

# The Effect of Blood Transfusion on Outcomes in Aortic Surgery

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## Abstract

### Keywords

- ▶ cardiac surgical procedures
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- ▶ dissection

The use of blood transfusion in cardiac surgery varies widely. The beneficial effects of blood products are offset by an increase in morbidity and mortality. Despite multiple studies showing an association between blood product exposure and adverse short- and long-term events, it is difficult to determine causality. Nevertheless, the implication is sufficient to warrant the search for alternative strategies to reduce the use of blood products while providing a standard of care that optimizes postoperative outcomes. Aortic surgery, in particular, is associated with an increased risk of bleeding requiring a blood transfusion. There is a paucity of evidence within aortic surgery regarding the deleterious effects of blood products. Here, we review the current evidence regarding patient outcomes after blood transfusion in cardiac surgery, with special emphasis on aortic surgery.

Blood transfusion is the most common form of transplantation in current practice. Worldwide, 75 million units of blood are donated every year. Of these, 24 million units are transfused in the United States reflecting a high economic and health care burden.<sup>1–3</sup> In cardiac surgery, 50% of patients receive transfusions, and up to a fifth of these patients utilize the majority of blood products intraoperatively.<sup>2</sup> This translates to 20% of the available U.S. supply.<sup>4</sup>

Notwithstanding its well-known complications, there is increasing evidence suggesting that blood transfusion is associated with an increase in morbidity and mortality, in both the short and long term. However, the evidence is conflicting, and transfusion policies in cardiac surgery vary widely. This absence of consensus is even greater in aortic surgery, where research does not adequately address the issue of outcomes.<sup>4–6</sup> Transfusion policies are often extrapolated from studies examining other cardiac procedures

(e.g., coronary artery bypass grafting [CABG], valve replacement). Here, we briefly summarize the benefits and risks of blood transfusion before reviewing current practices in cardiac surgery. We focus on the effects of perioperative transfusion on outcomes, with an emphasis on the management of patients undergoing aortic procedures.

## Benefits and Risks of Blood Transfusion

The role of blood transfusion (specifically, packed red blood cells—PRBC) is twofold: oxygen transport and volume expansion. Since intravascular volume can be expanded effectively using crystalloids and other colloids, the primary function of PRBC transfusion is the increase in oxygen-carrying capacity of the circulation to provide sufficient oxygen to meet the metabolic demands of body tissues.<sup>7</sup> In trauma, hemorrhage results in ischemia and metabolic

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acidosis due to anaerobic metabolism. Blood transfusion is required to reverse this derangement. Severely anemic patients also exhibit organ dysfunction due to the reduced oxygen-carrying capacity.<sup>8,9</sup> Therefore, the true benefits of transfusion are limited to these specific indications.

Despite its beneficial effects, blood transfusion is not without harm. Adverse effects are well documented and include acute and chronic hemolytic reactions, nonimmune hemolysis, anaphylaxis, transfusion-related acute lung injury, graft versus host disease, circulatory overload, and infectious disease transmission.<sup>1</sup>

Immunomodulatory effects influence short- and long-term outcomes. Outcomes are affected by duration of storage, as well as leukocyte level in the PRBC units. Blood products stored for longer than 14 days are associated with an increased risk of prolonged intubation, renal failure, sepsis, multiorgan failure, and in-hospital death, together with a reduction in survival during the first 6 months. The mechanism is not completely understood but might be related to the development of a "storage lesion" decreasing the availability of oxygen delivery, impeding microvascular flow, and increasing systemic inflammation.<sup>10</sup> Moreover, white blood cells contribute to transfusion-related immunomodulation. Nonleukoreduced blood activates the host immune system, changing the immune modulatory profile. There is a decrease in circulating lymphocytes, modification of the T-cell helper/suppressor ratio, and downregulation of the antigen-presenting cell. These changes make patients increasingly vulnerable to external insults.<sup>11</sup>

## Blood Transfusion in Cardiac Surgery

Cardiac surgical procedures are associated with an increased risk of bleeding.<sup>12</sup> The extent of blood utilization varies widely across institutions, ranging from 3 to 92% of patients.<sup>12</sup> The proportion receiving only one unit of PRBC is 22 to 67%, while 5 to 25% of patients received greater than five units, independent of hospital characteristics.<sup>3</sup>

Blood products are used to treat coagulopathies and anemia, thereby limiting bleeding and augmenting oxygen-carrying capacity.<sup>2</sup> Multiple intrinsic and extrinsic factors contribute to the need for blood transfusion. These factors are patient-related and procedure-related. Some patient factors include coagulopathy and platelet disorders, while procedure-related factors include hypothermia and qualitative platelet defects secondary to cardiopulmonary bypass (CPB).<sup>2</sup>

Many studies have shown an association between transfusion and increases in short- and long-term mortality, resulting in a shift from the liberal use of blood to a more restrictive and goal-directed strategy. The aims are more efficient blood utilization and reduction in the rate of transfusion-related complications, with an expected improvement in outcomes and long-term quality of life.<sup>2,12,13</sup> Koch et al<sup>14</sup> identified a biphasic pattern of mortality after CABG, with an early peak at 6 months, and a later peak at about 10 years after surgery in those who were transfused. The risk-adjusted reduction in survival was  $0.34 \pm 2$  ( $p < 0.0001$ ) for the early phase, and

$0.074 \pm 0.016$  ( $p < 0.0001$ ) for the late phase. This study and corroborating research highlighted the deleterious effects of a liberal transfusion policy. They likened the liberal use of blood transfusion to arbitrary antibiotic administration to every patient with fever, stressing that blood transfusion has specific indications and should not be used indiscriminately.<sup>12</sup> Yu et al<sup>15</sup> observed an incremental increase in the rate of postoperative complications with each additional unit of PRBC transfused (0, 0.35, 2.29% for septicemia; 0, 0.7, and 2.29% for pneumonia, for one, two, and three units, respectively). The intubation time was also prolonged from 11 hours with one unit to 13 hours with three units. Their demonstration of the cumulative adverse effects of blood transfusion suggested the benefit of reducing transfusion volume. Surgenor et al<sup>16</sup> showed, after adjusting for variables, that a lower intraoperative nadir hematocrit was associated with developing low-output heart failure (odds ratio [OR], 1.27; 95% confidence interval [CI], 1–1.61;  $p = 0.047$ ). Furthermore, Koch et al identified perioperative blood transfusion as the single most reliable factor associated with postoperative morbidity.<sup>17</sup> They described an increase in mortality (OR, 1.77; 95% CI, 1.67–1.87;  $p < 0.0001$ ), renal failure (OR, 2.06; 95% CI, 1.87–2.27;  $p < 0.0001$ ), prolonged ventilator support (OR, 1.79; 95% CI, 1.72–1.86;  $p < 0.0001$ ), severe infection (OR, 1.76; 95% CI, 1.47–1.63;  $p < 0.0001$ ), cardiac complications (OR, 1.76; 95% CI, 1.47–1.63;  $p < 0.0001$ ), and neurologic events (OR, 1.37; 95% CI, 1.30–1.44;  $p < 0.0001$ ).

Importantly, the retrospective nature of these observational studies makes it difficult to assess the exact relationship between blood transfusion and adverse events. The association may be influenced by numerous confounders that might not be accounted for during the statistical analysis.<sup>14–17</sup> One potential confounder that may impact outcomes is the severity of clinical presentation. Inherently high-risk patients, such as those with multiple comorbidities, complex clinical presentations, and emergent operations, naturally tend to have lower survival. Nevertheless, even in studies that evaluate nonhigh-risk patients, the outcomes are still conflicting. For instance, while Paone et al showed an increased morbidity and mortality after on-pump CABG with as little as one or two units of PRBC, Koster et al did not show an increase in mortality or adverse perioperative outcomes in patients receiving equal amount of blood products.<sup>18,19</sup>

Some centers give blood transfusions to patients with stable cardiovascular disease in anticipation of intraoperative hemorrhage. Paone et al<sup>18</sup> described the routine use of one to two units of PRBC, and showed an association with increased mortality after propensity adjustment (OR, 1.86; 95% CI, 1.21–2.87;  $p = 0.005$ ). Murphy et al<sup>20</sup> analyzed the effect of giving increasing volumes of blood, comparing outcomes with patients who did not receive transfusions. Patients receiving only one unit of PRBC had a 63% increase in ischemic complications and a 46% increase in infectious complications, while those exposed to two units had an increase of 130% and 136%, respectively. Moreover, they demonstrated an 11% and 21% increase in transfusion cost with one and two units, respectively. They showed not only the adverse association with increasing quantities of blood transfusion but also its existence

even with low blood product use, highlighting the harmful effect of this practice.<sup>18</sup>

## Age

Age is another factor that influences outcomes, and elderly patients invariably have more comorbidities than their younger counterparts. Cardiac surgery is increasingly performed in older patients. Preoperative anemia is common in this population, with a prevalence of one in eight patients older than 65 years;<sup>21</sup> and this is reflected in their greater use of blood products.<sup>22</sup> In spite of this, studies have not shown a statistically significant association between transfusion and adverse events in these patients. Yun et al<sup>22</sup> found no association between early and late mortality with the use of one to two PRBC units in octogenarians (early mortality hazard ratio [HR], 1.47; 95% CI, 0.84–2.56;  $p > 0.05$  and late mortality HR, 0.92; 95% CI, 0.50–1.69;  $p > 0.05$ ). Meanwhile, Carrascal et al<sup>23</sup> did not report a significant change in early or late survival with the use of one to two units of PRBC. However, transfusion may be of benefit in the elderly. Although not in the context of cardiac surgery, Wu et al<sup>24</sup> demonstrated an improvement in 30-day mortality in patients undergoing transfusion who experienced an acute myocardial infarction with low hematocrit ( $< 24\%$ ).

## Confounders

Many other variables influence outcomes and act as confounders in any observational study. Indeed, the surgery itself is a risk factor due to the systemic inflammatory response precipitated by the procedure and the use of CPB.<sup>12</sup> Thus, the etiologic association of blood transfusion with mortality is difficult to establish in the complex cardiac surgical patient.

## Counterevidence

Recent studies have challenged the negative association of transfusion in cardiac surgical patients. Koster et al<sup>19</sup> did not find an increase in 30-day mortality in patients undergoing CABG exposed to one to two units of PRBC (OR, 0.29; 95% CI, 0.06–1.50;  $p = 0.14$ ). Apart from a prolonged intensive care unit (ICU) stay (longer than 48 hours), there was no statistical difference in any other major clinical complication such as stroke, the requirement of hemofiltration, low cardiac output, wound infections, and prolonged mechanical ventilation. Dardashti et al<sup>25</sup> did not find an association between PRBC transfusion and reduced long-term survival after adjusting for hemoglobin (Hg) and glomerular filtration rate in patients undergoing CABG. Although Warwick et al<sup>26</sup> showed an increase in long-term mortality with the use of one unit of PRBC (by univariate analysis), they failed to show this relationship with Cox regression and propensity models. They identified preoperative anemia as a significant confounding factor ( $p = 0.02$ ) but concluded that a single unit transfusion policy is safe.<sup>26</sup>

Differences in methodology, the retrospective and observational nature of the studies, and the lack of randomized trials likely underlie the heterogeneity of the results in the

literature (► **Tables 1** and **2**). The ethical considerations and impracticality of a randomized clinical trial with a lifesaving procedure, such as blood transfusion, may jeopardize research in this area (► **Table 1**).

## Blood Transfusion in Aortic Surgery

Within cardiac surgery, aortic surgery is considered an especially high-risk subspecialty, with many surgeries carrying a considerable risk of bleeding. Complex aortic reconstruction, urgent presentations, multiple suture lines, prolonged CPB, and hypothermia account for the higher risk.<sup>6</sup> Unsurprisingly, there is a greater likelihood of exposure to blood products.<sup>2,13</sup> Nevertheless, most studies have excluded this group of patients from their analysis, and consequently, current transfusion guidelines are based on literature addressing nonaortic procedures. Current practices in aortic surgery are therefore not based on firm evidence.

The few studies that have addressed this issue have focused on comparisons between conventional (i.e., liberal transfusion) and conservative transfusion strategies, and as such can offer indirect insight into morbidity and mortality after blood product use. Smith et al<sup>5</sup> demonstrated that patients receiving two or more units of PRBC were more likely to have suffered complications than those requiring zero to one unit ( $p < 0.001$ ). Cambria et al<sup>27</sup> found that PRBC transfusion was one of the independent risk factors for mortality in patients undergoing thoracoabdominal surgery (OR, 1.4; 95% CI, 1.1–1.7;  $p = 0.005$ ). Chu et al,<sup>6</sup> in their evaluation of transfusion practices, found that the patients in the blood conservation group did indeed have less blood transfused, and had lower morbidity than the control group. However, a difference in mortality was not seen. Argalious et al<sup>11</sup> studied the effect of blood transfusion in patients undergoing endovascular aortic repair. Although they found an association with in-hospital morbidity and mortality in the univariate analysis (OR, 2.94; 95% CI, 1.96–4.46;  $p < 0.001$ ), propensity matching, and multivariate analysis yielded no statistically significant association (OR, 2.7; 95% CI, 0.8–9.0;  $p = 0.11$ ). To the best of our knowledge, this is the only study in the field of aortic intervention that directly relates transfusion with outcomes. The endovascular nature of the procedure studied, with its presumably lesser proinflammatory stimulus, may account for the disparity in results compared with the majority of the cardiac surgery literature (► **Table 2**).<sup>11</sup>

## Impact and Management of Perioperative Anemia

Among cardiothoracic surgery patients, some variables have been found to correlate with the likelihood of receiving a transfusion. These include advanced age, low preoperative hemoglobin concentration, preoperative antiplatelet, and antithrombotic medication, complex cardiac procedures, and redo surgeries, emergency surgery, and noncardiac comorbidities.<sup>2,12</sup> Among these, anemia is an independent risk factor associated with worse outcomes and has been

**Table 1** Summary of studies in cardiac surgery evaluating the effect of blood transfusion on morbidity and mortality

Study	Number of patients	Patient group	Mortality				Morbidity			Additional information	
			Yes		No	N/A	Yes	No	N/A		
			Early	Late							
Koch et al <sup>14</sup>	10,289	CABG	X	X					X	Biphasic pattern of mortality: 6 mo (early) and 10 y (late)	
Yun et al <sup>22</sup>	17,026	Octogenarians and CABG, isolated valve, CABG+ valve			X					X	Increased early death in patients < 80 y
Paone et al <sup>18</sup>	22,785	CABG	X					X			Evaluation of the effect of 1–2 units of PRBC
Koster et al <sup>19</sup>	3,006	CABG			X				X		Evaluation of the effect of 1–2 units of PRBC
Jakobsen et al <sup>43</sup>	20,001	CABG, isolated valve, CABG+ valve	X							X	Increased mortality in patients with EUROSCORE 0–4% compared with EUROSCORE > 5%
Murphy et al <sup>20</sup>	8,598	CABG, isolated valve, CABG+ valve	X	X				X			Increased ICU and hospital LOS with transfusion
Surgenor et al <sup>16</sup>	3,254	CABG				X	X				PRBC and nadir hematocrit were independently associated with LOHF
Kleczyński et al <sup>44</sup>	101	TAVR		X						X	Transfusion was associated with increased LOS
Surgenor et al <sup>45</sup>	9,079	CABG, isolated valve, CABG+ valve	X							X	N/A
Engoren et al <sup>46</sup>	1,915	CABG		X						X	N/A
Koch et al <sup>17</sup>	11,963	CABG	X					X			Stepwise increment in risk for adverse events with additional units of PRBC
Santos et al <sup>47</sup>	3,004	CABG	X	X						X	EUROSCORE < 2% and patients < 60 y are associated with increased mortality
Isil et al <sup>21</sup>	288	CABG, isolated valve, CABG+ valve			X			X			Transfusion was associated with renal failure and thrombocytopenia
Dardashti et al <sup>25</sup>	5,261	CABG			X					X	GFR and Hg are confounders for decreased survival
Warwick et al <sup>26</sup>	4,615	CABG			X					X	Preoperative anemia is a confounder for decreased survival
Yu et al <sup>15</sup>	745	CABG and reoperation with CPB				X	X				Stepwise increase in postoperative complications with additional PRBC units
Engoren et al <sup>48</sup>	940	CABG				X	X				PRBC transfusion is associated with a 20% increase in graft occlusion

Abbreviations: CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; GFR, glomerular filtration rate; Hg, hemoglobin; ICU, intensive care unit; LOHF, low-output heart failure; LOS, length of stay; N/A, not applicable; PRBC, packed red blood cells.

**Table 2** Summary of studies in aortic surgery evaluating the effect of blood transfusion on morbidity and mortality

Study	Number of patients	Patient group	Mortality				Morbidity			Additional information	
			Yes		No	N/A	Yes	No	N/A		
			Early	Late							
Yaffee et al <sup>4</sup>	132	Thoracic aortic aneurysm and dissection	X				X			Evaluation of the effectiveness of BCS	
Chu et al <sup>6</sup>	189	Ascending aortic and arch surgeries				X				X	Evaluation of the effectiveness of BCS
Smith et al <sup>5</sup>	63	Aortic replacement procedures				X				X	Evaluation of the effectiveness of BCS
Argalious et al <sup>11</sup>	510	EVAR			X			X			Endografts: Abdominal aortic, descending thoracic, and fenestrated
Cambria et al <sup>27</sup>	337	Thoracoabdominal aneurysm repair	X				X				Statistical significant association with spinal cord ischemia

Abbreviations: BCS, blood conservation strategies; EVAR, endovascular aortic repair; N/A, not applicable.

identified as a modifiable preoperative variable. Muñoz et al<sup>28</sup> found that patients with uncorrected preoperative anemia (men Hg < 13 g/dL, women Hg < 12 mg/dL) were more likely to receive transfusion and inotropic support postoperatively. They also had longer ICU stays than non-anemic patients. Hogervorst et al<sup>29</sup> established a direct relationship between the degree of intraoperative anemia and adverse outcomes, with an increase in side effects as the degree of intraoperative anemia increased.

Consequently, judicious evaluation and treatment of preoperative anemia are required to avoid transfusion and improve postoperative outcomes. A patient's tolerance of blood loss is linked to the amount by which Hg decreases from preoperative baseline levels. Therefore, the lowest perioperative Hg level should not be the only guide that triggers transfusion. Rather, the percentage drop of Hg from baseline should play a major role in clinical decision-making. Karkouti et al<sup>30</sup> described an increased risk of adverse events (hospital death, stroke, and acute kidney injury) with a greater than 50% decrease in the Hg concentration from preoperative baseline levels (adjusted OR, 1.53; 95% CI, 1.12–2.08;  $p = 0.007$ ). This carries significant therapeutic implications when evaluating the need for transfusion, as patients with a relatively lower decrease from baseline Hg levels may compensate better for the anemic state than patients with larger declines from baseline values.

It is a common observation among aortic surgeons that anemia begets bleeding. That is, the blood needs to be “thick” enough to clot properly. Many feel that a hematocrit greater than 30% is required for optimal coagulation.

## Transfusion Thresholds

Transfusion thresholds provide guidance on when to transfuse the anemic patient. An appropriate threshold should balance the benefits of increased oxygen delivery with the risks of PRBC transfusion. A Cochrane review of clinical trials in noncardiac surgery and critical care<sup>31</sup> found that transfusing at a lower level (Hg 7–8 g/dL) compared with a higher level (Hg 9–10 g/dL) was associated with a 43% reduction in PRBC requirement (relative risk [RR], 0.57; 95% CI, 0.49–0.65). There was no evidence that transfusing at this more restrictive level impacted 30-day mortality, development of cardiac events, stroke, pneumonia, thromboembolism, and infection (RR, 0.97; 95% CI, 0.81–1.16). Notably, cardiac patients with “active” disease were not studied. Thus, it is difficult to extrapolate the results above to cardiac surgical patients. Those with coronary artery disease (especially acute coronary syndromes) require higher Hg levels to maintain adequate oxygen delivery to the myocardial tissue. A fall in Hg increases the risk of ischemia with ensuing negative outcomes.<sup>32</sup> For cardiac surgical patients, Murphy et al<sup>33</sup> did not find a difference in the occurrence of severe infections, myocardial infarction, mesenteric infarction, or acute kidney injury between a liberal and restrictive strategy (33 vs. 35.1%; OR, 1.11; 95% CI, 0.91–1.34;  $p = 0.30$ ). However, the mortality rate was higher in the restrictive group compared with the liberal group (4.2% vs. 2.6%; HR, 1.64; 95% CI, 1–2.67;  $p = 0.045$ ). Also in cardiac

surgical patients, Carson et al<sup>31</sup> found that the development of myocardial infarction or unscheduled revascularization at 30 days was higher in the restrictive group compared with the liberal group (25.5 vs. 10.9% of patients;  $p = 0.054$ ), with higher mortality in the restrictive group (13%;  $p = 0.032$ ).

## Blood Conservation Strategies in Cardiac and Aortic Surgery

Given the deleterious effects of transfusion, there has been a drive toward reducing exposure to blood products in cardiac surgery. Although this is challenging in the surgical patient, techniques have emerged to reduce PRBC use while maintaining homeostasis. Various blood conservation strategies (BCS) have been developed to decrease perioperative complications, improve outcomes, and reduce health care costs.

Avgerinos et al<sup>34</sup> implemented a BCS comprising aggressive intraoperative autologous donation and utilization of shorter CPB circuits. In their study, they compared 1,126 patients with this strategy with a control group of 3,758 patients. Their protocol not only enabled use of a lower prime volume, but showed a significant reduction in the overall use of blood products (49–29%;  $p = 0.02$ ), postoperative respiratory failure (7–3%;  $p = 0.03$ ), pneumonia (3.1–1%;  $p = 0.01$ ), chest tube output (mean, 730–350 mL;  $p = 0.01$ ), reoperation for bleeding (2.5–1.2%;  $p = 0.04$ ), and length of stay (8.2–6.1 days;  $p = 0.05$ ).

Ad et al<sup>35</sup> used a BCS involving expanded use of cell salvage blood in place of cardiomy suction, acute normovolemic hemodilution, and retrograde autologous priming. Their protocol showed a reduction in the use of blood products from 54 to 25% ( $p = 0.001$ ), as well as a lower incidence of postoperative renal failure (4–2.6%;  $p = 0.04$ ), reoperation for bleeding (4–2%;  $p = 0.004$ ), and 30-day readmission (12–6%;  $p < 0.001$ ), with no difference in operative mortality.

Although scarce, the majority of transfusion research within aortic surgery is focused on BCS. Yaffee et al<sup>4</sup> studied the effects of BCS in high-risk aortic procedures. The minimization of intraoperative hemodilution, tolerance of perioperative anemia, and education of the multidisciplinary cardiac surgery team did not yield a difference in morbidity ( $p = 0.9$ ) or mortality ( $p = 0.4$ ). There was a 58% reduction in the number of PRBC units given in the blood conservation group. This resulted in a total cost saving of \$10,135.50 (\$349.50 per patient).

Smith et al,<sup>5</sup> using a similar strategy, showed that 74% of patients did not require intraoperative PRBC transfusion, with a 35% decrease in the rate of complications in the group exposed to up to one unit compared with those receiving greater than two units. There was a lower rate of major complications (respiratory/renal failure, sepsis, mortality) in patients receiving up to one unit of PRBC compared with those with more than two units (0 vs. 38%,  $p < 0.001$ ).

Parenthetically, implementation of electronic decision tools has provided insight into transfusion practices, showing that physician decisions sometimes do not comply with guidelines and clinical evidence. Razavi et al<sup>36</sup> used a clinical decision support tool within the electronic medical record that required a physician to give their rationale when ordering

cross-matched blood for cardiothoracic surgery patients. They showed an association with fewer transfusions (50.3–40.8%), lower infection rates (3.3–1.1%), and reduced health care costs after its implementation.

## Blood Transfusion in Other Specialties

The negative effects of liberal transfusion practices extend well beyond the field of cardiac surgery. However, the evidence in medical and noncardiac surgical areas is also controversial. Elmi et al<sup>37</sup> used the American College of Surgeon National Surgical Quality Improvement Program database to investigate the effect of blood transfusion on patients undergoing gastric resection. They found that PRBC use was independently associated with an increase in 30-day mortality (RR, 3.1; 95% CI, 1.9–5.0;  $p < 0.001$ ), significant morbidity (RR, 1.4; 95% CI, 1.1–1.6;  $p < 0.001$ ), respiratory failure (RR, 2.3; 95% CI, 1.6–3.3;  $p < 0.001$ ), infections (RR, 1.4; 95% CI, 1.1–1.6;  $p < 0.001$ ), and length of stay (RR, 1.2; 95% CI, 1.1–1.2;  $p < 0.001$ ). They advocate for the implementation of blood management strategies to reduce the use of blood products after gastrectomy for gastric cancer. Martin et al<sup>38</sup> found that perioperative blood transfusion in patients undergoing hepatectomy is independently associated with postoperative morbidity (OR, 4.18; 95% CI, 2.18–8.02;  $p = 0.0001$ ) and mortality (OR, 14.5; 95% CI, 3.08–67.8;  $p = 0.001$ ).

The effect of blood transfusion also impacts the pediatric population. Stone et al<sup>39</sup> found an association with increased mortality in pediatric trauma patients who received transfusion within 24 hours of admission. Demaret et al<sup>40</sup> studied the effect of blood transfusions in critically ill children. They showed an association between blood transfusion and the development of multiorgan dysfunction (OR, 3.85; 95% CI, 2.38–6.24;  $p < 0.001$ ), prolonged ventilation time ( $14.1 \pm 32.6$  vs.  $4.3 \pm 9.6$  days,  $p < 0.001$ ) and increased pediatric ICU stay ( $12.4 \pm 26.2$  vs.  $4.9 \pm 10.2$  days,  $p < 0.001$ ).

Conversely, Zheng et al<sup>41</sup> in a systematic review evaluating adult ICU patients concluded that there is a lack of strong evidence to support the negative effect of PRBC. After adjusting for confounders, they did not show a transfusion-related increase in in-hospital mortality.

## Possible Solutions

Overall, the evidence points preponderantly toward a more conservative transfusion policy in cardiac surgery. The complexity and bleeding potential of aortic surgery warrants a more individualized approach, incorporating an assessment of the potential for operative mortality, and bleeding. In those patients with a high bleeding risk, efforts can be made to permit yet minimize the amount of administered blood transfusion.

- Preoperatively: Investigate and treat anemia, for example, erythropoietin, iron
- Intraoperative factors: meticulous surgical hemostasis, shorter CPB circuits, point of care testing for coagulopathy; salvage procedures (e.g., autologous blood transfusion, cell

saver), correction of coagulopathy (antifibrinolytics, fresh frozen plasma, platelets, cryoprecipitate, factor VII)

- Availability of traditional and recombinant agents (aminocaproic acid, tranexamic acid, factor VII, and topical hemostatic agents) is laudable. Cardiac surgeons worldwide still bemoan the loss of aprotinin, which produced remarkably dry surgical fields<sup>42</sup>
- Postoperative: Careful surveillance for bleeding, regular Hg and hematocrit monitoring, treatment of sepsis (and other complications)

In cases where transfusion is required, it is important to consider the nature of blood being transfused. Specifically, leukoreduced blood and blood that has been stored for less than 14 days have a better safety profile with regards to immediate postoperative and long-term complications.<sup>10</sup>

Furthermore, the development of a multidisciplinary transfusion team (with surgeons, anesthesiologists, intensivists, perfusionists, nurses, and blood bankers) may help to ensure judicious use of blood products.<sup>2,13</sup>

Although each case should be considered on an individual basis, the current guidelines serve as an adjunct for decision-making. Medical and asymptomatic noncardiac surgical patients may benefit from a more restrictive approach, with an Hg threshold of less than 6 to 7 g/dL. For cardiac surgical patients and those with acute coronary syndromes, we must recognize that a more liberal approach (Hg threshold 9–10 g/dL) is beneficial to ensure sufficient oxygen delivery.<sup>2,13</sup>

## Conclusion

Blood transfusion is undoubtedly a lifesaving procedure if used appropriately. Nevertheless, it is not without harm, and there is much controversy surrounding the effects of transfusion on surgical outcomes. Despite the paucity of studies investigating this practice specifically in aortic surgery, there is some evidence showing an association between transfusion and adverse outcomes warranting greater vigilance regarding the use of blood products. Since aortic surgery is a particularly high risk, we advocate a thorough evaluation of the patient that balances the consequences of bleeding and anemia with the putative decreased survival associated with blood products. Further research is required to better define the effect of transfusion on short- and long-term outcomes in aortic surgery patients.

### Conflict of Interest

None.

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