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Blood Transfusion and Infection After Cardiac Surgery

Keith A. Horvath, MD[1], **Michael A. Acker, MD**[2], **Helena Chang, MS**[3], **Emilia Bagiella, PhD**[3], **Peter K. Smith, MD**[4], **Alexander Iribarne, MD, MS**[3], **Irving L. Kron, MD**[5], **Pamela Lackner, BA**[6], **Michael Argenziano, MD**[7], **Deborah D. Ascheim, MD**[3], **Annetine C. Gelijns, PhD**[3], **Robert E. Michler, MD**[8], **Danielle Van Patten, BA**[7], **John D. Puskas, MD**[9], **Karen O'Sullivan, MPH**[3], **Dorothy Kliniewski, RN, BSN**[2], **Neal O. Jeffries, PhD**[10], **Patrick T. O'Gara, MD**[11], **Alan J. Moskowitz, MD**[3], and **Eugene Blackstone, MD**[6]

[1]Cardiothoracic Surgery Research Program, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland [2]Department of Surgery, Division of Cardiovascular Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania [3]International Center for Health Outcomes and Innovation Research (InCHOIR) in the Department of Health Evidence and Policy, Mount Sinai School of Medicine, New York, NY [4]Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University, Medical Center, Durham, North Carolina [5]Division of Thoracic and Cardiovascular Surgery, University of Virginia School of Medicine, Charlottesville, VA [6]Department of Cardiothoracic Surgery, Heart and Vascular Institute, The Cleveland Clinic, Cleveland, Ohio [7]Division of Cardiothoracic Surgery, Department of Surgery, College of Physicians and Surgeons, Columbia University, New York, New York [8]Department of Cardiothoracic Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, New York City, New York [9]Clinical Research Unit, Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, Georgia [10]Office of Biostatistics Research, National Heart, Lung, and Blood Institute, Bethesda, Maryland [11]Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts

Abstract

Cardiac surgery is the largest consumer of blood products in medicine; although believed life saving, transfusion carries substantial adverse risks. This study characterizes the relationship between transfusion and risk of major infection after cardiac surgery.

5,158 adults were prospectively enrolled to assess infections after cardiac surgery. The most common procedures were isolated coronary artery bypass grafting (31%) and isolated valve surgery (30%); 19% were reoperations. Infections were adjudicated by independent infectious

Corresponding author: Alan J. Moskowitz, MD, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1077, New York, NY 10029, Phone: 212-659-9567, Fax: 212-423-2998, alan.moskowitz@mountsinai.org.

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disease experts. Multivariable Cox modeling was used to assess the independent effect of blood and platelet transfusions on major infections within 60±5 days of surgery.

Red blood cells (RBCs) and platelets were transfused in 48% and 31% of patients, respectively. Each RBC unit transfused was associated with a 29% increase in crude risk of major infection ($P<0.001$). Among RBC recipients, the most common infections were pneumonia (3.6%) and bloodstream infections (2%). Risk factors for infection included postoperative RBC units transfused, longer duration of surgery, and transplant or ventricular assist device implantation, in addition to chronic obstructive pulmonary disease, heart failure, and elevated preoperative creatinine. Platelet transfusion decreased the risk of infection ($P=.02$).

Greater attention to management practices that limit RBC use, including cell salvage, small priming volumes, vacuum-assisted venous return with rapid autologous priming, and ultrafiltration, and pre- and intraoperative measures to elevate hematocrit could potentially reduce occurrence of major postoperative infections.

Keywords

Bleeding; reoperation; surgery; complications; cardiopulmonary bypass; CPB; CPB; cell saver; wound infection

Introduction

Cardiac surgery has the largest consumption of blood products of any field in medicine (10% to 15% of the US blood supply), with half of patients undergoing cardiac surgery receiving blood products (1). Although prescribed for many reasons based on the belief that transfusion improves oxygen transport, they carry substantial adverse risks (2). Blood conservation practices in cardiac surgery were introduced in the 1970s because of the scarcity and cost of this limited resource, awareness of transfusion-borne infections such as Hepatitis B and C and human immunodeficiency virus (HIV), and increasing awareness of immunologic implications of this allogeneic exposure (3). Starting in the mid-1980s, a dose-response relationship was demonstrated between the quantity of packed red blood cells (RBCs) transfused and infections in various settings including cardiac surgery (4, 5). Yet the net effect of this information, neutral results of studies of liberal versus restrictive blood usage (6), and transfusion guidelines (7), coupled with an increasing number of patients coming to operation on anti-platelet medication or anticoagulants (8) is negligible reduction of blood usage in cardiac surgery. Moreover, substantial variation in transfusion practices among centers remains (9). Only recently has investigation begun regarding the optimal balance between the risks of anemia – an independent risk factor for morbidity and mortality after cardiac surgery – and those associated with RBC transfusion (10, 11).

The Cardiothoracic Surgical Trials Network (CTSN) has conducted a unique prospective multi-institutional observational study, with an overall aim to identify modifiable management practices, such as transfusion, associated with infections occurring up to 65 days following cardiac surgery. The primary objectives of the present study were to 1) investigate the association of RBC transfusion and postoperative infection, including type

and microbiology, and 2) identify patient and operative risk factors for infection, including use of RBCs and platelets, cell salvage, and timing of transfusion (intraoperative vs. postoperative).

Patients and Methods

Study design and patients

This observational study of postoperative infections among adults undergoing cardiac surgery at 10 centers in the United States and Canada was funded by the National Institutes of Health and Canadian Institutes of Health Research. Its overall objective was to identify management practices associated with risk for infections. *Inclusion criteria* were a clinical indication for a cardiac surgical intervention and age ≥ 18 years. Patients with active systemic infection at enrollment (most commonly hospital transfer patients and those with long preoperative length of stay) were excluded.

The study sample size was not predetermined; rather, enrollment continued until a pre-specified minimum of 200 patients with a major infection were identified. This is the number needed to make valid inferences about 20 risk factors for infection based on reliable multivariable models. Data were transmitted from sites using a web-based electronic data capture system to a secure server administered by the Data Coordinating Center (DCC). Each study site and the DCC received Institutional Review Board approval for the registry. All patients provided written informed consent to participate in the study and to release their medical information during this time frame.

From February 2010 through September 2010, 5,158 consecutive adult cardiac surgery patients were prospectively enrolled in the study. Patients were followed for 65 days after surgery with 2 planned post-discharge assessments at 30 and 60 days after surgery. The last date of follow-up was November 29, 2010.

Patients had a mean age of 64±13 years and preoperative hemoglobin of 13±1.8 g/dL; 33% were women and 19% had undergone prior cardiac surgery (Table 1). The most common procedures were isolated coronary artery bypass grafting (CABG) (31%) and isolated valve surgery (30%) (Table 2).

Endpoints

All infections were reviewed by an independent event adjudication committee consisting of 3 infectious disease experts. The final date of event adjudication for this manuscript was April 28, 2011. Infections were classified according to definitions from the Centers for Disease Control and the National Healthcare Safety Network (CDC/NHSN) surveillance (12). These definitions were slightly revised to accommodate the clinical characteristics of cardiac surgery patients (Appendix 1).

This study focused on *major infections*, which included 1) deep incisional surgical site infection occurring at the primary chest incision site, 2) deep incisional surgical site infection occurring at a secondary incision site (e.g. saphenous harvest site, groin cannulation site), 3) mediastinitis, 4) infectious myocarditis or pericarditis, 5) endocarditis,

6) cardiac device infection, 7) pneumonia, 8) empyema, 9) *Clostridium difficile* colitis, and 10) bloodstream infection.

Data analysis

Categorical variables were summarized by frequencies and percentages, and continuous variables by means and standard deviations, or medians and interquartile ranges if their distributions were skewed. Because infection occurred in a time-related fashion, time from surgery to infection was described using Kaplan-Meier curves. We recognized there would be a strong association between type of procedure, risk of infection, and risk of transfusion. Consequently, the case mix of our institutions affects distribution of infection among sites. Therefore, our strategy was to adjust for patient-level characteristics in the multivariable analysis, but not site. Adjusting for site runs the risk of obscuring variation in transfusion practices that is central to the question addressed in the current study.

We used Cox proportional hazard regression to identify the association of blood product utilization with risk of infection after adjusting for patient-level risk factors for major infection and those that would affect clinical decision making about transfusion. Variables tested included demographics, baseline laboratory values, comorbidities, surgical procedure, and surgery time. After performing the analysis using this strategy, we performed a secondary analysis that took into account patient clustering within sites using a marginal Cox proportional hazards model. Results were consistent with the primary analysis reported. All tests were conducted at the 2-sided .05 significance level. All analyses utilized SAS statistical software (SAS® v9.2; Cary, NC).

Results

Infections after cardiac surgery

Overall, 5,158 patients experienced 298 major infections (5.8%). The most commonly occurring major infections were pneumonia, *C. difficile* colitis, and bloodstream infections. Surgical site infections were uncommon (Table 3). Over 40% of major infections occurred after hospital discharge.

Prevalence of transfusion

Overall, 2,481 (48%) patients received at least 1 unit of RBCs, with close to half of transfused patients receiving 1 or 2 units (48%). Although percentage of patients transfused ranged from 33% to 74%, practice was relatively homogeneous across sites. Median number of units transfused was 2 at 8 sites and 3 at 2. Of patients transfused RBCs, 27% (n=1385) received them only in the operating room, 38% (n=1941) only postoperatively, and 35% (n=1805) both intra- and postoperatively (Figure 1). In those transfused, median number of RBC units transfused was 3 (interquartile range [IQ] 2-5). The highest volume of RBCs was given during transplant, left ventricular assist device (LVAD) implantation, and thoracic aorta procedures (see Table 2). Timing of transfusion (see Figure 1) was strongly related to volume of units given, with the majority of patients receiving intraoperative RBCs receiving only 1 to 2 units. Platelets were administered to 31% of patients and 85% received cell salvage blood. In this latter group, 38% received cell salvage blood only.

Transfusion and infection

There was a dose-related association between quantity of RBCs transfused and risk of infection, with crude risk increasing by an average of 29% with each RBC unit ($P<0.001$, Figure 2). Although in univariate analysis, platelet transfusion was associated with a greater risk of infection, once adjusted for quantity of transfused RBC units, platelet transfusion was protective (Figure 3). Specifically, lower risk of infection was observed when platelets were transfused with more than 4 units of RBCs.

In addition to patient characteristics such as chronic obstructive pulmonary disease, heart failure, and elevated preoperative serum creatinine, other relevant risk factors for major infection included longer duration of surgery and whether patients received a transplant or LVAD (Table 4). However, risk did not appear to be increased after reoperations nor after postoperative reoperations for bleeding. Use of cell salvage was not associated with increased risk of infection. Interestingly, diabetes (even when restricting patients to those receiving insulin or oral medications) and body mass index were among the baseline characteristics that were not predictive of infection.

The association of RBC transfusion with infection differed depending on type of infection observed. Thus, although transfused patients had a higher risk of any type of infection, the relationship was particularly strong for pneumonia and bacteremia (see Table 3).

Comment

Principal findings

This unique contemporary multi-institutional study of infections occurring up to 65 days after a variety of cardiac surgical operations, with well adjudicated events, revealed that RBC transfusion, particularly postoperative transfusion, was strongly associated with major postoperative infections in a dose-related fashion. Use of platelets appeared to have a mitigating effect, especially for those receiving higher numbers of RBC units. The association between RBC transfusion and infection was particularly strong for pneumonia and bacteremia.

Transfusion and infection

There is a more than 20-year history and over 200 reports of mostly observational studies demonstrating a relationship between transfusion and postoperative infection (13-20). This finding is not unique to cardiac surgery, as demonstrated by the meta-analysis of Hill and colleagues in trauma and elective general surgery patients (21). However, there have been some notable exceptions. Ali and colleagues, for example, did not find such a relation and suggested that “Clinicians should reconsider withholding blood transfusion in patients solely owing to concerns of predisposition to infection” (22). Vamvakas and Moore reviewed the evidence reported up to 1994 and concluded that a causal pathway was not established and that there were multiple confounders that could render transfusion merely a surrogate marker for infection and other adverse outcomes (5). These include extent of surgical trauma, which itself is an immune modulator, surgical bleeding and factors leading to coagulopathy, reoperation for bleeding, and unanalyzed patient and operative factors. In

studies before 2004, the effect of transfusions may have been in part related to low-dose bacterial contamination from the phlebotomy site and methods of blood handling and storage (23). Yet studies since then continue to demonstrate this association, including our contemporary multi-institutional study.

Several mechanisms have been proposed to explain this association. The most frequently cited is immune modulation (24). This is proposed as the mechanism for transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO). However, as Koch and colleagues demonstrate, a large proportion of patients after cardiopulmonary bypass – which renders the lungs relatively ischemic – meet qualitative criteria for TRALI, whether they are transfused or not (25). There is some controversy as to whether immune modulation is mediated by white blood cells (WBC) contained in the transfusion, with demonstrated reduction in natural killer cell function. The several randomized trials of WBC-depleted transfusions are inconclusive (13, 26). In addition, bactericidal permeability increasing protein (BPI) increases during blood storage, indicating presence of activated WBCs, and in transfused patients in the 1990s this serum biomarker was substantially increased along with other inflammatory mediators known to promote infection (27). WBC-depleted and irradiated blood transfusion is now routinely practiced throughout the world, but not necessarily in the United States. The sites in our Network, however, all used leukocyte-reduced blood, and most sites used irradiated blood for special patient categories such as transplants. As such, this mechanism is not likely to play a role in our observations.

The most recent theory relates to circulating non-transferrin-bound iron, which promotes proliferation of pathogenic bacteria (28, 29). The longer blood is stored before transfusion, the higher the serum iron concentration and transferrin saturation after transfusion of human volunteers (30). Further, growth of *E. coli* is enhanced when exposed to serum samples of volunteers with elevated non-transferrin-bound iron. The increase in iron is correlated with elevation in bilirubin levels, indicating that the mechanism for transferrin saturation is likely more rapid destruction of erythrocytes from older stored blood (31).

Attenuation of the relationship of transfused blood to infection was seen after administration of platelets. This observation has been reported by others (19). Banbury and colleagues speculated that this phenomenon may be related to co-transfusion of immunoglobulin with platelet-rich plasma, which has been demonstrated in other settings to reduce postoperative infections (32).

Although an increase in infections may itself explain the relation between RBC transfusion and prolonged postoperative length of stay and increased mortality, it also has been demonstrated that the number of transfusions given during and after cardiac surgery appears to be associated with not only increased early mortality, but a substantial increase in late risk of death (14, 16, 18, 33, 34).

Limitations

Because this is an observational hypothesis-generating study, the reported associations cannot be considered causal. Participating institutions were generally high-volume tertiary

referral centers performing a substantial number of complex operations leading to heterogeneity of procedures and patients. Surgeon-specific data for each procedure was not recorded. Moreover, we do not know the exact timing of transfusion in relation to postoperative infection; most transfusions are given intraoperatively and in the intensive care unit after surgery. Generally, infections are not manifest by that time, with many infections occurring after hospital discharge. We also do not know the age of transfused units, which may affect the relationship to infection (31), nor if the units came from a male or female donor. Transfused units were not independently audited. Finally, we also do not know the clinical triggers or reasons for transfusion; indeed, no attempt was made to control transfusion or any other institutional behaviors. We simply observed. We recognize that anemia is also associated with risks (10), as are measures to elevate or maintain hemoglobin levels before and during cardiac surgery. This study focuses only on transfusion risks, and cannot address the important clinical dilemma of when to transfuse to realize benefits of transfusion that outweigh the risks of anemia.

Clinical implications

Even recent guidelines advocating blood conservation continue to stress resource utilization and blood-borne viruses, without much consideration given to elevation of postoperative morbidity such as infections (7). All risks, and benefits, of transfusion must be weighed against the risks of anemia, which itself is associated with adverse outcomes (10). Given the high prevalence of preoperative antiplatelet therapy, particularly in patients with coronary artery disease, surgeons can take some solace in the relative safety of administering platelets.

There are a number of process measures that can be employed to avoid transfusion (7, 35). These include use of cell salvage (which in our study was not associated with increased risk of infection), use of small priming volume cardiopulmonary bypass circuits, minimizing hemodilution by crystalloid fluids, use of vacuum-assisted venous return (36, 37) with rapid autologous priming (38), increase in hematocrit by modified ultrafiltration (39), elevation of preoperative hematocrit in elective cases by iron and B-complex vitamin administration, and, possibly, the selective use of erythropoetin, although not approved by the FDA for this indication (40, 41). In addition, attention to intraoperative hemostasis, establishment of protocols for transfusion and reoperation for bleeding, use of anti-fibrinolytics, and a tolerance for mild-to-moderate anemia are reasonable means to reduce use of a scarce resource (35).

APPENDIX 1. Infection Definitionsa

Deep incisional surgical site infection (SSI), primary (DIP)

An SSI that is identified in the primary chest incision and meets all of the following criteria:

1. Infection occurs within 60 days after the operative intervention
2. Infection involves deep soft tissues (e.g., fascial and muscle layers)
3. Patient has at least 1 of the following:

a. Purulent discharge from the deep incision, but not from the organ/space component of the surgical site

b. A deep incision spontaneously dehisces or is deliberately opened by a surgeon and is culture positive, or not cultured[b] when the patient has at least one of the following: fever >38°C, localized pain or tenderness

c. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination

d. Diagnosis of deep incisional SSI by the surgeon or attending physician

Deep incisional surgical site infection, secondary (DIS)

An SSI that is identified in the secondary incision (e.g., donor site [leg] incision for CABG) in a patient who has had an operation with 1 or more incisions and meets all of the following criteria:

1. Infection occurs within 60 days after the operative intervention
2. Infection involves deep soft tissues (e.g., fascial and muscle layers)
3. Patient has at least 1 of the following:
    a. Purulent discharge from the deep incision, but not from the organ/space component of the surgical site
    b. A deep incision spontaneously dehisces or is deliberately opened by a surgeon and is culture positive, or not cultured[b] when the patient has at least 1 of the following: fever (>38°C), localized pain or tenderness
    c. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination
    d. Diagnosis of deep incisional SSI by the surgeon or attending physician

Empyema

Pyothorax (empyema thoracis) is the accumulation of pus within the pleural cavity. Empyema can occur in the setting of thoracic surgery, instrumentation of the pleural space (thoracentesis, chest tube placement), and suppurative lung disease (i.e., pneumonia, lung abscess, bronchiectasis). Empyema is characterized by bacterial organisms seen on gram stain or the aspiration of pus on thoracentesis. A positive culture is not required for diagnosis since there are several reasons why bacteria may not be cultured from an empyema: anaerobic organisms are difficult to culture; sampling is often performed after a patient has received antibiotics; and sterile inflammatory fluid can be aspirated adjacent to an infection.

[b]A culture-negative finding does not meet this criterion.

Endocarditis (ENDO)

Endocarditis of a natural or prosthetic heart valve must meet at least 1 of the following criteria:

1. Direct evidence of endocarditis based on histological findings
2. Positive gram stain results or cultures of specimens obtained from surgery or autopsy
3. 2 major clinical criteria
4. 1 major and any 3 minor clinical criteria
5. 5 minor clinical criteria

Major Clinical Criteria

1. Positive blood cultures
    a. Typical microorganism for infective endocarditis from 2 separate blood cultures
    b. Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from blood cultures drawn more than 12 hours apart or all of 3 or a majority of 4 or more separate blood cultures, with first and last drawn at least 1 hour apart
    c. Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1:800
2. Evidence of endocardial involvement
    a. Positive echocardiogram for infective endocarditis
    b. New valvar regurgitation

Minor Clinical Criteria

1. Predisposition
    a. Heart condition
    b. Intravenous drug use
2. Fever >38°C
3. Vascular phenomena
    a. Major arterial emboli
    b. Septic pulmonary infarcts
    c. Mycotic aneurysm
    d. Intracranial hemorrhage
    e. Conjunctival hemorrhages

   f. Janeway lesions

4. Immunologic phenomena
   a. Glomerulonephritis
   b. Osler's nodes
   c. Roth spots
   d. Rheumatoid factor
5. Microbiologic evidence
   a. Positive blood culture, but not meeting major criteria as noted previously
   b. Serologic evidence of active infection with organism consistent with infective endocarditis
6. Echocardiographic minor criteria eliminated

Infectious myocarditis or pericarditis (CARD)

Infectious myocarditis or pericarditis must meet at least 1 of the following criteria:

1. Patient has organisms cultured from pericardial tissue or fluid obtained by needle aspiration or during a surgical operation
2. Patient has at least 2 of the following signs or symptoms with no other recognized cause: fever >38°C, chest pain, paradoxical pulse, or increased heart size, *and* at least 1 of the following:
   a. Abnormal EKG consistent with myocarditis or pericarditis
   b. Positive antigen test on blood (e.g., *H. influenzae, S. pneumoniae*)
   c. Evidence of myocarditis or pericarditis on histologic examination of heart tissue
   d. 4-fold rise in type-specific antibody with or without isolation of virus from pharynx or feces
   e. Pericardial effusion identified by echocardiogram, CT scan, MRI, or angiography

Mediastinitis (MED)

Mediastinitis must meet at least 1 of the following criteria:

1. Patient has organisms cultured from mediastinal tissue or fluid obtained during a surgical operation or needle aspiration
2. Patient has evidence of mediastinitis seen during a surgical operation or histopathologic examination
3. Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever >38°C, chest pain, or sternal instability, *and* at least 1 of the following:

a. Purulent discharge from mediastinal area

b. Organisms cultured from blood or discharge from mediastinal area

Pneumonia (PNEU)

Clinically defined pneumonia must meet all of the following criteria:

1. At least 1 or more chest radiographs no earlier than 2 days post surgery, with at least 1 of the following:
   a. New or progressive and persistent infiltrate
   b. Consolidation
   c. Cavitation
2. Patient has at least 1 of the following signs or symptoms: fever >38°C with no other recognized cause, leukopenia (<4,000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3), or altered mental status with no other recognized cause (for patients ≥ 70 years old), *and* at least 2 of the following:
   a. New onset of purulent sputum, change in character of sputum, increased respiratory secretions, or increased suctioning requirements
   b. New onset or worsening cough, dyspnea, tachypnea
   c. Rales or bronchial breath sounds
   d. Worsening gas exchange (e.g. O_2 desaturations, increased oxygen requirements, increased ventilator demand)

Bloodstream infection (BSI)

A BSI must meet at least 1 of the following criteria:

1. Patient has a recognized pathogen cultured from 1 or more blood cultures *and* organism cultured from blood is *not* related to an infection at another site
2. Patient has at least 1 of the following signs or symptoms: fever >38°C, chills, or hypotension, *and* signs and symptoms and positive laboratory results are *not* related to an infection at another site *and* common skin contaminant (i.e., diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative staphylococci, viridians group streptococci, *Aerococcus* spp, *Micrococcus* spp) is cultured from 2 or more blood cultures drawn on separate occasions

Cardiac device infection

A cardiac device infection must meet at least 1 of the following criteria:

1. A positive culture from the skin and/or tissue surrounding a percutaneous cable, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis

2. A positive culture from the tissue surrounding the generator pocket, electrode leads, or external housing of a device implanted within the body, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis

3. Infection of blood-contacting surfaces of an LVAD documented by positive site culture

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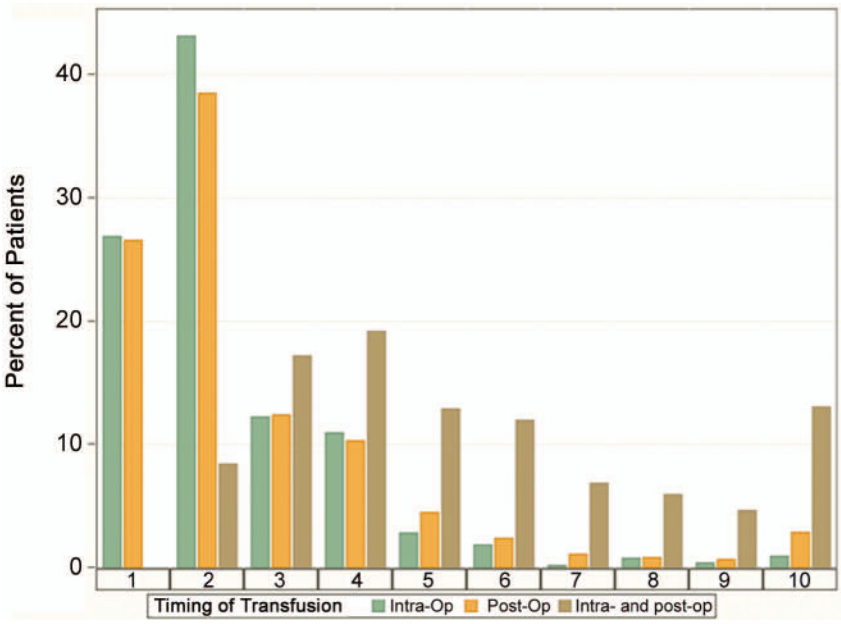

Figure 1.
Distribution of transfusions by intra- versus postoperative timing, or both.

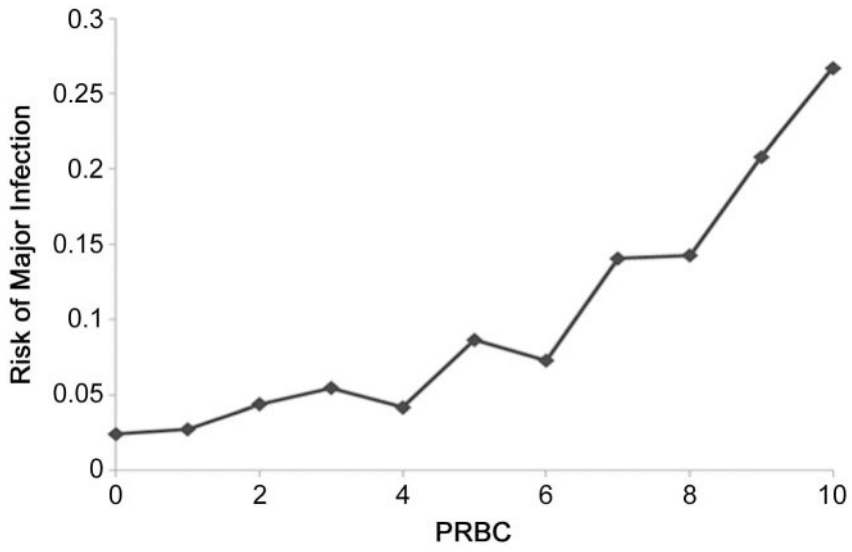

Figure 2.
Risk of major infection as a function of number of red blood cell (RBC) units transfused.

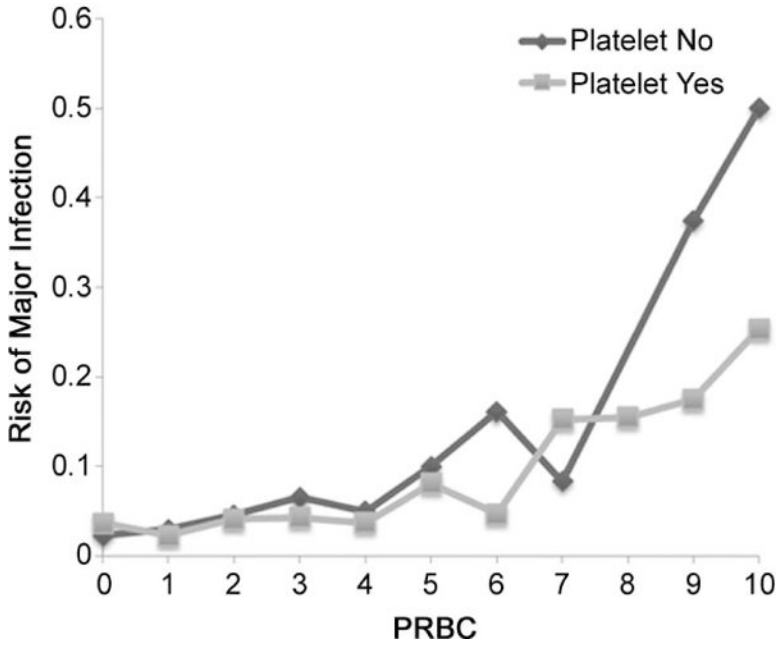

Figure 3.

Risk of major infection as a function of number of red blood cell (RBC) units transfused, with and without platelet transfusion.

Table 1
Patient and Operative Characteristics

Characteristic	No. (%)
Demographics	
Age (y) (mean ± SD)	64 ± 13
Male	3451 (67)
White	4322 (84)
Body mass index ($kg \cdot m^{-2}$) (mean ± SD)	29 ± 5.9
Cardiac morbidity	
Heart failure	1505 (29)
Ejection fraction (%) (median, [IQR])	55 (48, 60)
Previous cardiac surgery	958 (19)
Noncardiac comorbidity	
Hemoglobin ($g \cdot dL^{-1}$) (mean ± SD)	13 ± 1.8
Diabetes	1382 (27)
COPD	
None	4412 (86)
Mild or moderate	644 (12)
Severe	102 (2.0)
Operative	
Cardiopulmonary bypass time (min) (median, [IQR])	105 (78, 140)
Procedure	
Isolated CABG	1596 (31)
Isolated valve	1544 (30)
CABG + valve	589 (11)
Transplant or LVAD	121 (2.4)
Thoracic aorta	292 (5.7)
Other	1016 (20)

Key: *CABG*, coronary artery bypass grafting; *COPD*, chronic obstructive pulmonary disease; *IQR*, interquartile range; LVAD, left ventricular assist device; *SD*, standard deviation.

Table 2

Procedure and Transfusion

		Transfusion		Units	
Procedure	**n**	**No.**	**%**	**Median[a]**	**(25th, 75th percentiles)**
Isolated CABG	1596	721	45	2	(2, 4)
Isolated valve	1544	620	40	2	(2, 4)
CABG + valve	589	382	65	3	(2, 5)
Transplant or LVAD	121	102	84	5	(3, 8)
Thoracic aorta	292	185	63	4	(2, 7)
Other	1016	471	46	3	(2, 5)
Overall	**5158**	**2481**	**48**	**3**	**(2, 5)**

[a]Median units among those transfused (n=2481).

Key: *CABG*, coronary artery bypass grafting; *LVAD*, left ventricular assist device.

Table 3

Infections and Transfusions

	Patients Transfused			Patients not Transfused		
Infection	**No. of Events**	**No. of Patients**	**% of Patients (N=2481)**	**No. of Events**	**No. of Patients**	**% of Patients (N=2677)**
Pneumonia	91	89	**3.59**	33	33	**1.23**
Deep incision surgical site (chest)	14	14	**0.56**	11	11	**0.41**
Deep incision surgical site (groin, leg)	8	8	**0.32**	2	2	**0.07**
Bloodstream	51	48	**1.93**	7	7	**0.26**
Empyema	4	3	**0.12**	--	--	--
Endocarditis	3	3	**0.12**	--	--	--
Myocarditis or pericarditis	5	4	**0.16**	--	--	--
Mediastinitis	9	9	**0.36**	3	3	**0.11**
Device-related percutaneous site	2	2	**0.08**	1	1	**0.04**
Pocket	2	2	**0.08**	--	--	--
C. difficile colitis	35	33	**1.33**	17	17	**0.64**

Table 4
Risk Factors for Infection within 65 Days of Cardiac Surgery

Risk Factor	Coefficient ± SE	Hazard Ratio	95% CL	*P*
RBCs transfused (per unit)	0.21 ± 0.025	1.23	1.17 – 1.29	<.0001
Platelets transfused (yes/no)	−0.42 ± 0.17[a]	0.66[a]	0.47 – 0.92	.02
Heart failure	0.29 ± 0.15	1.34	1.01 – 1.78	.04
COPD (vs. no COPD)				
Mild or moderate	0.35 ± 0.17	1.42	1.02 – 1.98	.04
Severe	0.68 ± 0.31	1.98	1.07 – 3.67	.03
Serum creatinine > 1.5 mg·dL^{-1}	0.50 ± 0.17	1.66	1.20 – 2.29	.002
Duration of surgery (hours)	0.16 ± 0.040	1.17	1.08 – 1.26	<.0001
Procedure (vs. isolated CABG)				
Isolated valve	0.085 ± 0.20	1.09	0.74 – 1.61	.7
CABG + valve	0.016 ± 0.24	1.02	0.64 – 1.62	.9
Transplant or LVAD	1.1 ± 0.26	2.90	1.74 – 4.83	<.0001
Thoracic aorta	0.12 ± 0.30	1.13	0.63 – 2.03	.7
Other	0.36 ± 0.20	1.43	0.97 – 2.13	.07

[a] Protective

Key: *CABG*, coronary artery bypass grafting; *CL*, confidence limit; *COPD*, chronic obstructive pulmonary disease; *LVAD*, left ventricular assist device; *RBC*, red blood cell; *SE*, standard error.