

## Preoperative predicted risk does not fully explain the association between red blood cell transfusion and mortality in coronary artery bypass grafting

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**Objective:** Perioperative red blood cell transfusion is associated with increased morbidity and mortality after coronary artery bypass grafting (CABG). Whether transfusion is a cause of these outcomes or serves as a surrogate for a high-risk patient population remains uncertain. This retrospective study tested the hypothesis that increased preoperative risk profile of patients receiving transfusion would explain the relationship between red blood cell transfusion and operative mortality in isolated CABG.

**Methods:** A total of 31,818 patients undergoing isolated CABG were entered into a statewide collaborative database between January 2006 and June 2010. With the Society of Thoracic Surgeons risk calculator, patient cohorts were stratified into 4 groups by predicted risk of mortality (PROM) of less than 2%, 2% to 5%, more than 5% to 10% and more than 10%. The association between blood transfusion and mortality was tested at each stratum with a  $\chi^2$  test. A Breslow-Day test for homogeneity of odds ratios was used to test whether the 4 odds ratios of the strata were similar, and a Cochran-Mantel-Haenszel test was used to test the association between blood transfusion and mortality while controlling for predicted risk mortality strata.

**Results:** In all, 17,720 (55.7%) of all patients were transfused during the hospitalization. Incidence of transfusion increased stepwise with risk level; 93.3% of patients with PROM greater than 10% received blood. Operative mortality was 2.1% overall, 0.6% among the 44.3% of patients who were not transfused, and 3.3% in the transfused group (odds ratio, 6.19;  $P < .0001$ ). The association between blood transfusion and mortality was significant within each predicted risk stratum. Increased mortality associated with transfusion was statistically equivalent across all predicted risk strata ( $P = .1778$ ). The association between blood transfusion and mortality for all patients lessened somewhat when controlling for PROM (odds ratio, 2.99 vs 6.19), yet remained highly significant ( $P < .0001$ ).

**Conclusions:** The association between red blood cell transfusion and mortality after CABG is highly significant and independent of increased preoperative risk status. The correlation persists after controlling for increased PROM. (*J Thorac Cardiovasc Surg* 2012;143:178-85)

Perioperative red blood cell transfusion is associated with increased morbidity and both short- and long-term mortality after coronary artery bypass grafting (CABG).<sup>1-5</sup> The many articles reporting these relationships have repeatedly documented that the demographic risk profile of patients

who receive transfusion differs significantly from those who do not. Consequently, whether transfusion is a cause of these adverse outcomes or serves as a surrogate marker for a patient population at higher risk remains uncertain. This retrospective study tests the hypothesis that an increased preoperative risk profile of patients receiving transfusion would explain the relationship between red blood cell transfusion and operative mortality in isolated CABG.

### MATERIALS AND METHODS

#### Patient Population

The Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative is a multidisciplinary group consisting of all 33 hospitals that perform adult cardiac surgery in the state of Michigan.<sup>6</sup> All programs use the Society of Thoracic Surgeons (STS) data collection form and submit data on a quarterly basis to both the STS database and the collaborative. Data managers meet quarterly for ongoing education and training in data abstraction and outcomes reporting. In addition, there are scheduled conference calls and web-based seminars that focus specifically on issues

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### Abbreviations and Acronyms

CABG = coronary artery bypass grafting

PROM = predicted risk of mortality

STS = Society of Thoracic Surgeons

related to institutional quality initiatives or data definitions. Data audits are conducted annually to ensure data integrity. Seventy-six data elements are audited from a random sample of 20 cases at each center. These data elements include STS morbidity and mortality risk model variables, intraoperative data, and process and outcome measures. Data managers are instructed to correct data abstraction errors and submit corrected data to the STS during the next data harvest. For consistency, all audit visits are conducted by the same 2 quality collaborative nurses. The last yearly audit, completed in 2010, revealed 97% accuracy with 100% documentation of 30-day follow-up.

Between January 2006 and June 2010, a total of 31,818 patients undergoing isolated CABG were entered into the statewide collaborative database and form the basis of this report. Patients undergoing both on-pump and off-pump procedures were included. Through application of the STS risk calculator,<sup>7</sup> patient cohorts were stratified into 4 groups according to predicted risk of mortality (PROM) of less than 2%, 2% to 5%, greater than 5% to 10%, and greater than 10%. The STS risk model for CABG predicts the risk of operative mortality and morbidity on the basis of 30 preoperative patient demographic and clinical variables and can adjust for case mix when comparing outcomes across institutions with different patient populations.<sup>7</sup>

### Statistical Analyses

The response rates for each of 23 preoperative patient characteristics that were considered clinically relevant were summarized. The relationships between these variables and both blood transfusion and mortality were assessed in separate univariate analyses. Quantitative variables were compared with 2-sided 2-sample *t* tests. Categorical variables were compared between groups with  $\chi^2$  tests for association.

Because the distributions of PROM observed for both transfused and nontransfused patients were severely skewed, a 2-sided Mann-Whitney-Wilcoxon test was used to test whether there was a statistically significant difference in the distribution of PROM between the 2 groups. A  $\chi^2$  test was used to test whether there was an association between mortality and blood transfusion. An odds ratio and a 95% confidence interval were computed to estimate the strength of the association. The association between blood transfusion and mortality was tested at each PROM stratum with a  $\chi^2$  test. A Breslow-Day test for homogeneity of odds ratios was used to test whether the 4 odds ratios among the strata were similar, and a Cochran-Mantel-Haenszel was used to test the association between blood transfusion and mortality while controlling for PROM strata.

A Cochran-Armitage trend test was used to test for a trend in transfusion rate by increasing ordinal PROM strata. PROM was used as a predictor of transfusion in a simple linear regression model. The effects of each risk stratum in reference to the less than 2% PROM group were assessed with the Wald  $\chi^2$  estimates.

A propensity score analysis was performed in a 2-step process to adjust statistically for group differences in preoperative characteristics of patients who received transfusion versus patients who did not. In step 1, the propensity score was obtained by calculating the predicted probabilities in a multiple logistic regression on predicting transfusion. The model included 17 preoperative variables that had significant relationships with both transfusion and mortality according to univariate testing. Several other variables were excluded because of limited responses. Patient records missing 1 or more responses for any of the 17 variables used in

the model were excluded, reducing the final sample size to 29,526. In step 2, the strength of blood transfusion in predicting mortality was then tested in another multiple logistic regression model after adjustment for the propensity score.

Finally, as a sensitivity analysis, an additional multiple logistic regression model to test for a relationship between transfusion and mortality was constructed. This model had as predictors, in addition to blood transfusion, each of the 17 individual preoperative variables originally used to build the propensity score.

Statistical analyses were performed with SAS statistical software (version 9.2; SAS Institute, Inc, Cary, NC).

### RESULTS

Preoperative characteristics, including univariate comparisons for both transfusion status and mortality, are listed in Table 1. The large majority of studied variables were significantly related to both outcomes ( $P < .001$ ). Preoperative aspirin use within 5 days of surgery was the only variable studied not significantly associated with either transfusion status ( $P = .690$ ) or mortality ( $P = .298$ ). A total of 17,720 patients (55.7%) received red blood cell transfusions during the index hospitalization. This transfusion rate is comparable to the rate of 55.0% from the STS database in a similar time frame.<sup>8</sup>

The incidence of transfusion increased stepwise with risk level; 45% of patients at the lowest (<2% PROM) risk stratum were transfused, and this rate increased to 93.3% for patients with PROM greater than 10% (Table 2). Every PROM stratum had a significantly higher transfusion rate in reference to the lowest (<2% PROM) group, and this trend was significant ( $P < .0001$ ). PROM for the 44.3% of patients not transfused was 1.3%, compared with 3.3% for the transfused group ( $P < .0001$ ).

Operative mortality was 2.1% for the entire group. There was a significant association between blood transfusion and mortality; 0.6% of those patients not receiving transfusion died, compared with a mortality of 3.3% in the transfused group (odds ratio, 6.19;  $P < .0001$ ). The association between blood transfusion and mortality was also significant within each PROM stratum (Table 3). Overall, there was no significant difference between odds ratios when comparing them across the PROM strata ( $P = .1778$ ). The association between blood transfusion and mortality for all patients decreased when controlling for the PROM (odds ratio, 2.99 vs 6.19) yet remained highly significant ( $P < .0001$ ).

Sixteen of the 17 preoperative variables in a multiple logistic regression model were statistically significant predictors of blood transfusion. Although left main coronary disease was not significant, it was still considered in the propensity model because it had a significant association with mortality (Table 4). After adjustment for group differences built into the propensity score, blood transfusion remained a highly significant predictor of mortality (odds ratio, 2.88;  $P < .001$ ). Finally, a multiple logistic regression model

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