Infectious Complications After Cardiac Surgery: Lack of Association With Fresh Frozen Plasma or Platelet Transfusions

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Objective: **The purpose of this study was to examine the effect of perioperative transfusion of platelets and fresh frozen plasma (FFP) on infection rates after cardiac surgery.**

Design: **Retrospective study comparing infection rates after cardiac surgery among patients receiving combinations of packed red blood cells (PRBCs), platelets, and FFP.**

Setting: **Tertiary care university teaching hospital.**

Participants: **All elective primary coronary artery bypass (CABG) surgery patients from July 1995 to January 1998 before introduction of leukocyte-reduced blood products.**

Interventions: **Multivariate logistic and linear regression models were applied to identify clinical risk factors for postoperative infection and to determine the relationship between perioperative administration of PRBCs, platelets, and FFP with postoperative infection.**

Measurements and Main Results: **Transfusion of PRBCs, diabetes, age, preoperative hematocrit, and the duration of cardiopulmonary bypass were significantly associated with postoperative infection; platelet or FFP transfusion added no additional risk to PRBC transfusion alone.**

Conclusions: **Infectious complications in a population of adult primary CABG surgery patients were not increased by transfusion of platelets or FFP. It is PRBC transfusion that confers an increased risk of postoperative infection in this population.**

KEY WORDS: cardiopulmonary bypass, human, adult, coronary artery bypass, postoperative complications, blood transfusion, blood component transfusion, erythrocyte transfusion, platelet transfusion, plasma, infection

CORONARY ARTERY BYPASS graft (CABG) surgery consumes more health care dollars than any other single medical treatment.[1] In 1997, approximately 500,000 patients in the United States underwent cardiac surgery with cardiopulmonary bypass (CPB).[2] Infectious complications add to perioperative morbidity, mortality, and cost[3] after this common procedure, representing a serious public health risk. Transfusion of blood products is common during CABG surgery[4,5] and both immunomodulatory effects and direct bacterial contamination of blood products may predispose to infection in this setting.

Infectious complications after cardiac surgery occur in as many as 7% of patients, and bacterial contamination of blood products has been implicated as contributing to perioperative infections.[3,6] Platelet bacterial contaminants frequently are identical to bacterial organisms associated with invasive monitoring catheter infections. In addition, freeze thawing of fresh frozen plasma (FFP) results in leukocyte lysis and release of immunomodulating bioactive substances into plasma. These effects are in addition to the well-established immunomodulating effects of intact leukocytes in packed red blood cell transfusions. The authors postulated that perioperative transfusion of platelets and/or FFP, before the introduction of leukocyte-depleted blood products, would increase postoperative infections after CABG surgery. In this investigation, the association between perioperative transfusion of nonautologous, blood component transfusions and infection rates for patients undergoing primary CABG surgery at a tertiary care medical center between July 1995 and January 1998 is reported.

MATERIALS AND METHODS

After approval by the Duke University Institutional Review Board for Human Studies for waiver of patient consent, data for all elective primary CABG surgery patients between July 1995 and January 1998 who received packed red blood cells (PRBCs), FFP, and/or platelets within 48 hours from the start of surgery were reviewed. Exclusion criteria included cryoprecipitate use; patients undergoing reoperation, or patients who underwent emergency, valvular, or transplant surgery. Patients on immunosuppressive drugs, patients with metastatic malignancies, or patients with preexisting coagulopathies were excluded.

Anesthetic management consisted of fentanyl and midazolam infusions supplemented with isoflurane (0.5%-1.5%). Patients received epsilon-aminocaproic acid during the study period (10-g intravenous bolus before CPB and then 1 g/h for 5 hours). Hypothermic CPB was performed between 25°C and 34°C (nasopharyngeal temperature) using a Cobe CML membrane oxygenator (Cobe laboratories, Lakewood, CO), Sarns 7000 MDX pump (Sarns Inc, Ann Arbor, MI), and Pall SP 3840 (Pall Biomedical Products Co, Glencove, IL) 40-μm arterial filters. All patients received cefuroxime, 1.5 g intravenously, before surgical incision and 1.5 g after separation from CPB.

Infectious complications recorded included pneumonia, acute respiratory distress syndrome, mediastinitis, leg wound infection, sternal wound infection, nosocomial infection, invasive catheter-related sepsis, urinary tract infection, decubitus ulcers, and positive blood cultures. Pneumonia was diagnosed by clinical findings, new infiltrates on chest radiography, and isolation of a pathogen on gram stain. Diagnostic criteria for acute respiratory distress included a PaO_2 $<$50 mmHg despite an F_IO_2 $>$50% and/or capillary wedge pressure $<$18 mmHg. Leg wound infections were identified by local erythema and tenderness requiring dressings and intravenous antibiotic administration. Nosocomial infections were defined as occurring at least 48 hours after hospital admission. Urinary tract infections were identified by positive urine cultures and decubitus ulcers by loss of skin integrity. Catheter-related sepsis was based on identification of pathogens isolated from blood cultures and excluded as sources of other ongoing infection.

Blood bank records were the source for transfusion data. Transfusion of blood products occurred at the discretion of the attending surgeon and anesthesiologist. Cryoprecipitate use was rare and most often administered for prophylactic treatment of von Willebrand's disease or

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Table 1. Patient Demographics

Age (y)	63 (11)
Weight (kg)	81 (17)
Female (%)	36
Cigarette use (%)	42
Diabetic (%)	30
Preoperative creatinine (mg/dL)	1.21 (0.93)
Preoperative hematocrit	38.7 (5.5)
LVEF	52 (14)
CPB time (min)	118 (74)
Total units	1.3 (2.5)

NOTE. Descriptive data are presented as percentages or mean (± standard deviation).

Abbreviation: LVEF, left ventricular ejection fraction.

Table 2. Incidence of Infection

Infection Type	Total (n = 418)
UTI	150 (2.17%)
Pneumonia	124 (1.8%)
Positive blood cultures	52 (0.75%)
Leg wound	38 (0.6%)
Mediastinitis	49 (0.7%)
ARDS	31 (0.5%)
Sternal wound	46 (0.7%)
Monitoring catheter sepsis	13 (0.2%)
Nosocomial	16 (0.2%)
Decubitus ulcer	15 (0.22%)

Abbreviations: UTI, urinary tract infection; ARDS, acute respiratory distress syndrome.

other coagulopathies. Demographic variables were gathered for each patient. Clinical covariates were chosen as previously described[7-9] and included duration of CPB, weight, age, sex, preoperative hematocrit and creatinine, history of cigarette use, and diabetes.

Demographic data were described as percentages or means with standard deviation. Infection rates were described as percentages (±95% confidence limits on the risk estimates, as groupings were of widely varying size) and number of units transfused as median (interquartile range). Comparisons of infection rates between groups used chi-square testing. Multivariate logistic regression modeling was employed to describe associations between blood component transfusion and clinical covariates (as predictors) and infectious complications (as outcomes). Results were reported as odds ratios (95% confidence limits). Linear regression models were constructed to describe associations between the total number of units of blood components transfused and infectious complications after logarithmic transformation of the blood product data. Models were reported as unadjusted or adjusted for the effect of clinical covariates. Statistical analysis was performed using SAS (Cary, NC) software version 8.02; a p value <0.05 was considered significant. Given the sample size, there was an 80% power to detect a difference of postoperative infection of 3% or greater; that is, the group without platelets had a risk of infection of 6%, and the group given platelets had a risk of infection of 9%, assuming a 2-sided chi-square test of general association and an alpha level of 0.05.

RESULTS

Patient demographics appear in Table 1. Between July 1995 and January 1998, 6721 patients underwent elective primary cardiac surgery at Duke University; 2,657 patients required a blood product transfusion within the first 48 hours postoperatively. During this period, 1,803 received PRBC transfusions alone; 326 received only PRBCs and FFP; 184 received only PRBCs and platelets; and 344 received PRBCs, FFP, and platelet transfusions. Patients excluded (n = 406) were those receiving other combinations of blood products including cryoprecipitate. Of the 6,721 patients examined, 418 patients experienced at least 1 infectious complication postoperatively. Frequency of infection varied from least common (monitoring catheter sepsis, n = 13, 0.2%) to most common (urinary tract infection, n = 150, 2.2%) (Table 2). Chi-square comparisons identified the group receiving no transfusion as having a significantly lower infection rate ($p < 0.001$) than groups receiving transfusions (5.1% [4.5-5.9] *v* 7.5% [6.3-8.8], 6% [3-10.4], 7% [4-11.1], and 8.1% [5.4-11.5]) (Fig 1).

Of the clinical covariates tested (age, weight, diabetes, smoking, preoperative creatinine, preoperative hematocrit, left ventricular ejection fraction and CPB duration), only CPB duration, age, preoperative hematocrit, and diabetes were significantly associated with infection (Table 3), although this association only persisted for CPB duration and diabetes when blood transfusion was considered as a linear variable (total units transfused, Table 4).

A multivariate logistic regression model (Table 3) including binary identifiers of PRBCs, FFP, and platelet transfusion as predictors and infection as an outcome identified that blood component transfusion increased the risk of infection (odds ratio 1.45 [1.19-1.77], $p = 0.0002$). A more detailed model (Table 3 model A) indicates that PRBC transfusion is a significant predictor of infection ($p = 0.0002$), whereas FFP ($p = 0.25$) or platelet

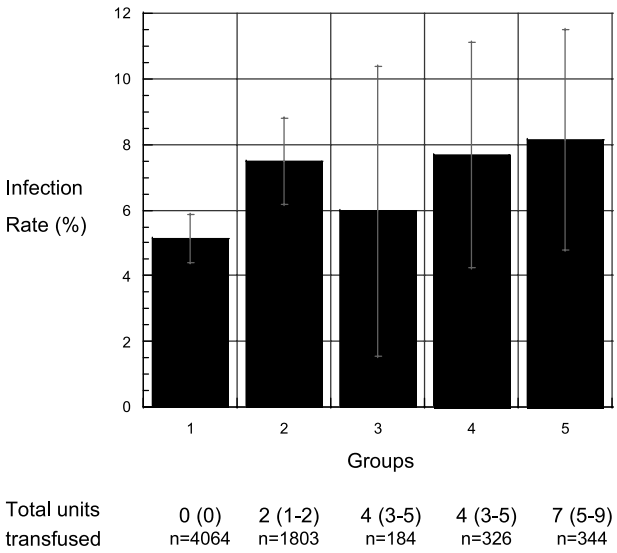

Fig 1. Infection rates and total number of units transfused (all blood components) grouped according to types of blood components received. Group 1, no transfusion; group 2, PRBC transfusion only; group 3, PRBC and platelet transfusion; group 4, PRBC and FFP transfusion; and group 5, PRBC, FFP, and platelet transfusion. Chi-square testing comparing infection rates shows a significant difference exists among these groups ($p < 0.001$); with removal of the no-transfusion group, there is no significant difference among groups ($p = 0.18$).