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Original Article

Morbidity and Mortality Associated With Blood Transfusions in Elective Adult Cardiac Surgery

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Objectives: Perioperative transfusion thresholds have garnered increasing scrutiny as restrictive strategies have been shown to be noninferior. The study authors used data from a statewide academic collaborative to test the association between transfusion and 30-day mortality.

Design: All adult patients undergoing coronary artery bypass grafting (CABG) and/or valve surgeries between 2013 and 2019 in the authors' Academic Cardiac Surgery Consortium were examined. The relationship between the number of overall packed red blood cell (pRBC) and coagulation product (CP) (fresh frozen plasma, cryoprecipitate, platelets) transfusions on 30-day mortality was evaluated. Multivariate regression was used to evaluate predictors of transfusion and study endpoints. Machine learning (ML) models also were developed to predict 30-day mortality and rank transfusion-related features by relative importance.

Setting: At an Academic Cardiac Surgery Consortium of 5 institutions.

Participants: Patients ≥18 years old undergoing CABG and/or valve surgeries.

Measurements and Main Results: Of the 7,762 patients (median hematocrit [HCT] 39%, IQR 35%-43%) who were included in the final study cohort, >40% were transfused at least 1 unit of pRBC or CP. In adjusted analyses, higher preoperative HCT was associated with reduced odds of mortality (adjusted odds ratio [aOR] 0.95, 95% CI 0.92-0.98), renal failure (aOR 0.95, 95% CI 0.92-0.98), and prolonged mechanical ventilation (aOR 0.97, 95% CI 0.95-0.99). In contrast, perioperative transfusions were associated with increased 30-day mortality after adjustment for preoperative HCT and other baseline features. The ML models were able to predict 30-day mortality with an area under the curve of 0.814-to-0.850, with perioperative transfusions displaying the highest feature importance.

Conclusions: The present analysis found increasing HCT to be associated with a lower incidence of mortality. The study authors also found a direct dose-response association between transfusions and all study endpoints examined.

Key Words: heat valve prosthesis implantation; coronary artery bypass; health care economics and organizations; outcome assessment, health care; quality of health care

WITH MORE THAN HALF of cardiac surgical patients receiving allogeneic blood products, perioperative transfusion practices have garnered much scrutiny.[1-4] Although critical for augmenting oxygen-carrying capacity, stored packed red blood cell (pRBC) transfusions are associated with a multitude of complications, including infections, acute kidney injury, postcardiotomy syndrome, and even mortality.[5-7] However, several studies also have demonstrated the deleterious effects of anemia and low hematocrit (HCT) on outcomes after cardiopulmonary bypass, and have advocated for pRBC transfusion in select patients.[8,9] Prior work examining the independent impact of anemia and transfusions on clinical outcomes has

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yielded conflicting conclusions. This uncertainty is largely because transfusions and preoperative anemia are correlated and associated with adverse outcomes. In a study of >33,411 patients undergoing coronary artery bypass grafting, LaPar et al. found anemia and transfusions to increase the odds of mortality and major complications, although the latter exerted a more profound impact.[10]

To better standardize transfusion practices, threshold hemoglobin levels have been suggested by several groups, with safe levels generally exceeding 7 g/dL.[11] However, wide variability in center-level transfusion rates persists, with 7.8%-to-92.8% of CABG patients receiving stored red cells, among national and international reports.[4] A landmark randomized study of restrictive or liberal transfusion strategies in the United Kingdom failed to demonstrate the ability of the former to reduce morbidity and healthcare costs.[12] Furthermore, the impact of coagulation products (CP), such as cryoprecipitate, plasma, and platelets, on perioperative outcomes of cardiac surgeries has not been examined broadly. In the present study, the study authors used data from a statewide collaborative of academic hospitals to test whether transfusions of pRBC or CP would be associated with increased risk of 30-day mortality, prolonged mechanical ventilation, acute kidney injury, and stroke. They hypothesized that increased morbidity and mortality were associated with pRBC and CP transfusions in a dose-dependent fashion.

Methods

Data for the present study were obtained from the authors' Academic Cardiac Surgery Consortium repository. Founded in 2013, this consortium is a collaborative encompassing 5 academic hospitals within their state. Data elements, including those submitted to the Society of Thoracic Surgeons (STS), are collected prospectively and linked to financial data in compliance with policies of individual institutions and approved by a cross-campus system-wide Institutional Review Board.

All adult patients undergoing isolated CABG, isolated valve, CABG and single valve, and multivalve surgeries between 2013 and 2019 were identified within the Academic Cardiac Surgery Consortium. Patients with infective endocarditis, preoperative HCT <20% (first percentile) or >45% (90th percentile), as well as those receiving >50 transfusions throughout the index hospitalization, were excluded to maintain generalizability of the study findings (Fig 1). Additionally, those requiring extracorporeal life support, left ventricular assist devices, or transcatheter valve surgery during the index hospitalization were not considered for further analysis (Fig 1). Patients who received at least one unit of either pRBC or CP (ie, intraoperative or postoperative fresh frozen plasma, cryoprecipitate, or platelets) comprised the transfusion group.

Patient characteristics (ie, age, sex, urgent and/or emergent status, and comorbid conditions) and surgical category (ie, isolated CABG, isolated valve, CABG and single valve, and multivalve surgeries) were defined according to the STS Adult Cardiac Surgery Database dictionary.[13] Preoperative HCT was treated as a continuous variable to reduce bias. In addition, 30-day, all-cause mortality was defined in congruence with the STS definition, as were postoperative prolonged mechanical ventilation (>24 hours of mechanical ventilation after operating room exit), acute renal failure (increase in serum creatinine level 3-times greater than baseline or serum creatinine ≥4 mg/dL or new requirement in dialysis postoperatively) and stroke.[13]

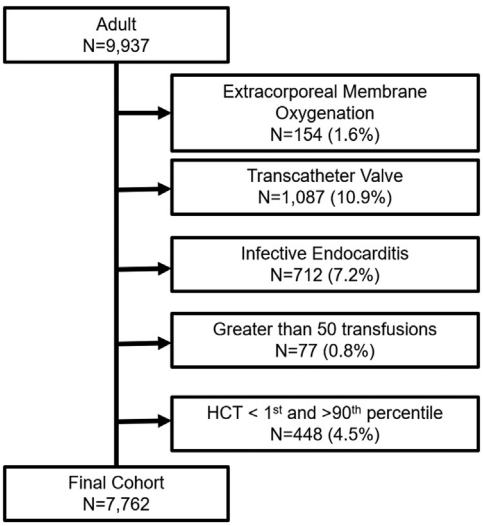

Fig 1. Study consort diagram. HCT, hematocrit.

The present study had the following 2 main objectives: (1) delineate the independent association between preoperative HCT and transfusion status on outcomes of interest and (2) develop machine learning (ML) models to predict 30-day mortality and rank transfusion-related covariates based on relative feature importance.

First, logistic regression with adjustment for age, sex, urgent and/or emergent status, surgical group, institution, and surgical year was developed to evaluate the association of preoperative HCT with postoperative outcomes. Marginal analysis was used to obtain predicted risk of mortality at various HCT levels. Subsequently, the Least Absolute Shrinkage Operator regularization was used to select additional relevant variables, including race, diabetes, end-stage renal disease requiring dialysis, body mass index (BMI), prior myocardial infarction, congestive heart failure, cerebrovascular disease, peripheral vascular disease, preoperative albumin, and a number of coronary arteries with significant disease.[14] Using this model with additional covariates, the association between preoperative HCT and outcomes of interest was reassessed. The study authors then tested for an independent association between preoperative HCT and outcomes of interest while adjusting for the aforementioned patient and surgical factors as well as transfusion status. Marginal analysis was performed to assess the predicted risk of mortality at various HCT levels with and without the inclusion of transfusion as a regression covariate.

Second, the authors developed 3 Random Forest classification models to predict 30-day mortality. Each model adjusted for baseline patient and surgical characteristics (described above), in addition to either total transfusions, pRBC transfusions, or CP transfusions. Models were trained using a random

70% subsample of data and evaluated with the remaining 30%. They obtained cross-validated performance metrics by repeating the random subsampling, derivation, and validation process 10 times. Model performance metrics are reported as means with 95% CIs. In addition, the study authors queried model attributes to rank covariates by their relative feature importance. This concept is often used to identify explanatory variables that are most influential in an ML model's decision-making because feature importance represents the overall improvement in accuracy and/or predictive power attributable to a certain covariate.

The continuous variables are reported as medians with IQR, and were compared using the Mann-Whitney *U* test. The categorical variables are reported as proportions and were compared between groups using the Adjusted Wald test. The area under the receiver operating characteristic (C-statistic) was examined to evaluate logistic regression and Random Forest models. Logistic regression outputs are reported as adjusted odds ratios (aOR) with 95% CIs. Statistical analysis was performed using Stata 16.0 (StataCorp, LLC, College Station, TX) and Python 3.9 (Python Software Foundation, Wilmington, DE). It was not appropriate or possible to involve patients or the public in the design, conduct, reporting, or dissemination plans of the authors' research. The study was approved by each Institutional Review Board as well as the cross-campus Institutional Review Board agency.

Results

Over the study period, 7,762 patients (median HCT 39%, IQR 35%-43%) met the inclusion criteria, with case distribution reported in Table 1. Overall, 30-day mortality was 2.4%, although 9.9% of patients suffered prolonged postoperative mechanical ventilation, 1.5% postoperative stroke, and 3.3% postoperative renal failure. During the intraoperative and postoperative phases of care, 62.0% of patients underwent pRBC or CP transfusion. Further stratification by category of transfusion revealed that 48.6% were transfused with at least 1 unit of pRBC and 46.4% with at least 1 unit of CP. The overall distribution of pRBC and CP use is shown in Fig 2, A and B, respectively. Expectedly, the median preoperative HCT was lower for the transfusion group (Table 1).

Patients requiring transfusions were older, more commonly female and of Asian race. In addition, compared to others, the transfused group had a lower median BMI (Table 1). The STS predicted morbidity (8.7 *v* 14.3%, $p < 0.001$) and mortality (0.8 *v* 1.7%, $p < 0.001$) scores were significantly higher for patients receiving a transfusion. Several chronic medical conditions, such as peripheral vascular disease, dialysis dependence, and liver dysfunction, were also more prevalent in the transfusion cohort (Table 1). Moreover, intra-aortic balloon pumps were more commonly employed among patients who received a transfusion (7.8 *v* 2.2%, $p < 0.001$). Relative to others, the transfusion cohort had longer median cross-clamp time (94 *v* 108 minutes, $p < 0.001$) and greater operative complexity, with a more frequent performance of CABG and single-valve (7.0 *v* 17.4%, $p < 0.001$) and multivalve (2.8 *v* 7.6%, $p < 0.001$) surgeries. Significant center-level variation was noted also, with a transfusion rate ranging from 8.3%-to-35.7% of patients at each center ($p < 0.001$).

Risk-adjusted predictors of perioperative transfusion included increasing age, non-White race, history of prior cardiac surgery, preoperative congestive heart failure, dialysis dependence, cerebrovascular disease, peripheral vascular disease, number of diseased coronary vessels, and intra-aortic balloon pump use (Fig 3). Furthermore, preoperative HCT was associated inversely with the risk-adjusted predicted rate of blood product use (Fig 4). Risk-adjusted analysis also demonstrated center-level variation in odds of transfusion, as 2 centers had significantly different odds of blood receipt, compared to the reference institution (aOR 0.34, 95% CI 0.23-0.40; aOR 1.49, 95% CI 1.22-1.82).

The parsimonious risk-adjusted model of mortality, with age, sex, operative type, baseline HCT, elective and/or urgent or emergent surgery, and operative year as covariates, revealed a 5% reduction of odds of 30-day mortality with every 1-point increase in preoperative HCT (aOR 0.95, 95% CI 0.92-0.98; Fig 5, A). However, with additional adjustment for BMI, dialysis-dependence, race, preoperative serum albumin levels, and preoperative HCT were no longer associated with the odds of 30-day mortality (aOR 1.03, 95% CI 0.99-1.08; Fig 5, B). In contrast, the total number of transfusions exhibited a dose-dependent relationship with mortality despite adjustment for preoperative HCT (Fig 6, A). Stratification by pRBC and CP transfusions demonstrated similar results, as shown in Figure 6, B and C, respectively.

Increasing preoperative HCT was associated with a reduction in the odds of prolonged ventilation (aOR 0.97, 95% CI 0.95-0.99) and acute renal failure (aOR 0.95, 95%CI 0.92-0.98). In contrast, blood transfusions were not associated with increased odds of prolonged ventilation (aOR 1.02, 95% CI 0.99-1.04) and renal failure (aOR 0.99, 95% CI 0.95-1.02). Regardless, incremental increases in the odds of prolonged ventilator support, postoperative renal failure, and stroke were noted for every additional unit of pRBC or CP transfused (eFigures 2-4).

In a secondary analysis, the study authors created 3 unique models for the prediction of 30-day mortality, each adjusted for baseline patient and surgical characteristics, in addition to either total transfusions, RBC transfusions, or CP transfusions. The area under the curves for these 3 models were 0.850, 0.830, and 0.814, respectively. Feature importance of included variables for each model is represented visually in Figure 7, with transfusion variables carrying the most importance for predictive performance and accuracy.

Comment

Blood-component therapy remains a critical facet of perioperative management in cardiac surgical patients. Given the association of transfusions with worse clinical outcomes reported, concerted efforts have been made to reexamine transfusion thresholds and practices. The present study provides a contemporary perspective on the impact of blood component

Table 1
Patient and Operative Characteristics Stratified by Transfusion Cohort Status

Patient/Surgical Characteristic	No Transfusion n = 2,943	Transfusion n = 4,819	Overall N = 7,762	p Value
Age, median (IQR), y	63 (55-70)	66 (58-73)	65 (57-72)	< 0.001
Female sex, n (%)	675 (22.9)	1,566 (32.5)	2,241 (28.9)	< 0.001
Race category (n = 7,075), n (%)				< 0.001
White	1,678 (65.3)	2,431 (58.3)	4,109 (61.0)	
Black	120 (4.7)	258 (6.2%	378 (5.6)	
Hispanic	566 (22.0)	815 (19.6)	1,381 (20.5)	
Asian	207 (8.1)	663 (15.9)	870 (12.9)	
BMI (N = 7,740), median (IQR), kg/m^2	28.1 (25.1-31.9)	26.7 (23.6-30.4)	27.2 (24.1-30.9)	< 0.001
Cerebrovascular disease, n (%)	396 (13.5)	818 (16.7)	1,214 (15.6)	< 0.001
Chronic lung disease, n (%)	483 (16.4)	950 (19.7)	1,433 (18.5)	< 0.001
Hypertension, n (%)	2,212 (75.2%	3,803 (78.9)	6,015 (77.5)	< 0.001
Diabetes, n (%)	999 (33.9%	1,813 (37.6)	2,812 (36.2)	0.001
Peripheral arterial disease, n (%)	193 (6.6)	543 (11.3%	736 (9.5)	< 0.001
Renal failure (hemodialysis), n (%)	63 (2.1)	379 (7.9)	442 (5.7)	< 0.001
Liver disease	140 (4.8)	355 (7.4)	495 (6.4)	< 0.001
Total albumin (N = 6249), median (IQR)	4.1 (3.8-4.4)	3.9 (3.5-4.3)	4.0 (3.6-4.3)	< 0.001
Previous MI, n (%)	809 (27.5)	1,569 (32.6)	2,378 (30.6)	< 0.001
CHF, n (%)	2,639 (49.8)	2,824 (36.4)	5,463 (41.8)	< 0.001
NYHA class, n (%)				< 0.001
None	2,205 (74.9)	3,035 (63.0)	5,240 (32.8)	
I	111 (15.0)	212 (11.9)	323 (4.1)	
II	285 (38.6)	558 (31.3)	843 (10.9)	
III	289 (39.2)	734 (41.1)	1,023 (13.2)	
IV	53 (7.2)	280 (15.7)	335 (4.3)	< 0.001
Ejection fraction (N = 7,361), median (IQR), %	60 (52-65)	58 (48-63)	60 (50-65)	0.001
Left main disease >50%, n (%)	2,345 (79.7)	3,979(82.6)	6,324 (81.5)	0.47
Vessel disease (N = 6,926), n (%)				0.27
Single	814 (30.4)	1,202 (28.3)	2,016 (29.1)	
Double	243 (9.1)	387 (9.1)	630 (9.1)	
≥3	1618 (23.4)	2,662 (38.4)	4,280 (61.7)	
Last preoperative HCT, median (IQR), %	41 (38-44)	38 (33-42)	39 (35-43)	< 0.001
Lowest HCT, median (IQR), %	27 (24-31)	23 (20-26)	25 (21-28)	< 0.001
Predicted risk of mortality, median (IQR), %,	0.4 (0.2-0.7)	1.0 (0.5-2.3)	0.7 (0.3-1.6)	< 0.001
Operative characteristics (N = 7,760)				
Bypass support, n (%)	2,361 (80.3)	4,605 (95.6)	6,966 (89.8)	< 0.001
None, n (%)	581 (19.8)	213 (4.4)	794 (10.2)	
Operative status (N = 7,728), n (%)				< 0.001
Elective	1,944 (66.4)	2,550 (53.1)	4,494 (58.2)	
Urgent	963 (32.3)	2,024 (42.2)	2,987 (38.7%	
Emergent	21 (0.7)	220 (4.6)	241 (3.1)	
Emergent salvage	0	6 (0.1)	6 (0.08)	
Cardiopulmonary bypass time (N = 6,907), median (IQR), min	131 (103-169)	152 (117-204)	144 (111-191)	
Aortic cross-clamp time (N = 6,657), median (IQR), min	94 (75-121)	108 (81-143)	103 (78-135)	
Lowest intraoperative HCT (N = 6,036), median (IQR), %	27 (24- 30)	23 (20-26)	25(21-28)	
Postoperative HCT (N = 2,910)	30 (27-33)	28 (25-30)	28 (26-31)	
IMA use (N = 4,694), n (%)				< 0.001
LIMA	1,495 (83.4)	2,454 (84.0)	3,940 (83.9)	
RIMA	29 (1.6)	27 (0.9)	56 (1.2)	
BIMA	158 (8.9)	149 (5.1)	307 (6.5)	
None	100 (5.6)	291 (10.0)	391 (8.4)	
IABP, n (%)	65 (2.2)	374 (7.8)	439 (5.7)	< 0.001
Total all blood product use, median (IQR)	0	4 (2-8)	2 (0-5)	< 0.001
Total number of pRBC, median (IQR)	0	2 (1-4)	0 (0-2)	< 0.001
Total number of coagulation Products, median (IQR)	0	2 (0-5)	0 (0-3)	< 0.001
Preop anemia, n (%)	67 (2.3)	665 (13.)	743 (9.5)	
Operative group, n (%)				< 0.001
Isolated CABG	1,578 (53.6)	2,094 (43.5)	3,672 (47.3)	
Isolated valve	1,077 (36.6)	1,520 (31.5)	2,597 (33.5)	
CABG/valve	207 (7.0)	837 (17.4)	1,493 (19.2)	
Multivalve	81 (2.8)	368 (7.6)	449 (5.8)	

Abbreviations: BIMA, bilateral internal mammary artery; BMI, body mass index; CABG, coronary artery bypass graft; CHF, congestive heart failure; HCT, hematocrit; IABP, intra-aortic balloon pump; IMA, internal mammary use; LIMA, left internal mammary artery; MI, myocardial infarction; NYHA, New York Heart Association Classification; preop, preoperative; pRBC, packed red blood cell; RIMA, right internal mammary artery.

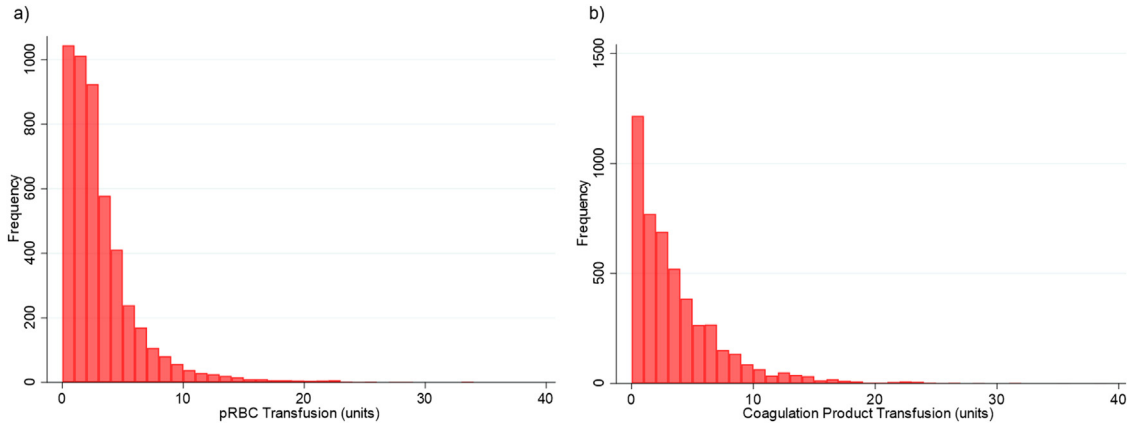

Fig 2. Frequency of (A) packed red blood cells and (B) coagulation product transfusions for overall study cohort. Histogram of packed red blood cells and coagulation product transfusion for the final study cohort. CPT, coagulation product transfusion; pRBC; packed red blood cell.

therapy, including pRBC and coagulation products, on perioperative outcomes after elective adult cardiac surgeries. Transfusion of blood products was common in the authors' academic statewide collaborative, with pRBC and CP transfusions demonstrating a dose-dependent association with outcomes of interest, such as 30-day all-cause mortality, perioperative renal failure, and prolonged mechanical ventilation. Secondarily, the authors created ML models with moderately high predictive accuracy for 30-day mortality, which was driven in large part by perioperative transfusion exposures.

Consistent with the literature, the authors' study demonstrated the association of preoperative HCT with 30-day all-cause mortality, prolonged postoperative mechanical ventilation, and renal failure. Not surprisingly, the impact of preoperative anemia was diminished with the addition of patient and operative characteristics, as well as the total number of pRBC and CP transfusions. The present analysis adds to a growing body of literature that has demonstrated that although preoperative anemia is a significant contributor to perioperative morbidity and mortality,[10] pRBC and CP transfusions may have a profound effect on outcomes regardless of the baseline HCT level. Consistent with another institutional study from the Maryland Cardiac Surgery Quality Initiative,[15] the study authors found a dose-response association between the number of transfusions and risks of mortality, prolonged ventilatory support, postoperative renal failure, and stroke. Although the study by Ad et al. shared a number of similarities in design, the present analysis excluded patient outliers in regard to preoperative HCT and the number of transfusions used in order to improve generalizability.[15] Finally, the authors' analysis spanned a shorter period of time during which the evolution of blood transfusion practice was inevitable, and they employed ML algorithms to validate the prior hierarchical modeling. The addition of feature importance and ML analysis further amplified previous analyses that have attempted to perform hierarchical modeling of the relationship among anemia, transfusions, and mortality. Furthermore, the study authors acknowledge the potential for preoperative HCT, which thereby mediates the effect of transfusions on outcomes. Although the transfusion decision straddles concerns regarding tissue hypoxia in patients with potentially limited cardiopulmonary reserve, the authors' findings add further support to restrictive transfusion policies when clinically feasible.

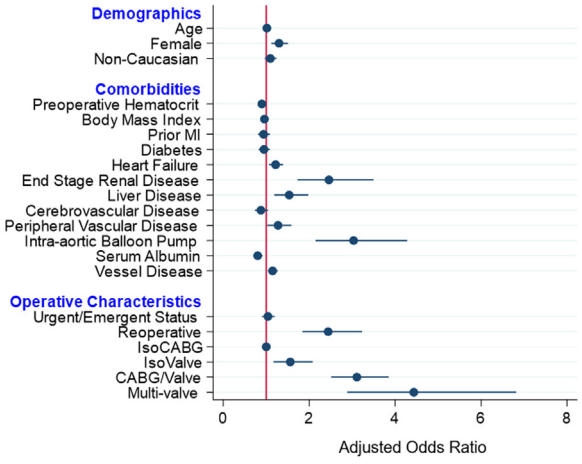

Fig 3. Risk-adjusted patient and surgical factors associated with perioperative transfusion. The *red vertical bar* is used as reference. *Horizontal blue* error bars represent 95% CI. CABG, coronary artery bypass graft; CABG/Valve, combined coronary artery bypass graft/valve; IsoCABG, isolated CABG; IsoValve, isolated valve; MI, myocardial infarction; multivalve, multiple cardiac valve operations without coronary artery bypass..

Similar studies examining coagulation products are sparser than the literature examining the outcome of pRBC on perioperative outcomes of cardiac surgery, with a general lack of prospective studies examining platelet and plasma transfusion. One such meta-analysis performed by Yanagawa et al. aimed to address the apparent surgical equipoise regarding the impact of platelet transfusions in patients undergoing cardiac surgery, with no significant increases in postoperative death, stroke, myocardial infarction, reoperation for bleeding, infection, or dialysis associated with platelet transfusion.[16] However, this analysis was underpowered and suffered from study heterogeneity due to the pooling of observational studies and variability in quantity and type of platelet transfusion. Another retrospective analysis of >32,000 isolated CABG patients found no increase in morbidity with empirical platelet transfusion for microvascular bleeding.[17] In the present work, the study authors performed a composite analysis of coagulation products, considering plasma, platelet, and cryoprecipitate

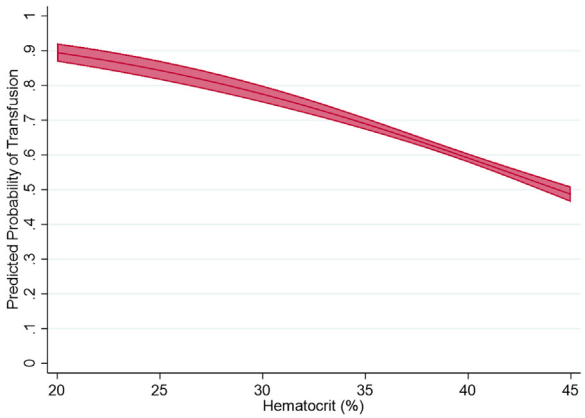

Fig 4. Predicted probability of rate of transfusion by preoperative hematocrit. Risk-adjusted predicted probability of transfusion across range of preoperative hematocrit. Model not inclusive of transfusions received.

transfusions in one group, given the difficulty in identifying the distinct effects of transfusion on study outcomes. Their findings of increased morbidity and mortality with coagulation product transfusion were consistent with a separate pooled analysis of 2 randomized controlled studies that demonstrated increased all-cause mortality with plasma transfusions and infectious-related mortality with platelet transfusions.[18] Given the potential for adversely impacting perioperative outcomes, the need for goal-directed treatment of coagulopathy is warranted and remains a relevant concern for cardiac surgeons.

The degree of variability among 5 academic institutions with a statewide health system underscores the numerous factors that contribute to transfusion decision-making. Even within a relatively homogeneous system with a unified overlying advisory board, the extent of variation was notable. These findings were consistent with numerous observational studies that demonstrated significant variation in transfusion practices.[19,20] Whether this was related to the documented risk profile and limitations in capturing patient acuity and severity within an administrative database versus inherent biases in transfusion practices is unknown. Across all institutions, viscoelastic coagulation testing was employed, but the authors were unable to obtain assay results to standardize transfusion indications in a retrospective manner. Various groups have shown that a programmatic focus on blood conservation has significantly improved transfusion rates over time.[21] Nonetheless, perioperative transfusions remain an elusive opportunity for quality improvement that is intertwined with the value of care delivered, and standardized thresholds and definitions are needed.[22]

Regardless of transfusion thresholds, the present analysis built upon a vast literature demonstrating an association between blood transfusions and adverse events after cardiac surgery.[5-7,23,24] Although interpretation of this association warrants consideration that transfusions serve as a surrogate marker of patient severity and adverse outcomes may not be an inherent consequence of transfusion itself, a number of theories are postulated on how transfusions may be harmful—triggering systemic inflammatory response and adverse immunomodulatory effects through reduction of circulating lymphocytes, to mention a few. Recent results from a randomized controlled study of short-term combination treatment of intravenous iron, subcutaneous erythropoietin alpha, vitamin b12, and folic acid were associated with reduced RBC and total allogeneic transfusions in patients with preoperative anemia undergoing elective cardiac surgery, and may reflect the evolving trends in management beyond modification of transfusion thresholds.[25] Not unexpectedly, female patients, those of Asian self-declared race, and those with a lower BMI received higher rates of perioperative transfusion. Thus, the inclusion of these factors in ML models, able to account for interactions among various confounders, may allow for optimized transfusion triggers.

Limitations

The present study had several limitations that warrant further discussion. First, although patient preoperative, intraoperative, and postoperative HCT was available, the decision for transfusion administration was not documented, and clinical context prompting transfusion was not prospectively collected.

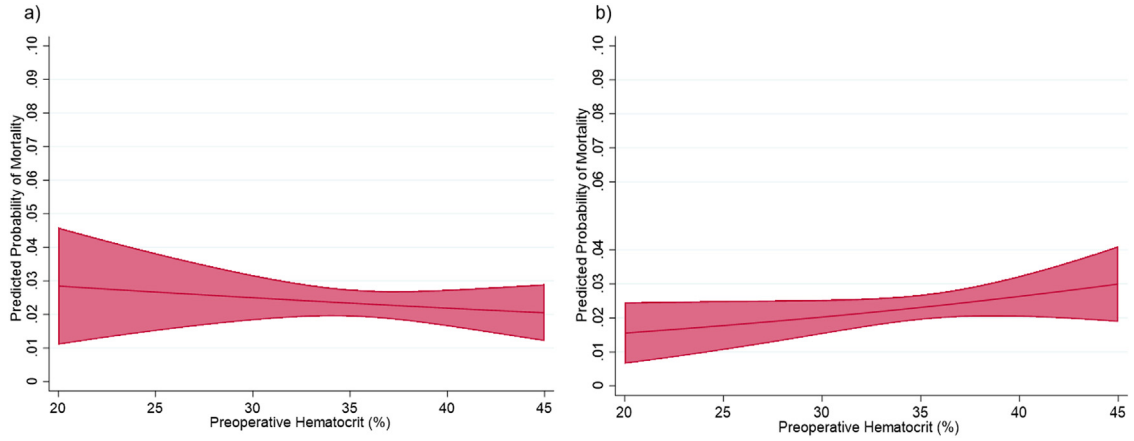

Fig 5. Risk-adjusted predicted 30-day mortality by preoperative hematocrit (A) with and (B) without adjustment for transfusion status. Risk-adjusted predicted probability of mortality across range of preoperative hematocrit.

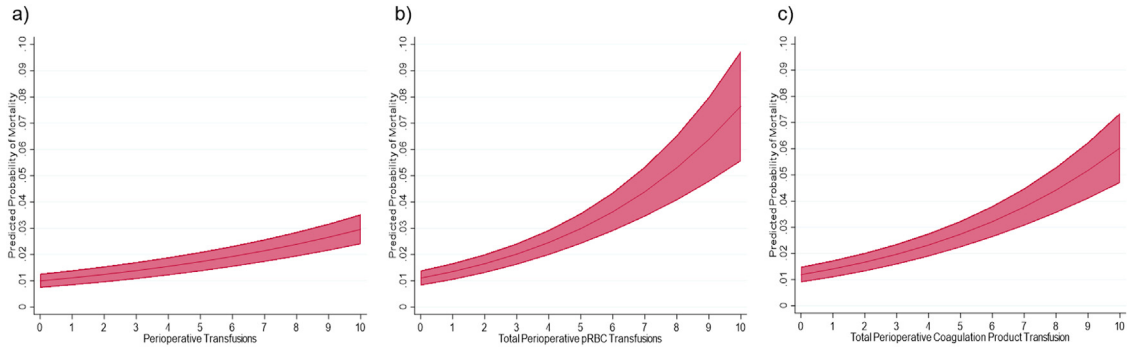

Fig 6. Risk-adjusted predicted 30-day mortality by number of (A) overall transfusions, (B) packed red blood cells, and (C) coagulation product transfusions. Incremental increase in perioperative mortality when considering number of perioperative transfusions overall and when stratifying by category of transfusion product. CPT, coagulation product transfusion; pRBC; packed red blood cell.

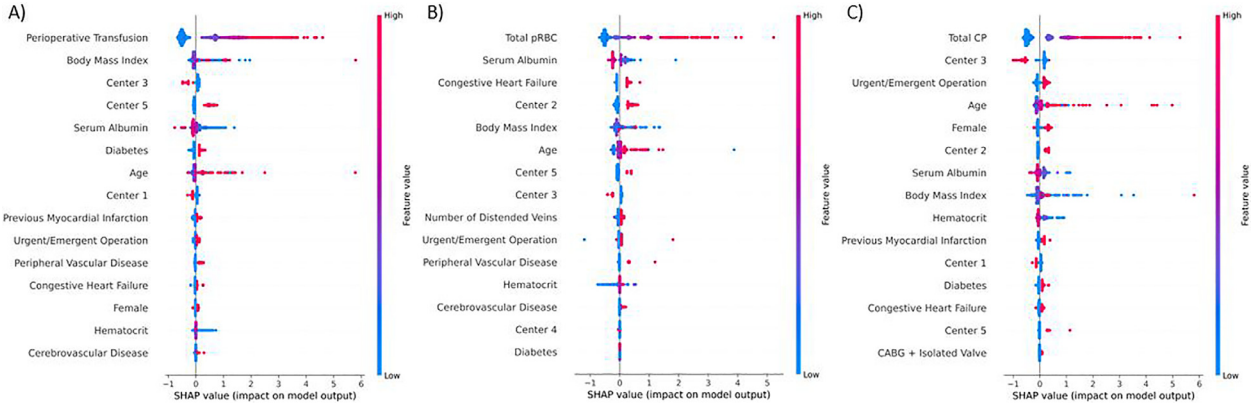

Fig 7. Feature importance for individual Random-Forest risk models for (A) overall transfusions, (B) packed red blood cells, and (C) coagulation product transfusion. Model coefficients ranked by absolute value as defined by the multivariate logistic regression analysis. Feature impact on model output is ranked in descending order. *Positive values* signify that as the variable increases, the risk of mortality increases. *Negative values* signify that as the variable increases, the risk of mortality decreases. *Dots* are colored according to the values of features for the respective patient and accumulate vertically to depict density. *Red* represents higher feature values. *Blue* represents lower feature values. CABG, coronary artery bypass graft; CP, coagulation product; pRBC; packed red blood cell; SHAP, SHapley Additive exPlanations.

Furthermore, the period of surveillance was limited to the first 30 days after hospitalization. Given the composite analysis of intraoperative and postoperative transfusions, the study authors are further unable to provide a cause-effect analysis of transfusions and perioperative complications, such as renal failure, prolonged intubation, and stroke. These events also may be associated with the need for additional transfusions, thus confounding the interpretation of the present analysis. Hemodynamic parameters and vasopressor support, which may often dictate the indication for transfusion to optimize oxygen-carrying capacity or address clinically significant coagulopathy, were also not characterized in a continuous fashion. Furthermore, posttransfusion response was not noted.

Conclusion

In conclusion, blood product transfusion remains prevalent and highly variable within the authors' consortium of academic health centers. Higher preoperative HCT was associated with lower mortality and adverse events. The relationship between preoperative HCT and mortality was attenuated with the inclusion of perioperative transfusions, suggesting that at least some of the effect of HCT on mortality is mediated by perioperative transfusions. Finally, the authors developed ML models for the prediction of 30-day mortality, for which perioperative transfusions displayed the greatest feature importance.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2022.11.012.

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