Blood Transfusions in Cardiac Surgery: Indications, Risks, and Conservation Strategies

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Although red blood cell (RBC) transfusions are frequently used in cardiac operations, an increasing amount of data has demonstrated deleterious consequences. Consequently, the appropriate use of this limited resource is unclear. In this review, we discuss the relationship between anemia and the outcomes of cardiac surgical procedures, the risks associated with RBC transfusion, and the impact of blood transfusions on mortality and morbidity after cardiac operations.

The discovery of circulation and the first attempted blood transfusions performed in animals dates back to the 1600s, but not until the 1800s was the first successful human transfusion performed [1, 2]. In the early 1900s, preservation techniques for storing blood and blood banking matured, enabling the practice to become more widespread [3]. Red blood cell (RBC) transfusions were performed with limited understanding of their complications until the latter half of the 20th century. In the modern era, however, an increasing amount of data has demonstrated deleterious consequences of RBC transfusions. As a result of these recognized transfusion-related risks and the fact that blood is a limited resource, randomized trials have been conducted to better define transfusion strategies. Furthermore, to salvage as much of the patient’s own native RBCs and to focus attention on critical thinking regarding transfusion, blood conservation techniques and protocols have been developed.

Rationale for Review

Although cardiac surgical procedures represent a limited fraction of overall surgical procedures, they are responsible for approximately 2.5 million, or 20%, of the annual transfusions in the United States [4]. Although the figure is variable, approximately 60% of coronary bypass (CABG) patients receive transfusions [5–7].

Given the significant use of blood products in cardiac operations, and the wide disparity in transfusion rates among cardiac surgical centers, it is important to understand the growing evidence regarding the risks and benefits of transfusions in this specific cohort of patients. In this literature review, we summarize relevant data regarding RBC transfusions as they relate to the patient undergoing cardiac surgical procedures. Specifically, we discuss the relationship between preoperative, intraoperative, and postoperative anemia and the outcomes of cardiac surgical procedures; the risks associated with RBC transfusion; and the impact of blood transfusions on mortality and morbidity after cardiac operations. The review concludes with a discussion of randomized trials comparing restrictive versus liberal transfusion strategies and a consideration of blood conservation techniques.

Patients and Methods

A search was conducted on MEDLINE of studies published between January 1, 1980, and February 1, 2013. The search terms included “anemia,” “red blood cells,” “blood transfusion,” “blood utilization,” “cardiac surgery,” and “blood conservation” or any combination thereof. We excluded studies in languages other than English. Otherwise, there were no exclusion criteria, and we included all types of articles.

Results

Correlation Between Anemia and Outcomes of Cardiac Surgical Procedures

Preoperative or Intraoperative Anemia. Multiple studies have demonstrated a significant correlation between preoperative anemia and worse outcomes after cardiac operations (Table 1) [8–11]. Two large-cohort, risk-adjusted analyses demonstrated associations between preoperative anemia and postoperative mortality [8, 10]. One study of 3,500 patients found a risk-adjusted twofold increase in the composite outcome of inhospital mortality, stroke, or acute kidney injury in patients who were anemic preoperatively [9]. A worldwide study involving 70 institutions and 5,065 CABGs determined that preoperative anemia was a significant risk
factor for noncardiac complications, in particular renal dysfunction or failure [11].

With regard to intraoperative anemia, multiple large-cohort studies have demonstrated that nadir hematocrit during cardiopulmonary bypass has a significant impact on postoperative mortality (Table 1) [12–14]. An analysis of 7,957 patients demonstrated that lower nadir hematocrit during bypass was associated with worse renal function, more myocardial injury as measured by troponin levels, longer ventilator support, and longer hospital stays, in addition to increased mortality [14]. Another study of 10,949 patients found an association between lower nadir hematocrit during bypass and an increased risk of postoperative stroke [15].

**POSTOPERATIVE ANEMIA.** A study of patients undergoing cardiac surgical procedures who refused blood transfusions for religious reasons found a 0% mortality rate but a 9.4% morbidity rate in those with a postoperative hemoglobin of 7.1 to 8.0 g/dL (Table 2) [16]. Progressive decreases in hemoglobin levels were met with steep increases in mortality risk, with a 34% observed mortality rate for those with a hemoglobin of 4.1 to 5.0 g/dL. A retrospective analysis of data from 2,553 patients from the IMAGINE trial, a negative study designed to look at the benefit of early institution of angiotensin-converting enzyme inhibition in CABG, demonstrated that 44% of patients sustained postoperative anemia for more than 50 days after CABG [17]. Decreasing hemoglobin was associated with significant increases in adverse cardiovascular events and all-cause mortality. Another single-institution series of 617 patients found that lower hemoglobin levels after cardiopulmonary bypass were associated with higher odds of postoperative stroke.

### Table 1. Studies Evaluating Preoperative or Intraoperative Anemia and Outcomes in Cardiac Operations

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Outcomes</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Straten et al [8]</td>
<td>10,025</td>
<td>Mortality (early: within 30 days; late: after 30 days)</td>
<td>Preoperative anemia significant risk factor for early and late mortality</td>
</tr>
<tr>
<td>Karkouti et al [9]</td>
<td>3,500</td>
<td>Composite outcome of in-hospital mortality, stroke, or acute kidney injury</td>
<td>Preoperative anemia significant risk factor for composite outcome in multivariable logistic regression and propensity-matched analyses</td>
</tr>
<tr>
<td>Hung et al [10]</td>
<td>2,688</td>
<td>Primary: perioperative red blood cell transfusion</td>
<td>Preoperative anemia significant risk factor for transfusion, in-hospital mortality, and prolonged intensive care unit stay</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secondary: in-hospital mortality, length of intensive care unit stay, costs of transfusion</td>
<td></td>
</tr>
<tr>
<td>Kulier et al [11]</td>
<td>5,065</td>
<td>In-hospital cardiac and noncardiac morbidity and mortality</td>
<td>Low preoperative hemoglobin significant independent predictor of noncardiac adverse events</td>
</tr>
<tr>
<td>Fang et al [12]</td>
<td>2,738</td>
<td>Postoperative mortality</td>
<td>Minimum hematocrit significant risk factor for postoperative mortality</td>
</tr>
<tr>
<td>DeFoe et al [13]</td>
<td>6,980</td>
<td>In-hospital mortality, need for intraaortic balloon pump, stroke, return to bypass, reoperation for bleeding</td>
<td>Lowest hematocrit significantly associated with increased risk of in-hospital mortality, need for intraaortic balloon pump, and return to cardiopulmonary bypass</td>
</tr>
<tr>
<td>Loor et al [14]</td>
<td>7,957</td>
<td>In-hospital mortality and morbidity, markers of end-organ dysfunction, use of resources, long-term survival</td>
<td>Lowest hematocrit significantly associated with worse renal function, more myocardial injury, longer ventilator support, longer hospital stay, and increased mortality</td>
</tr>
<tr>
<td>Karkouti et al [15]</td>
<td>10,949</td>
<td>Postoperative stroke</td>
<td>Lowest hematocrit associated with increased risk of postoperative stroke</td>
</tr>
</tbody>
</table>

### Table 2. Studies Evaluating Postoperative Anemia and Outcomes in Cardiac Operations

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Outcomes</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carson et al [16]</td>
<td>300</td>
<td>Primary: in-hospital mortality within 30 days</td>
<td>0% mortality and 9.4% morbidity if hemoglobin 7.1–8.0 g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secondary: 30-day mortality or in-hospital 30-day morbidity</td>
<td>34% mortality if hemoglobin 4.1–5.0 g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mortality odds increased 2.5 times for each gram decrease in hemoglobin level below 8 g/dL.</td>
</tr>
<tr>
<td>Westenbrink et al [17]</td>
<td>2,553</td>
<td>Adverse cardiovascular events and all-cause mortality</td>
<td>Decreasing hemoglobin significantly associated with increased risk of adverse cardiovascular events and all-cause mortality</td>
</tr>
<tr>
<td>Bahrainwala et al [18]</td>
<td>617</td>
<td>Postoperative stroke</td>
<td>Lower hemoglobin levels significantly associated with increased risk of postoperative stroke</td>
</tr>
</tbody>
</table>
Although these studies demonstrated significant associations between postoperative anemia and worse outcomes, specific hematocrit thresholds below which risk increased were not collectively well defined.

Risks Associated With RBC Transfusions

Although these studies demonstrate that perioperative anemia is associated with adverse outcomes, the decision to transfuse might be more straightforward if not for its associated risks and for the data demonstrating that transfusions in and of themselves can be associated with deleterious consequences. The risks of transfusion range from the remote but lethal risk of transmitting a bacterial infection, to transfusion-related acute lung injury (TRALI), to the more common febrile transfusion reactions.

TRALI. Acute lung injury is defined by acute onset, lack of left atrial hypertension, bilateral infiltrates on chest roentgenogram, and hypoxemia with a PaO₂/FiO₂ ratio of ≤ 300 [19]. TRALI is defined as an acute lung injury that occurs within 6 hours of transfusion. Although there are approximately 150,000 cases of acute lung injury in the United States each year, the estimated incidence of TRALI is roughly 1 per 1,000 transfusions [20]. Importantly, this incidence is not well established, with a recent study demonstrating a TRALI rate of 2.4% specifically in patients undergoing cardiac surgical procedures [21]. This may in part be due to an incomplete understanding of this complication by providers and therefore a resultant underreporting of its occurrence.

The central feature of acute lung injury is increased permeability in the pulmonary microvasculature with protein-rich edema fluid. In TRALI, the presence of donor antibodies to recipient leukocytes is thought to be responsible for the ensuing lung damage and capillary leak [20]. Another proposed mechanism of TRALI involves a predisposing patient condition, such as sepsis or a surgical procedure, that causes neutrophil sequestration in the lungs. Exposure to biologically active substances, which occurs with blood transfusions, activates these neutrophils, again leading to lung injury [22]. Patients with TRALI typically improve clinically within 48 to 96 hours after onset, with resolution of pulmonary infiltrates within days, and no long-term adverse effects [23]. Nevertheless, almost certainly because of associated underlying conditions, the mortality rate associated with TRALI is 5% to 15% [21, 23].

IMMUNOMODULATION. The concept of immunomodulation related to transfusions was sparked by the observation that renal transplant patients had improved graft survival if they underwent transfusion before transplantation [24]. Despite this beneficial effect, additional observational studies demonstrated an increased risk of postoperative bacterial infections and higher rates of cancer recurrence in patients receiving blood transfusions, all of which supported the notion that transfusions induce immunosuppression [25]. Although the mechanisms remain incompletely understood, proposed causes of transfusion-related immunomodulation involve immunologically active donor white blood cells, soluble white blood cell—derived immune mediators in stored blood, and soluble human leukocyte antigen peptides circulating in allogeneic plasma [26]. Perhaps most convincing of this complication was a randomized trial demonstrating that patients undergoing cardiac surgical procedures had reduced multiorgan failure and mortality when receiving only leukoreduced transfusions, compared with nonreduced transfusions—a finding that was not entirely explained by lower infection rates in the cohort receiving leukoreduced transfusions [27].

TRANSFUSION REACTIONS. Simple allergic reactions occur in approximately 1 of 100 transfusions, typically manifest immediately after transfusion, and are the result of a type I hypersensitivity reaction [28]. Antihistamines are the treatment of choice. Anaphylactic transfusion reactions usually occur as a result of anti-immunoglobulin A antibodies in the recipient [28]. Patients with a history of anaphylactic reactions to RBC transfusions should therefore be screened for the presence of these antibodies in their own blood before undergoing transfusion, and they should receive saline-washed RBCs or immunoglobulin A–deficient products.

Febrile nonhemolytic transfusion reactions are thought to be due to transfusion of leukocyte antigens or pyrogenic cytokines that accumulate in stored blood [29]. In one study, leukoreduction decreased the incidence of febrile nonhemolytic reactions from 0.33% to 0.19% [30]. Acute hemolytic transfusion reactions are most commonly the result of inadvertent transfusing RBCs that are incompatible with antibodies present in the recipient. This reaction occurs in approximately 1 in 6,000 to 20,000 transfusions, with hallmark symptoms including fevers, chills, rigors, hypotension, hemoglobinuria, renal failure, back or flank pain, and disseminated intravascular coagulation [31, 32]. Delayed transfusion reactions can also occur, generally 1 to 3 weeks after transfusion. Most commonly, delayed transfusion reactions are due to antibodies to minor blood group antigens, such as anti-Duffy or anti-Kidd antibodies, which are frequently stimulated by previous transfusion or pregnancy [33, 34]. Very rarely, transfusion-associated graft-versus-host-disease can occur, usually a week after transfusion. Generally, it is characterized by a rapid downward course that can lead to death within 1 to 3 weeks after the initial presence of symptoms [32]. This complication develops after the transfusion of immunocompetent T-lymphocytes into an immunocompromised host. The transfused lymphocytes can proliferate, activate, and reject host tissue. Gamma irradiation of transfused blood products is essential to preventing the occurrence of this serious complication [35].

INFECTIOUS COMPLICATIONS OF TRANSFUSIONS. The estimated transmission risks of human immunodeficiency virus (1 in 2.3 million), hepatitis B (1 in 300,000), hepatitis C (1 in 1.8 million), and human T-lymphotrophic virus (1 in 2.9 million) are extremely low with transfusions [36]. Human herpesvirus-8, Epstein-Barr virus, West Nile virus, and the other hepatitides are also rarely transmitted. On the
other hand, more than 50% of blood donors are thought to be cytomegalovirus positive, and the transmission of cytomegalovirus can cause significant morbidity in immunocompromised recipients [36].

Bacterial contamination of RBCs occurs in approximately 1 in 38,000 units, with septic reactions occurring in 1 in 250,000 units transfused—rates that are, interestingly, much lower than those reported with platelet transfusions [32]. The clinical presentation of high fever, rigors, and hypotension shortly after transfusion raises clinical suspicion for bacterial contamination. The mortality associated with transfusion of RBCs contaminated with bacteria is over 60%, even higher if it is due to gram-negative organisms [36, 37].

Correlation Between RBC Transfusions and Outcomes of Cardiac Surgical Procedures

IMPACT OF BLOOD TRANSFUSIONS ON MORTALITY AFTER CARDIAC OPERATIONS. All studies examining the effect of transfusions on mortality after cardiac operations suffer from the criticism that someone who needs blood postoperatively is quite likely not to be doing as well as someone who does not need blood. Multivariate risk analyses and propensity analyses have attempted to address that study limitation, and all have found that transfusion is an independent risk factor for morbidity and mortality (Table 3). A study of 10,425 patients [38] found that RBC transfusion was an independent and dose-dependent risk factor for early mortality after CABG. Another study of 3,024 CABG patients similarly found that blood transfusions were associated with significantly increased 30-day and 1-year mortality, even after baseline risk, reoperations for bleeding, perioperative blood loss, and postoperative complications were accounted for [39].

Of importance is that even if short-term survival is disregarded, long-term survival after cardiac operations is negatively affected by perioperative RBC transfusions [40–43]. A study of 8,598 patients [39] found that even after the exclusion of deaths within 1 year of operation, there remained a significant impact of perioperative transfusions on increased subsequent mortality [40]. Similarly, a single-institution series involving 1,915 CABG patients [40] demonstrated that the negative effect of transfusions on survival persisted when 1-year to 5-year mortality was specifically examined [41]. Another analysis of 10,289 patients [40] found an increased risk-adjusted odds of mortality occurring at least 6 months from CABG in patients undergoing transfusion [42]. As a follow-up to a prior study that demonstrated worse outcomes in anemic patients [13], a study of over 9,000 patients demonstrated a 16% increased risk of long-term mortality in patients undergoing transfusion [43].

The age of RBCs is another important concept. A propensity-matched analysis demonstrated that transfusion of RBCs that had been stored for more than 2 weeks was associated with an increased risk of postoperative complications and with short-term and long-term mortality [44]. An ongoing trial, the Red Cell Storage Duration Study (RECESS) randomizes patients to receive RBCs stored less than 10 days versus 21 or more days, with the primary outcome being change in the Multiple Organ Dysfunction Score by day 7 [45].

IMPACT OF BLOOD TRANSFUSIONS ON MORBIDITY AFTER CARDIAC OPERATIONS. Along with increased mortality, perioperative blood transfusions have been associated with increased morbidity. Perioperative RBC transfusions have been identified as an independent risk factor for postoperative atrial fibrillation after cardiac operations [46–48]. The rate of infectious complications after cardiac operations, including bacteremia, sternal wound infections, and *Clostridium difficile*-associated diarrhea, has also been shown to be increased in those receiving blood transfusions [7, 49–53] With regard to pulmonary morbidity, higher risk-adjusted rates of postoperative respiratory distress, respiratory failure, acute respiratory distress syndrome, and reintubation, and longer times on the ventilator, have been demonstrated in patients undergoing transfusion [54, 55].

In an analysis of 11,963 CABG patients, the risk-adjusted rates of postoperative renal failure and

Table 3. Studies Evaluating the Impact of Blood Transfusions on Mortality After Cardiac Operations

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Outcomes</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Straten et al [38]</td>
<td>10,425</td>
<td>Mortality (early: within 30 days; late: after 30 days)</td>
<td>Number of transfused RBCs predictor of early mortality compared to expected survival, receiving no RBC improved long-term survival whereas receiving ≥3 RBC decreased survival</td>
</tr>
<tr>
<td>Kuduvalli et al [39]</td>
<td>3,024</td>
<td>30-day and 1-year mortality</td>
<td>Transfusion significantly associated with 30-day and 1-year mortality</td>
</tr>
<tr>
<td>Engoren et al [41]</td>
<td>1,915</td>
<td>Long-term mortality</td>
<td>Patients undergoing transfusion had a 70% increased risk of long-term mortality</td>
</tr>
<tr>
<td>Koch et al [42]</td>
<td>10,289</td>
<td>All-cause mortality</td>
<td>Patients undergoing transfusion had higher risk-adjusted odds of early and late mortality</td>
</tr>
<tr>
<td>Surgenor et al [43]</td>
<td>9,079</td>
<td>Long-term mortality</td>
<td>Patients receiving transfusions of 1 or 2 RBC units had 16% higher odds of long-term mortality compared with patients not receiving transfusions</td>
</tr>
</tbody>
</table>

RBC = red blood cell(s).
neurologic events were higher in patients undergoing transfusion [56]. An analysis of 12,388 patients undergoing cardiac surgical procedures found that the risk of acute kidney injury increased proportionally with the number of RBCs transfused [57]. A study of gastrointestinal complications in patients undergoing cardiac surgical procedures found a low rate of such complications (0.5%), but nonetheless blood transfusions were found to be an independent risk factor for their occurrence [58]. An important study that used propensity matching found that Jehovah’s witnesses undergoing cardiac surgical procedures had fewer acute complications, including myocardial infarctions, reoperations for bleeding, prolonged ventilation, and shorter length of hospitalization, in addition to improved 1-year survival, than did well-matched patients receiving transfusions [59].

**Randomized Trials of Restrictive Versus Liberal Transfusion Strategies**

These published studies have increased our awareness that blood transfusions are not benign but rather are associated with increased morbidity, mortality, and cost and, in fact, may be causative. Specifically addressing the issue of an appropriate transfusion strategy, four randomized trials have been conducted to better define the risks and benefits of a restrictive transfusion trigger, although only one has addressed the postoperative cardiac operation population specifically (Table 4). In 1999, a multicenter randomized trial of Transfusion Requirements in Critical Care (TRICC) enrolled 838 critically ill patients and randomized them to a restrictive (transfuse if hemoglobin <7 g/dL) versus a liberal (transfuse if hemoglobin <10 g/dL) strategy [60]. The 30-day mortality rates, though better in the restrictive strategy group, did not reach statistical significance (p = 0.11). However, myocardial infarction and pulmonary edema occurred less frequently with the restrictive strategy. A subgroup analysis, which looked at younger patients (age <55) and patients who were less acutely ill (APACHE <20) showed significantly lower mortality rates with the restrictive strategy. Patients with known, significant cardiac disease had comparable mortality rates regardless of the transfusion strategy.

A more recent randomized trial, Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS), randomizing 2,016 patients with a history of, or with, risk factors for cardiovascular disease to a restrictive (transfuse with symptoms of anemia, or hemoglobin <8.0 g/dL) versus a liberal (transfuse if hemoglobin <10.0 g/dL) strategy [61]. The average age of the study population was 81.6 years. Both strategies were found to have comparable morbidity, mortality, and ability to walk independently at 30-day and 60-day follow-up.

Another recent randomized trial compared a restrictive (transfuse when hemoglobin <7 g/dL) with a liberal (transfuse when hemoglobin <9 g/dL) strategy in 921 patients with acute upper gastrointestinal bleeding [62]. The principal finding was that 6-week survival was significantly better in the restrictive cohort. The rates of adverse events and further bleeding were also significantly lower with the restrictive strategy.

Finally, only one randomized trial in cardiac surgical procedures has looked at appropriate hemoglobin triggers for transfusions. The Transfusion Requirements After Cardiac Surgery (TRACS) trial randomized 502 patients who had undergone cardiac surgical procedures with the use of cardiopulmonary bypass to a restrictive (maintain hematocrit ≥24%) versus a liberal (maintain hematocrit ≥30%) strategy [63]. The primary outcome of 30-day mortality and in-hospital major morbidity was comparable between transfusion strategies. In the restrictive strategy group, there was a 60% diminution in the number of transfused units. Furthermore, RBC transfusions were again found to be an independent risk factor for mortality.

**HEMOGLOBIN DRIFT.** A single-institution study of 199 cardiac surgical patients not receiving postoperative transfusions demonstrated that all patients’ hemoglobin levels initially dropped, with the average difference between minimum and maximum hemoglobin level being 1.8 g/dL, occurring on postoperative day 3 to day 4 [64]. The majority of patients (79%) recovered close to 40% of the initial drop, or an average of 0.7 g/dL, by discharge on postoperative day 7 through day 10. The almost universal upward hemoglobin trend before discharge is an important finding for those attempting to implement a restrictive transfusion strategy.

**BLOOD CONSERVATION.** In 2007, the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists released a clinical practice guideline that highlighted five techniques for blood conservation [65]. These included (1) drugs that increase preoperative blood volume or decrease postoperative bleeding, including erythropoietin or preoperative autologous donation, (2) devices that conserve blood such as the cell-saving device, (3) interventions that protect patients’ blood from operative stress, (4) the use of institution-specific transfusion algorithms, and (5) a multimodality approach to blood conservation. The utility of these conservation techniques was postulated to be most productive in high-risk patients, with high-risk criteria including older age, preoperative anemia, and redo or emergency procedures [65].

An update in 2011 added even more specific recommendations for blood conservation, including the use of minicircuits or modified ultrafiltration [66]. Minicircuits can reduce by 70% the priming volume needed; thus, they markedly decrease the amount of hemodilution that occurs on institution of cardiopulmonary bypass. A randomized study of 60 CABG patients found that minicircuits were associated with a 38% reduction in blood product use, reducing not only transfused volume but postoperative bleeding as well [67]. Minicircuits may also offer logistic advantages with reduced tubing length and fewer components compared with conventional circuits.

Despite these national guidelines, institutions continue to vary significantly in their blood use during cardiac surgical procedures. A multicenter study involving 17,252
Table 4. Randomized Controlled Trials Comparing Restrictive Versus Liberal Transfusion Strategies

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of Patients Enrolled</th>
<th>Cohorts (Transfusion Triggers)</th>
<th>Outcomes</th>
<th>Major Findings</th>
</tr>
</thead>
</table>
| TRICC [60]                    | 838                      | Restrictive: hemoglobin <7.0 g/dL  
Liberal: hemoglobin <10.0 g/dL | Primary: 30-day mortality  
Secondary: 60-day mortality, intensive care unit mortality, in-hospital mortality | Restrictive and liberal 30-day mortality comparable (18.7% vs 23.3%; $p = 0.11$)  
30-day mortality lower with restrictive strategy in less acutely ill and patients younger than 55 years  
In-hospital mortality rate lower in restrictive group (22.2% vs 28.1%; $p = 0.05$) |
| FOCUS [61]                    | 2,016                    | Restrictive: symptoms of anemia, or physician discretion if hemoglobin <8.0 g/dL  
Liberal: hemoglobin <10.0 g/dL | Primary: mortality or inability to walk 10 feet independently at 60-day follow-up  
Secondary: in-hospital myocardial infarction, unstable angina, or mortality  
Tertiary: in-hospital morbidity at 30 days | Primary outcome (34.7% vs 35.2%), in-hospital acute coronary syndrome and mortality, and 60-day mortality and morbidity each comparable between restrictive and liberal cohorts, respectively |
| Acute gastrointestinal bleeding [62] | 921                      | Restrictive: hemoglobin <7.0 g/dL  
Liberal: hemoglobin <9.0 g/dL | Primary: mortality within 45 days  
Secondary: in-hospital complications and further bleeding | Improved 45-day survival, lower complication and further bleeding rates with restrictive strategy |
| TRACS [63]                    | 502                      | Restrictive: hematocrit <24%  
Liberal: hematocrit <30% | Primary: composite of 30-day mortality and in-hospital severe morbidity  
Secondary: complications, intensive care unit and hospital lengths of stay | Primary outcome met in 11% and 10% of restrictive and liberal cohorts, respectively ($p = 0.85$)  
Number of transfused units independent risk factor for complications or death at 30 days |

FOCUS = Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair;  
TRACS = Transfusion Requirements After Cardiac Surgery;  
TRICC = Transfusion Requirements in Critical Care.
CABGs noted significant variability in institutional RBC transfusion rates (0% to 85.7%) [68]. Similarly, an analysis of 102,470 CABGs performed at 798 centers revealed an unexplained variability between hospitals in blood transfusion rates (8% to 93%), with hospital characteristics and case mix accounting for only 11% and 20% of the variation, respectively [69].

These data point out a lack of standardization and a need for the use of evidence-driven algorithms guiding blood transfusions in each cardiac surgery program. Attempting to systemize the approach to transfusions in CABG, 23 Ontario hospitals emphasized conservation education, preoperative autologous donation, erythropoietin use, and cell salvage, experiencing a significant 23% reduction in transfusion rates [70]. At a single institution, a multifaceted blood conservation strategy in cardiac surgical procedures involving restrictive transfusion triggers, algorithm-driven decisions, point-of-care testing, and use of low prime perfusion circuits reduced blood component use by 40%, with no detrimental effect on outcomes [71]. Yet another study compared transfusion rates and outcomes after CABG at an institution with a well-established blood conservation program compared with a propensity-matched cohort at other hospitals in which there were no identifiable, systematic approaches to blood conservation [72]. A significant absolute reduction in transfusion rates of 32% was observed at the institution with the conservation program, with transfusion again being identified as a risk factor for adverse outcomes in both cohorts. A recent analysis of 14,000 CAGB patients from a statewide dataset demonstrated that the implementation of transfusion guidelines was associated with significant reductions in morbidity, mortality, and use of resources [73].

Part of the issue may relate to effective delivery of evidence-based guidelines to providers and programs. One survey-based study found that only 20% of respondents reported having an institutional discussion after publication of the aforementioned 2007 guidelines [74]. These guidelines and the updates can be found online on the Society of Thoracic Surgeons website (http://www.sts.org/resources-publications/clinical-practice-credentialing-guidelines/blood-conservation-guidelines). A blood conservation webinar was also presented (http://www.sts.org/webinars/blood_conservation_webinar).

Summary

Over the past decade, an increasing amount of evidence points to the significant disadvantages associated with blood transfusions in all patients. In cardiac surgical procedures, the data are convincing that there are immediate and long-term negative consequences of transfusion. The randomized trials demonstrating the lack of benefit to a liberal transfusion strategy are very persuasive, but they have not yet appeared to have significantly changed the transfusion behavior within our specialty.

As our review highlights, both anemia and transfusion are each independently associated with adverse outcomes; yet, at a critical level of anemia, transfusion is lifesaving. Our deficit in identifying this critical level has undoubtedly contributed to the wide variability in transfusion practices. Although hemoglobin levels have been used as triggers in prior trials, oxygen extraction, oxygen content, and oxygen delivery are important measurements that may reflect the need for increased hemoglobin content. Citing lack of evidence, our preference is to transfuse at a hemoglobin of 8 g/dL, with exceptions including (1) a mixed venous saturation that cannot be made to go over 50% by increasing cardiac output safely, inasmuch as below 50% the PO2 is less than 27, and the driving force for oxygen and its availability and the capillary level may be too low to support aerobic energy production, (2) end-organ ischemia, (3) ongoing bleeding, and (4) hypotension recalcitrant to low-dose pressors after adrenal insufficiency has been ruled out.

Recent developments have significantly improved our techniques of blood conservation in cardiac operations and could help us substantially decrease the number of transfusions our patients receive. As the major user of blood in most hospitals, cardiac surgeons should lead the way implementing protocol-driven blood transfusion algorithms within their institutions in an effort to standardize transfusion behavior. In the near future, it is very likely that transfusions will be regarded as a quality measure in cardiac surgical procedures [69]. Improving the evidence associated with the indications for blood transfusions, and addressing the barriers within our specialty to widespread adoption of evidence-based guidelines, should be recognized as crucial elements in providing high-quality care to our patients. It is our hope that this review article will provide a knowledge base that lays the groundwork for improved transfusion practices that would benefit all of our patients.

References

BLOOD TRANSFUSIONS IN CARDIAC SURGERY

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KILIC AND WHITMAN

REVIEW


