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Blood products and liver transplantation: A strategy to balance optimal preparation with effective blood stewardship

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Abstract

Background: Unanticipated transfusion requirements during liver transplantation can delay lifesaving intraoperative resuscitation and strain blood bank resources. Risk-stratified preoperative blood preparation can mitigate these deleterious outcomes.

Study Design and Methods: A two-tiered blood preparation protocol for liver transplantation was retrospectively evaluated. Eleven binary variables served as criteria for high-risk (HR) allocation. Primary outcomes included red blood cell (RBC), plasma (FFP), and platelet (Plt) utilization. Secondary outcomes included product under- and overpreparation. Contingency tables for transfusion requirements above the population means were generated using 15 clinical variables. Modified protocols were developed and retrospectively optimized using the study population.

Results: Of 225 recipients, 102 received HR preoperative orders, which correlated to higher intraoperative transfusion requirements. However, univariate analysis identified only two statistical risk factors per product: Hgb ≤7.8 g/dl ($p < .001$) and MELD ≥38 ($p = .035$) for RBCs, Hgb ≤7.8 g/dl ($p = .002$) and acute alcoholic hepatitis ($p = 0.015$) for FFP, and Hgb ≤7.8 g/dl ($p = .001$) and normothermic liver preservation ($p = .037$) for Plts. Based on these findings, we developed modified protocols for individual products, which were evaluated retrospectively for their effectiveness at reducing under-preparatory events while limiting product overpreparation. Cohort statistics were used to define the preparation strategy for each protocol. Retrospective comparative analysis demonstrated the superiority of the modified protocols by improving the under-preparation rate from 24% to <10% for each product, which required a 1.56-fold and 1.44-fold increase in RBC and FFP overpreparation, respectively. Importantly, there was no difference in Plt overpreparation.

Joseph P. Connor and David P. Al-Adra are contributed equally.

Discussion: We report translatable data-driven blood bank preparation protocols for liver transplantation.

KEYWORDS

blood bank, blood product, liver transplant, plasma, platelet, preparation protocols, red blood cell, transfusion requirements

1 | INTRODUCTION

Orthotopic liver transplantation (OLT) is the standard of care for qualified candidates with end-stage liver disease; however, the peri- and intraoperative care of these complex patients requires intense resource utilization that can strain critical ancillary systems.[1] One prominent consideration involves blood bank preparedness and management, which represents a delicate balance between intraoperative need and product allocation. If mismanaged in the preoperative setting, inadequate supply can portend significant risk to the transplant recipient, as well as other non-transplant patients requiring blood transfusions within the system. Despite the gravity of these consequences, consensus blood bank preparation protocols for OLT recipients have not been established.

Historically, OLT had been characterized by high blood loss and aggressive product-based resuscitation; however, the resuscitative strategy has gradually shifted towards a more restrictive approach, which has been associated with improved recipient outcomes.[2–6] This paradigm, coupled with advancements in operative technique and graft preservation, has yielded an overall reduction in product utilization among OLT recipients, though the potential for massive intraoperative transfusion still exists.[7–10] The disparate range of blood product utilization in liver transplantation creates a logistical dilemma for operative and blood bank teams, characterized by an elusive balance between under-preparation leading to delayed intraoperative resuscitation, and over-preparation risking waste of perishable blood products such as platelets (Plts). Together, these conflicting priorities underscore the need for effective and applicable models to predict intraoperative transfusion requirements during OLT despite the complexities of end-stage liver disease and liver transplantation.

It is well known that end-stage liver disease yields significant aberrancies in traditional laboratory coagulation tests. However, contemporary understanding of physiologic hemostasis in cirrhotic patients is characterized by a rebalanced pro- and anti-thrombotic system, thus limiting the predictive value of standard preoperative laboratory tests in isolation.[11–13] Further, reperfusion of the allograft liver yields a dramatic physiologic shift that further complicates the systemic coagulation cascade.[13–15] While viscoelastic testing has emerged as an important guide for product resuscitation during transplantation, sole reliance on laboratory coagulation tests in the preoperative period yields a confounded assessment of hemostatic physiology, thus limiting their reliability for predicting intraoperative transfusion requirements.[13,16–18] It is therefore important to also consider physiologic and operative characteristics thought to be associated with increased blood loss when developing optimal blood bank allocation protocols to be implemented prior to reaching the operating room.

Several single center studies have described predictive models for blood product utilization during OLT; however, these reported strategies are limited to red blood cell (RBC) preparation alone and are often complex, thus limiting their applicability to the clinical setting.[19–22] At the University of Wisconsin (UW), the Division of Transplantation and the Transfusion Medicine Service jointly developed an algorithm aimed at predicting intraoperative transfusion requirements based on a series of binary laboratory, physiologic, and surgical factors. This system was a provider-driven protocol designed to allocate patients to standard-risk (SR) or high-risk (HR) cohorts, which corresponded to two different levels of preoperative blood product preparation by the blood bank. The purpose of this study was to evaluate the effectiveness of the original UW blood preparation system and to report optimization strategies for institutional, multi-product protocols based on risk factors for increased transfusion requirements during OLT.

2 | MATERIAL AND METHODS

We conducted a single center, retrospective analysis of all deceased donor orthotopic liver transplants at the UW from September 1, 2018, through October 9, 2020. Recipients of living donors and split allografts were excluded from this study. Data was acquired through a comprehensive clinical chart review, which was supplemented by an internal liver transplant archive: the Wisconsin Allograft Recipient Database. These sources were queried for recipient age, sex, weight, physiologic model for end-stage liver disease (MELD), cause of liver failure, history

of peritonitis, concomitant renal failure, donor type, and preoperative hemoglobin (Hgb), international normalized ratio (INR), partial thromboplastin time (PTT), Plt count, fibrinogen, total bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), albumin, creatinine, and blood urea nitrogen (BUN), as well as blood product transfusion requirements. The primary outcomes of this study included RBC, fresh frozen plasma (FFP), and Plt utilization. Secondary outcomes included blood product under- and overpreparation. This study was approved by the Institutional Review Board of the UW.

The original UW blood preparation protocol for liver transplantation was developed in 2018 to allocate recipients to standard-risk (oSR) or high-risk (oHR) cohorts based on a set of binary characteristics determined by staff liver transplant surgeons. Recipient variables included diagnosis of fulminant liver failure, acute alcoholic hepatitis or polycystic liver disease, history of spontaneous bacterial peritonitis (SBP) or prior OLT (redo), and need for pre-or intraoperative hemodialysis (HD), as well as preoperative laboratory values of Plt count <34,000/mcl and Hgb <8 g/dl. Operative variables included donation after circulatory death (DCD) and simultaneous liver/kidney (SLK) transplant. Per protocol, the presence of any one or more of these variables allocated the prospective recipient to the HR cohort. The transplant team was responsible for ordering the standard- or HR blood product order set as a part of the preoperative orders within the electronic medical record (EMR). Based on the order set placed, the UW blood bank prepared 10 units of RBCs, 10 units of FFP, and 4 units of Plts (10/10/4) for oSR patients versus 20 units of RBCs, 15 units of FFP, and 8 units of Plts (20/15/8) for oHR recipients. Intraoperative blood product transfusions were administered per the discretion of the transplant anesthesiology team based on the patient's hemodynamic status and viscoelastic data.

Statistical analysis was performed using Fisher's exact test to identify individual factors that were associated with high levels of blood product usage. Increased blood product utilization was defined as transfusion requirements greater than the population mean for each product. Continuous variables were evaluated in the univariable analyses based on their population means plus (age, MELD, INR) or minus (Hgb, Plt count, fibrinogen) their standard deviation (SD). Polycystic liver disease was excluded from univariate analysis based on its n value of one.

Optimized blood preparation protocols were developed based on the risk factors statistically associated with increased product utilization in univariable analyses. The modified protocols were retrospectively applied to the 225 recipients included in this study population. The preparation strategies (number of units prepared for the modified standard- and HR cohorts) were determined based on statistical values determined for each cohort. Comparative subanalyses were then performed retrospectively to evaluate product utilization, product under-preparation, and product overpreparation between the original UW protocol as it was implemented in practice (order sets placed clinically), an ideally applied original UW protocol, and an ideally applied modified UW protocol.

3 | RESULTS

3.1 | Study population and original blood preparation protocol

There were 225 deceased donor orthotopic liver transplants performed at the UW during the 25-month study period. Population characteristics are presented in Table 1. Blood product utilization among all recipients is shown in Figure 1. Average RBC use was 10.38 units with a SD of 14.94. Intraoperative use varied widely from 0–120 units, though the median was 7.0. FFP usage was characterized by an average of 8.29 units and an SD of 13.51. Median use was 4.0 units despite a range of 1–100. Plt transfusion requirements were more uniform with an average of 3.68 units and an SD of 3.92. Usage ranged from 0–25 units, with a median of 3.0 units.

All patients received standard- or HR preoperative blood product orders placed by transplant surgery providers per the original UW blood preparation protocol (Figure 2A). Among all recipients, 82 were positive for zero variables, while 74 had one factor, 44 had two, 21 had three, and four had four (Figure 2B). However, 123 total patients had oSR orders placed, while 102 received the oHR order set. Based on this retrospective review, 67.1% were correctly identified as standard- or HR, while the remaining 32.9% were misclassified at the time of preoperative order placement. Specifically, 21.9% of patients with zero factors had oHR orders initiated, while 41.3% of patients positive for one or more factors had oSR orders placed (Figure 2C). If ideally applied, the original UW protocol would have assigned 82 recipients to the oSR group and 143 to the oHR group.

3.2 | Risk factors for blood product transfusion

Fisher's exact tests for transfusion requirements above the population mean for each individual product are

TABLE 1 Descriptive statistics for all recipients of deceased donor liver transplants during the study period ($n = 225$)

	Binary statistics		Continuous statistics	
	N	%	Avg	SD
Recipient factors				
Age (years)			54.5	11.5
Weight (kg)			90.6	21.1
Physiologic MELD			25.1	10.7
Fulminant liver failure	4	1.78		
Acute alcoholic hepatitis	17	7.56		
Polycystic liver disease	1	0.44		
Hemodialysis	46	20.45		
History of SBP	61	27.11		
Preoperative laboratory values				
Hgb (g/dl)			9.9	2.1
INR			1.9	0.8
PTT (s)			48.7	74.4
Platelet count (per mcl)			96.0	61.9
Fibrinogen (mg/dl)			196.6	106.7
Total bilirubin (mg/dl)			10.8	12.5
Alkaline phosphatase (IU/L)			205.2	182.5
GGT (IU/L)			144.6	207.4
AST (IU/L)			73.7	63.6
ALT (IU/L)			60.6	142.8
LDH (IU/L)			261.9	84.0
Albumin (g/dl)			3.0	0.7
Creatinine (mg/dl)			1.7	1.5
BUN (mg/dl)			30.2	22.6
Transplant factors				
Cold ischemia time (h)			6.0	1.8
Operative time (h)			7.9	2.3
DCD	37	16.45		
Normothermic liver preservation	6	2.67		
Redo transplantation	11	4.89		
SLK transplant	15	6.67		

shown in Table 2. Binary cutoffs for continuous variables were determined by the population mean of each factor plus (age, MELD, INR) or minus (Hgb, Plt count, fibrinogen) their SD. Variables associated with RBC transfusion >10 units include Hgb ≤7.8 g/dl ($p < .001$) and MELD ≥38 ($p = .035$). Hgb ≤7.8 g/dl ($p = .002$) and acute alcoholic hepatitis ($p = .015$) were correlated to FFP requirements >8 units. Plt transfusions >4 units were associated with Hgb ≤7.8 g/dl ($p = .001$) and normothermic liver preservation ($p = .037$). Age ≥66 years, fulminant liver failure, pre-or intra-operative HD, history of SBP, INR ≥2.7, Plt count ≤34,000/mcl, fibrinogen ≤90 mg/dl, and redo, DCD, or SLK transplantation failed to reach significant statistical associations with high blood product utilization.

3.3 | Protocol optimization

A modified allocation protocol was developed for RBCs, FFP, and Plts individually, defined by variables statistically associated ($p < .05$) with transfusion requirements above the population mean in the univariate analysis (Table 3). Product preparation for the modified high-risk

(mHR) cohorts were determined by their mean product use plus the SD, while product preparation for the modified standard-risk (mSR) cohorts was defined by their median product use plus the SD. For all subsequent sub-analyses, the modified allocation protocol was retrospectively applied to all 225 deceased donor OLT recipients and compared to an ideally employed original allocation protocol as well as the actual order sets initiated clinically.

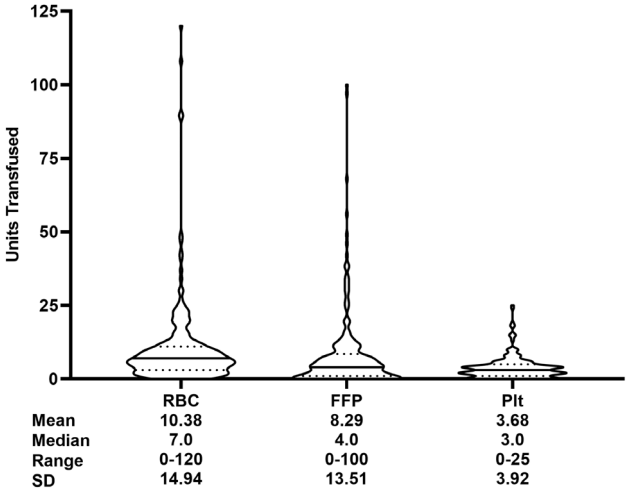

FIGURE 1 Violin plot of red blood cell (RBC), plasma (FFP), and platelet (Plt) utilization for the study population (solid line: Median; dotted lines: 25th and 75th quartiles). Mean, median, range, and standard deviation (SD) are given in units

Blood product utilization per preparation strategy is shown in Table 4. Those that received SR orders required an average of 8.32 units of RBCs, which was less than the 12.86 units of RBCs utilized by those that received HR orders ($p = .023$). Similar trends were observed between the standard- and HR order groups with respect to FFP (6.07 vs. 10.97; $p = .006$) and Plts (3.02 vs. 4.47; $p = .006$). If the original UW protocol was ideally applied, a similar trend was observed, with the oHR cohort requiring an average of 12.13 units of RBC (vs. 7.33; $p = .024$), 10.19 units of FFP (vs. 4.98; $p = 0.010$), and 4.36 units of Plt (vs. 2.50; $p = 0.004$) utilized by those positive for any combination of factors. However, sub-analysis of product utilization broken down by number of variables present, revealed no statistical difference in RBC, FFP, or Plt use between recipients positive for zero versus one of the original eleven variables. Retrospective application of the modified UW protocol yielded a 1.8-fold increase in RBC utilization (16.08 vs. 8.75; $p = .002$) among the mHR-RBC cohort. Similarly, the mHR-FFP group required a

(A)

Original UW Blood Preparation Procotol

Allocation System	Preparation (units)	Variables
Standard Risk (oSR)	10 RBC / 10 FFP / 4 Plt	None
High Risk (oHR)	20 RBC / 15 FFP / 8 Plt	Fulminant liver failure
		Acute alcoholic hepaitis
		Polycystic liver disease
		Hemodialysis
		History of SBP
		Hgb <8 g/dL
		Platelts ≤30,000/mcL
		Normothermic liver preservation
		Redo transplantation
		DCD
		SLK transplant

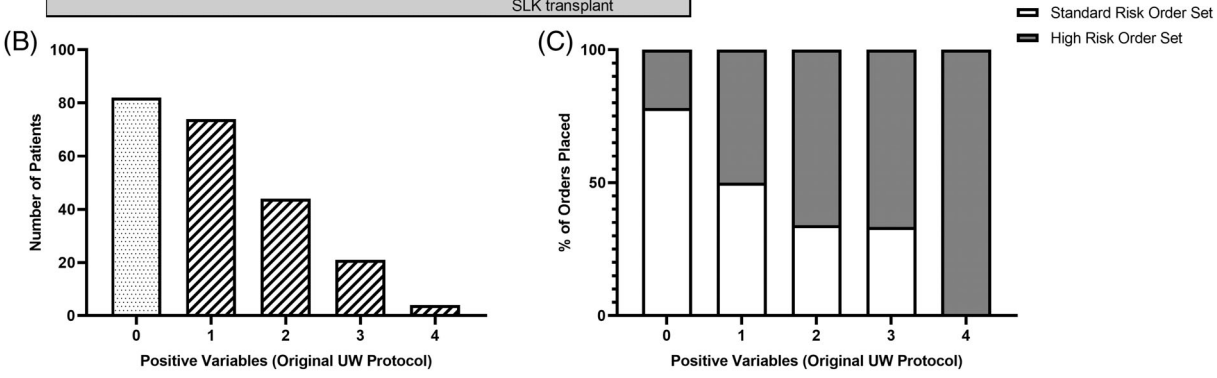

FIGURE 2 (A) Original UW blood preparation protocol demonstrating the unit preparation and allocation criteria for the oSR and oHR system. (B) Number of patients positive for the eleven variables included in the original UW protocol. (C) Clinical orders (standard-risk order set vs. high-risk order set) initiated in practice by transplant providers based on the original UW protocol (*y*-axis) versus the number of variables present for each recipient (*x*-axis)

TABLE 2 Univariate analyses for transfusion requirements greater than the population mean for RBCs, FFP, and Plts.

	RBC >10 units		FFP >8 units		Plt >4 units	
	%	*p* value	%	*p* value	%	*p* value
Recipient factors						
Age ≥66 years	24.24	.833	12.12	.081	12.12	.081
MELD ≥38	**44.44**	**.036**	40.74	.057	37.04	.158
Fulminant liver failure	0.00	.576	0.00	.574	0.00	.574
Acute alcoholic hepatitis	35.29	.402	**52.94**	**.015**	35.29	.384
Hemodialysis	34.78	.191	36.96	.054	30.43	.447
History of SBP	34.43	.127	34.43	.056	32.79	.124
Preoperative laboratory values						
Hgb ≤7.8 g/dl	**68.00**	**<.001**	**52.00**	**.002**	**60.00**	**<.001**
INR ≥2.7	37.84	.105	37.84	.060	32.43	.303
Platelets ≤34,000/mcl	50.00	.056	35.71	.347	42.86	.200
Fibrinogen ≤90 mg/dl	38.46	.153	38.46	.146	30.77	.484
Transplant factors						
Normothermic liver preservation	50.00	.194	33.33	.640	**66.67**	**.037**
Redo transplantation	36.36	.489	18.18	.736	18.18	.734
DCD	35.14	.224	27.03	.835	29.73	.537
SLK transplant	40.00	.236	33.33	.536	26.67	1.000

Note: Percentages (%) represent the fraction of recipients positive for the respective variable that required >10 units of RBCs, >8 units of FFP, or >4 units of Plts.
These are significant values as defined by $p < 0.0$

TABLE 3 Modified UW blood bank preparation protocol

	Preoperative preparation		Allocation criteria	
	Median + SD (units)	Mean + SD (units)	Risk factors	N
Modified RBC protocol				
mSR-RBC	21			175
mHR-RBC		30	Hgb ≤7.8 g/dl	26
			MELD ≥38	27
Modified plasma protocol				
mSR-FFP	14			183
mHR-FFP		38	Hgb ≤7.8 g/dl	26
			Acute alcoholic hepatitis	17
Modified platelet protocol				
mSR-Plt	6			196
mHR-Plt		11	Hgb ≤7.8 g/dl	26
			Normothermic liver preservation	6

2.9-fold increase in FFP (17.62 vs. 6.15; $p < .001$), while the mHR-Plt cohort required 2.0-fold greater units of Plts (6.62 vs. 3.24; $p < .001$) compared to their respective SR counterparts.

Analysis of blood product under-preparation per strategy is shown in Figure 3A. Among all 225 recipients who received standard-or HR orders, 54 (24.0%) patients required more blood product than was initially prepared. This resulted in 41 (18.2%) patients being underprepared for RBCs, 35 (15.5%) for FFP, and 35 (15.5%) for Plts. The ideally applied original UW protocol would have resulted in 42 (18.7%) total under-preparations, with 31 (13.8%) patients utilizing more units of RBCs than was initially prepared, 32 (14.2%) utilizing more FFP, and 29 (12.8%) utilizing more Plts. The retrospectively applied modified UW protocol improved on these percentages by yielding an under-preparation rate of <10% for all products. Specifically, compared to their projected preoperative preparations, 16 (7.1%) patients would have required more RBCs, 19 (8.4%) would have required more FFP, and 21 (9.3%) would have required more Plts. Compared to the original protocol, this reduced rate of under-preparation came at the cost of a 1.56-fold increase in RBC overpreparation and a 1.44-fold increase in FFP overpreparation, as measured by average units of product setup but not transfused (Figure 3B). Importantly, there was no difference in Plt overpreparation between the original and modified protocols.

TABLE 4 Blood product utilization statistics per standard-risk (SR) and high-risk (HR) groups for the study population defined by actual clinical orders placed, the ideally applied original UW protocol, and the retrospectively applied modified UW protocol (*$p < 0.05$, **$p < .001$ for increased mean HR utilization compared to the respective SR mean).

	RBC (units)			FFP (units)			Plt (units)		
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
Clinical orders placed									
SR orders ($n = 123$)	8.32	6.00	10.70	6.07	4.00	9.30	3.02	2.00	3.13
HR orders ($n = 102$)	12.86*	8.00	18.52	10.97*	5.50	16.88	4.47*	4.00	4.57
Original UW protocol									
oSR ($n = 82$)	7.33	5.00	12.18	4.98	3.00	8.34	2.50	2.00	2.67
oHR ($n = 143$)	12.13*	8.00	16.05	10.19*	6.00	15.41	4.36*	4.00	4.33
Modified UW protocol									
mSR-RBC ($n = 175$)	8.75	6.00	14.62						
mHR-RBC ($n = 50$)	16.08*	11.50	14.53						
mSR-FFP ($n = 183$)				6.15	4.00	10.18			
mHR-FFP ($n = 42$)				17.62**	8.50	20.47			
mSR-Plt ($n = 196$)							3.24	2.00	3.65
mHR-Plt ($n = 29$)							6.62**	5.00	4.40

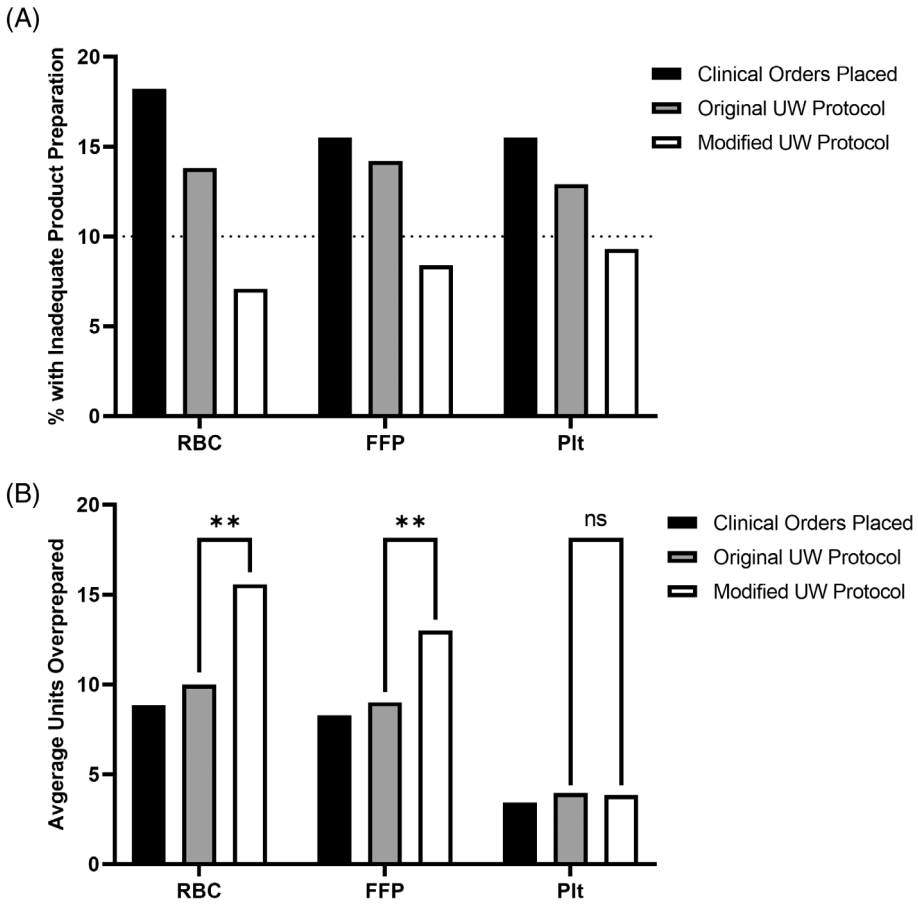

FIGURE 3 (A) Percentage of patients with inadequate preoperative product preparation compared to actual transfusion requirements intraoperatively. (B) Average units overprepared among patients that did not require more product than was setup preoperatively

4 | DISCUSSION

Given the significant variability of blood loss experienced during liver transplantation, it is imperative to reliably predict recipients at risk for increased transfusion requirements in order to maximize patient safety while preventing blood product waste and limiting the logistical burden assigned to the blood bank. In this study, we analyzed and refined an intraoperative blood product preparation strategy developed at the UW for OLT recipients. Based on an original set of eleven binary variables, patients were divided into standard- and HR protocols as described. We found that despite a high rate of misallocation by transplant providers, those that had HR orders placed did subsequently require more RBCs, FFP, and Plts compared to those that received SR orders, which was recapitulated retrospectively by ideally applying the original UW protocol to the overall population. These findings validated the utility of preoperative blood product allocation strategies, though this system yielded an unacceptably high rate of under-preparation, which portends significant risk to the transplant recipient due to delays in intraoperative resuscitation. Univariate models analyzing 15 variables for each individual product demonstrated that most factors serving as criteria for HR product preparation in the original protocol were not associated with increased utilization. These analyses did, however, identify a small subset of risk factors statistically associated with increased transfusion requirements over the population mean for each product. Higher RBC use was related to Hgb ≤7.8 g/dl and MELD ≥38, increased FFP utilization with Hgb ≤7.8 g/dl and acute alcoholic hepatitis, and greater Plt consumption with Hgb ≤7.8 g/dl and normothermic liver preservation. These risk factors were subsequently extrapolated to establish a data-driven, product-individualized blood bank preparation protocol, which was retrospectively optimized in this study prior to institutional implementation.

Prediction of intraoperative blood loss remains an elusive and conflicted target. A major factor complicating preoperative prognostication lies in the dynamic coagulopathies associated with progressive end-stage liver disease.[11–13,23] Across the wide spectrum of disease sequala and severity, heterogenous deficiencies in isolated pro- and anti-thrombotic cascades develop a cumulative, rebalanced hemostatic physiology within the systemic environment.[24–29] Though together these aberrations yield a relatively preserved equilibrium, conventional laboratory tests fail to accurately represent systemic hemostatic physiology.[13,16–18] INR and PTT time captures the deficit of extrinsic and intrinsic coagulation factors; however, the proportional decrease in anticoagulant proteins is not measured.[17,26] Similarly, low Plt count does not account for endothelial compensation observed in cirrhotic patients.[24,30] While viscoelastic testing can serve an important role in guiding intraoperative resuscitation, it is best implemented in series and is not routinely used as a standalone assay in the preoperative setting.[13] Furthermore, subjective interpretation is required, and availability is not ubiquitous across institutions, thus limiting its value as a preoperative predictor for increased product utilization during OLT.[13] Consistent with previously published reports, our analysis found that these conventional coagulation labs failed to capture the risk profile associated with increased transfusion requirements at our institution and were therefore not included in the modified protocol. These findings underscore the inadequacy of traditional laboratory hemostatic markers in the liver transplant population, thus supporting a multifactorial strategy incorporating patient and operative characteristics associated with increased blood loss.

Several studies have sought to identify consistent predictors for increased intraoperative blood loss; however, these reports are conflicting and limited largely to single-center experiences. Consequently, a wide spectrum of patient and operative characteristics have been described to portend increased operative bleeding, though no consensus risk factors have been clearly delineated across multiple centers.[31–36] Despite these consternations, there have been several reported predictive models for identifying patients at risk for high blood product utilization, though the majority are restricted to RBC use alone, and are complex, thus limiting their bedside utility.[19–22] McCluskey et al., however, did develop an applicable preoperative risk index derived from seven binary variables that were subsequently validated and modified to five binary factors by Pustavoitau et al.[20,21] While successful in developing applicable risk indices, both studies were restricted to RBC transfusion requirements and did not extend their predictive modeling to FFP or Plt utilization. We, therefore, sought to scrutinize the original multiyear protocol at UW, while exploring novel strategies to inform multi-product risk stratification and preparation moving forward.

The modified UW protocol was optimized through several iterations and sub-analyses, which consistently demonstrated the superiority of establishing individualized criteria for supplemented RBC, FFP, and Plt preparation as opposed to a single HR setup encompassing all three products. Though unified by the shared risk factor of Hgb ≤7.8, this allows for patients to receive customized preparations based on their individual risk profile, thus augmenting precise identification of HR utilizers while minimizing waste of unused product and limiting the logistical burden of overpreparation. We did test expanded criteria protocols to include factors with

p values <0.1 or <0.2 in an effort to capture as many high-utilizers as possible; however, these attempts resulted in heterogenous HR groups defined by poorly correlated variables. Accordingly, these strategies failed to substantially improve the rate of under-preparation, which was only overcome by unacceptable sums of compensatory overpreparation. Instead, we focused on creating smaller, homogenous HR populations characterized by significant ($p < .05$) risk factors for each product, which were augmented by statistically-driven unit setups for the redefined mSR (cohort median usage plus SD) and mHR (cohort mean usage plus SD) subgroups.

Application of the modified protocol to the 225 OLT recipients yielded a two-fold differential in blood product utilization between the mSR and mHR cohorts, indicating improved identification of high-utilizers for each product. Most importantly, the strategy dramatically improved the under-preparedness rate to <10% for each product, which accounts for nearly all non-outlier recipients. This achievement is of particular importance with respect to FFP, which can be delayed intraoperatively by the thawing process, and Plts, which are often limited by inventory and institutional quarantine prior to use. Mitigating under-preparation is inevitably associated with a higher degree of overpreparation, represented by the 1.56-fold increase in RBCs and 1.44-fold increase in FFP compared to the original protocol. However, the risk of wasting RBC and FFP secondary to product overpreparation is negligible at this institution. This is in contrast to Plts, which represent a valuable and highly perishable product that is at risk for waste if not transfused within 5 days of thawing. Importantly, our modified protocol yielded no increase in Plt overpreparation, despite improving its under-preparation rate to 9.3%. Taken together, we accept the small labor cost associated with RBC and FFP overpreparation in order to substantially improve the risk to OLT recipients potentiated by blood product under-preparation. It is important to note that this modified protocol was optimized based on our retrospective cohort and must be prospectively evaluated to determine its true effectiveness.

An important facet to consider is the high rate of non-compliance observed through analysis of standard- and HR order placements at this institution. We speculate that reducing the number of risk factors assigned to each product will simplify the ordering process and improve prospective order accuracy. Moreover, we posit that supplemental provider education and integrated blood product order sets in the EMR will further augment compliance and performance. The EMR order sets will consist of binary selections for each variable, which will then automatically direct the provider to the correct blood product request individualized for each product. We are currently implementing this updated protocol, with plans to rigorously evaluate its effectiveness and compliance in subsequent analyses.

The primary limitations of this study include the retrospective design and the relatively small sample size, which restricted the extent of our statistical analyses. The modified protocol was optimized based on a retrospective study population and evaluated within the same cohort. We theorize that these 225 patients accurately represent our current and future liver transplant population; however, variation will exist among prospective recipients underscoring the necessity of future analyses to evaluate the actual performance of our modified protocol. Though this was a single center study, we believe that our findings and optimization strategies are translatable across high-volume liver transplant centers with similar patient populations. Furthermore, the methodology represents a key feature of this report and can serve as an applicable template for widespread extrapolation across institutions with more disparate experiences. Moreover, we believe that although this modified UW protocol is similar to previously reported predictive models for intraoperative transfusion requirements during OLT, our methodology is uniquely strengthened by its simplicity, inclusivity of multiple blood products, and translatability across institutions.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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