum amplitude values (Table 5).

DISCUSSION

A recent in vitro study by Assen et al.[13] demonstrated significant decreases in platelet count and increases in ACT, *k* time, and MA with increasing WB cold-storage time. While worsening values were noted at 14 days, significant coagulation changes of WB were also noted after as little as 7 days of storage. Remy et al.[17] showed decreasing platelet numbers with 5 days of cold storage of WB, as well as decreased maximum clot firmness, MA, and platelet aggregation by day 15 of cold storage. Jobes et al.[18] similarly demonstrated a significant decrease in platelet number within 4 days of cold storage, decreased collagen-induced platelet aggregation by day 7, and decreased MA and α angle by day 14. Our study represents the first examination of the clinical sequelae of aging WB. Consistent with in vitro data, this study showed statistically significant improvements in the presenting r-TEG values of patients receiving young prehospital WB compared with products having spent >14 days in cold storage on univariate testing. Differences were observed in r-TEG parameters measuring clotting factor availability (ACT, *k* time), as well as platelet and fibrinogen availability and function (*k* time, α angle, platelet count, MA). Statistically significant differences were shown only in *k* time, α angle, and platelet count. On multivariate analysis, α angle and MA were seen to show the largest differences between young and old blood groups but did not achieve statistical significance. Age, sex, and ISS were seen to be statistically significant predictors of α angle and MA values. Differences in ACT values were not statistically significant in this small study. Fibrinogen and platelet activity–related parameters were the most affected by the cold-storage time of WB. Despite differences in the primary outcome of TEG parameters, clinically relevant endpoints such as mortality and transfusion volumes were not seen to be different.

The debate over the clinical impact of old versus young blood is not novel. The worsening in vitro performance of pRBCs, plasma products, and WB as they age in storage has all been demonstrated. Most recently, secondary analysis of patients enrolled in the (Prospective, Randomized Optimal Platelet and Plasma Ratios) trial demonstrated that the number of units of pRBCs transfused after ≥22 days of cold storage was an independent risk factor for mortality.[19] Retrospective literature in trauma had previously yielded similar results with respect to pRBCs.[20] Conversely, large multicentered trials in critical care and general hospital settings have shown no difference in mortality with increasing pRBC cold-storage time.[21–23] The results of these large trials have resulted in practice patterns, which do not discriminate among the age of blood products administered at transfusion. However, there is signal in the literature that trauma patients or, more specifically, patients suffering from massive hemorrhage may represent a specific subset of the overall hospital and critical care patient population who may benefit from the incremental benefit of young blood products.

The increasing recognition that traumatically injured patients require replacement of the hemostatic component of shed blood has led to increased focus on plasma, platelet, and WB resuscitation. Fresh frozen plasma demonstrates superior in vitro clotting potential and higher measured levels of coagulation factors with short cold-storage times.[24] After thawing, fresh frozen plasma begins to lose clotting potency within 24 hours.[25] Huish et al.[26] also demonstrated significant deterioration in clotting factor activity in the plasma component of WB after 14 days of cold-storage time and argued that its shelf life should be between 14 and 21 days. Unsurprisingly, the aforementioned in vitro studies on aging WB have likewise shown it to be likewise susceptible to deterioration in cold storage.[13,18,19] Previous work in aging WB has attributed time-related changes in hemostasis to the platelet storage lesion.[27] The complex interplay of clotting factors and platelets in the formation of a fibrin fortified platelet plug is adversely affected by the decrease in number and function of platelets in aged blood products. The effect of increased cold-storage time on clotting factors as well as von Willebrand factor has also been described in vitro.[28] This preliminary study demonstrates that the same platelet storage lesion and adverse effects on clotting factors, which are seen in vitro, may translate to the clinical setting.

The current study demonstrates that WB, which has spent ≤14 days in cold storage, may have superior hemostatic potential. Severely injured patients at risk of traumatic coagulopathy may benefit from preferential administration of fresh WB. Thromboelastography profiles demonstrating traumatic coagulopathy at presentation have been associated with increased transfusion requirement, time to hemostasis, and mortality.[29,30] While local logistical and economic factors may be prohibitive, the improvement of the presenting hemostatic profiles of trauma patients shows promise in improving outcomes. More specifically, the early administration of young nonleukoreduced group O whole blood, in addition to the well-established tenets of damage-control resuscitation and rapid achievement of hemostasis, may serve to improve outcomes. Whole blood products

in the prehospital setting are scarce and center specific. Improvement in blood product availability and distribution are thus necessary and worthwhile goals of the modern trauma system.

There are multiple limitations of this study. While we found reduced hemostatic potential in patients receiving old WB, this did not translate to decreased transfusion requirements or improved clinical outcomes. This study is a small, single-center retrospective study with limited power and, thus, is likely unable to detect concrete differences in clinical outcomes. Multiple r-TEG parameters were also found to approach clinical significance but failed to reach significant p values (ACT, MA). Multivariate analysis of α angles and MA again approximated but did not cross the threshold of statistical significance. This reflects a lack of power to delineate granular differences in each TEG parameter and the possibility of type II error in our study. In addition, the size of the study limits multivariate analysis. While the overall differences in patient presenting parameters are quite small, the influence of an undetected confounding factor remains a possibility. This preliminary study is limited in its ability to rule out the influence of these possible confounders. While the inability to achieve statistical significance in this study is possibly due to inadequate power, future statistical analysis of this patient population could include inverse probability weighting or propensity score matching. In addition, this preliminary data should be followed up with larger multicentered studies to further elucidate the effect of young WB. We also look at multiple clinical outcomes and the possibility of that any of these relevant outcomes is found to be significant by chance does increase with each outcome. This is a limitation but has been analyzed as such, to limit the possibility of type II error. Finally, the in vitro data published by Assen et al.[13] shows a remarkable decrease in platelet number and function within the first week of storage. These data may demonstrate that 14 days is still too old and that a 7-day cutoff may be more appropriate.

CONCLUSION

Previous in vitro data have suggested deterioration of platelet function in cold-stored WB after 14 days. The current study demonstrated decreased global hemostasis by clinically available laboratory tests, in older WB. This was most notable in values related to fibrinogen and platelet interactions. While changes were seen on univariate analysis, multivariate analysis failed to show significant differences. However, in this small single-center study, this did not translate into increased transfusion requirements. Further studies are needed to determine the optimal storage duration for cold-stored WB for transfusion in the bleeding trauma patient.

AUTHORSHIP

T.C., C.M., S.A., and B.A.C. contributed in the study design, data collection, data analysis, and drafting of the article. J.C., C.W., and D.M. contributed in the interpretation and analysis of data and drafting of the article.

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DISCLOSURE

The authors declare no conflicts of interest.

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DISCUSSION

JASON SPERRY, M.D., M.P.H. (Pittsburgh, Pennsylvania): I would like to thank the AAST Program Committee for the privilege to discuss this manuscript and for Dr. Clements, Dr. Cotton and colleagues out of the Red Duke Trauma Center at the University of Texas Health Science Center, Houston.

They continue to put out important science which has the potential to change and improve trauma care as it's practiced across the country.

The authors report on their retrospective analysis characterizing their prehospital whole blood experience and the arrival coagulation status of patients who receive either young whole blood, designated as less than or equal to 14 days of cold storage time, relative to old whole blood, defined as greater than 14 days cold storage time.

They report rapid TEG differences, which correspond to prior literature. And it is a nicely written manuscript. I do have a couple important questions.

Number 1. The methods detail that when a patient received a single unit of whole blood, either young or old, they were designated as such, irrespective of additional red cells or plasma.

My question is, were multiple unit of whole blood provided in any patients? And are the differences seen in rapid TEG most prominent in those that received only whole blood prehospital without confounding by other blood components or more than one unit of whole blood?

My second question, although the study is underpowered for outcome differences, will the current retrospective results lead you to change your practice and minimize old blood in the prehospital setting?

I appreciate the privilege of the podium to discuss this excellent manuscript.

THOMAS CLEMENTS, M.D. (Calgary, Alberta, Canada): Thank you very much, Dr. Sperry, for your very important and very relevant questions. I'd like to thank Dr. Malhotra for the introduction, and thank the AAST, as well.

In regards to Question Number 1, Dr. Sperry, based on previous in vitro data we tried to separate our patient groups in the manner we saw was the cleanest way possible, so we used the 14-day cutoff of less than or equal to 14 days being "young" blood and greater than 14 days being "old" blood.Because of this we didn't break down the patient populations to look at patients who received multiple products prehospital, so there is no specific breakdown of these subgroups.

We do have some numbers for who received additional product so of our 220 patients, 49 of them received a second unit of whole blood. Only 11 of them received packed red blood cells. And 13 of them received plasma. And those were all prehospital.

In terms of Question Number 2, while the results of this paper haven't led to a difference in the age of whole blood transfused, it has sparked talks with the blood bank about discontinuing the current practice of having our whole blood for seven days on the EMS-based ground units and then sending them to hospital to be used after that seven days.

Our current median age of our whole blood in-hospital is about 16 days. We have a 21-day expiry on those products, so hopefully this will lead to newer, fresher whole blood in our emergency department, and OR settings.

In terms of the prehospital whole blood, we have started discussions with our blood providers to get younger, fresher whole blood on our life flight helicopter program. Our current median age for the blood transfused on life flight is about 16 days of cold storage time.

This is a little bit more difficult to change as we don't have direct control over the blood provider regarding the blood products that they dispense to us.

Thank you, again, very much, for your questions.

MICHAEL W. CRIPPS, M.D. (Dallas, Texas): Nice talk. And with no difference in blood transfusion do the authors think that these differences in TEG values would have any real clinical significance?

THOMAS CLEMENTS, M.D. (Calgary, Alberta, Canada): This is an excellent question that we address in our manuscript. This study is underpowered, we think, to detect clinically-relevant changes in either the outcome or the transfusion volume of patients.

We think that we require a much larger group to be able to see this. And this data shows us what outcomes in terms of our clinical lab values only.

Additionally, there is some data in the literature that 14 days might in fact be too long, and that seven days might be a more appropriate cutoff. Studies show differences in platelet values and platelet function after only five days in cold storage, so another future direction of our study is to look at earlier cutoffs for our young whole blood.

MARTIN SCHREIBER, M.D. (Portland, Oregon): Would you really expect a single unit of whole blood to have an impact on your outcomes, whether old or young?

JASON SPERRY, M.D. (Pittsburgh, Pennsylvania): What if patients received large volumes of old versus young blood?

THOMAS CLEMENTS, M.D. (Calgary, Alberta, Canada): Yes, fantastic questions. Thank you for them. As mentioned with our data, our prehospital transport times are fairly short.

These patients don't have a large period to receive multiple units prehospital. So that rapid TEG that we see after a short prehospital time is often only with one or two units of product transfused.

The idea is that we are already seeing, even in the small numbers and single units of whole young blood, differences in our TEG values. So as this data pool expands and we look at more and more of these patients we would like to see if that, in fact, does play out as a clinical difference. Of course, this study doesn't necessarily prove that.