Prediction of Transfusions After Isolated Coronary Artery Bypass Grafting Surgical Procedures

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Background. **Although blood transfusions are common and have been associated with adverse sequelae after cardiac surgical procedures, few contemporaneous models exist to support clinical decision making. This study developed a preoperative clinical decision support tool to predict perioperative red blood cell transfusions in the setting of isolated coronary artery bypass grafting.**

Methods. **We performed a multicenter, observational study of 20,377 patients undergoing isolated coronary artery bypass grafting among patients at 39 hospitals participating in the Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative's PERFusion measures and outcomes (PERForm) registry between 2011 and 2015. Candidates' preoperative risk factors were identified based on previous work and clinical input. The study population was randomly divided into a 70% development sample and a 30% validation sample. A generalized linear mixed-effect model was developed to predict perioperative red blood cell transfusion. The model's performance was assessed for calibration and discrimination. Sensitivity analysis was performed to assess the robustness of the model in different clinical subgroups.**

Results. **Transfusions occurred in 36.8% of patients. The final regression model included 16 preoperative variables. The correlation between the observed and expected transfusions was 1.0. The risk prediction model discriminated well (receiver operator characteristic $[ROC]_{development}$, 0.81; $ROC_{validation}$, 0.82) and had satisfactory calibration (correlation between observed and expected rates was $r = 1.00$). The model performance was confirmed across medical centers and clinical subgroups.**

Conclusions. **Our risk prediction model uses 16 readily obtainable preoperative variables. This model, which provides a patient-specific estimate of the need for transfusion, offers clinicians a guide for decision making and evaluating the effectiveness of blood management strategies.**

(Ann Thorac Surg 2016;■:■–■)

Cardiac surgery accounts for nearly 25% of all blood use in the United States [1]. Although red blood cell (RBC) transfusions are certainly life preserving in many clinical circumstances, patients exposed to these transfusions are at increased odds of major morbidity and death [2, 3]. Indeed, patients exposed to RBC transfusions are more likely to have more resource use, including prolonged length of stay [4].

Despite these risks, more than 50% of patients undergoing coronary artery bypass grafting (CABG) surgical procedures continue to be exposed to RBC transfusions [4]. Prediction models were previously developed to provide accurate and reliable estimates of a patient's risk of being exposed to RBCs. In addition, these models may provide guidance to clinicians as they consider strategies for mitigating a patient's risk of exposure to RBC transfusions, including reducing circuit prime volume [5] or providing erythropoietin to increase hematocrit (Hct) [6]. Nonetheless, many of these studies included heterogeneous populations, including patients undergoing a variety of cardiac surgical procedures [7, 8], or they likely no longer reflect current surgical experiences given that they are more than a decade old [9, 10]. Contemporaneous, accurate, and reliable estimates are needed to

Accepted for publication July 5, 2016.

Presented at the Poster Session of the Fifty-second Annual Meeting of The Society of Thoracic Surgeons, Phoenix, AZ, Jan 23–27, 2016.

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0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.07.009

guide targeted quality improvement activities around blood management.

We leveraged a prospective, multiinstitutional database of patients undergoing isolated CABG operations to derive a model using preoperative factors to predict a patient's risk of being exposed to RBC transfusions in the setting of CABG surgical procedures.

Patients and Methods

This study (HUM00117106) was approved by the University of Michigan's Institutional Review Board.

Patient Population

The PERFusion measures and outcomes (PERForm) registry was established in 2010 as a voluntary database. Current efforts are focused on identifying perfusion practices associated with improved outcomes and providing benchmarking opportunities to support local and multiinstitutional quality improvement initiatives. It is organizationally structured within the Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative (MSTCVS-QC). The MSTCVS-QC began in 2001 as a cardiac surgeon–led quality collaborative embedded in the Michigan Society of Thoracic and Cardiovascular Surgeons, and in 2005 it became partially funded by Blue Cross/Blue Shield of Michigan. The Collaborative meets quarterly to review processes and outcomes and to facilitate and evaluate quality improvement studies.

All programs in the MSTCVS-QC use The Society of Thoracic Surgeons (STS) data collection form and submit data on a quarterly basis to both the STS database and the MSTCVS-QC data warehouse. The PERForm registry contains information related to the care and conduct of cardiovascular perfusion practices. (A list of fields and definitions may be found at http://www.mstcvs.org/perform-registry.) Each surgical record is merged with a record from the PERForm registry [11].

We excluded patients refusing blood transfusions (n = 102). The final dataset included 20,377 patients undergoing isolated CABG procedures at any of the 39 (32 of which are located in Michigan) centers participating in the MSTCVS-QC PERFusion database from July 1, 2011 to March 31, 2015.

Measures

The primary outcome of this study was the receipt of any RBC transfusion during the operation or before discharge. Variables investigated in univariate analysis were informed by previous work [7, 8], as well as by clinical input from our statewide collaborative. Variables under consideration included those reflecting patient-related demographic factors, medical history, acuity (ie, elective, urgent, emergency or salvage), admission status, comorbid disease, cardiac anatomy, and the institution performing the procedure.

Statistical Analysis

Categorical variables with less than 1% missing were imputed with their lowest risk values (eg, patients with missing information for diabetes were considered not to have diabetes). With some exceptions, missing values of continuous variables were imputed with the median. Missing data on ejection fraction were imputed to the median value of ejection fraction conditional on congestive heart failure and sex. Last preoperative Hct level was imputed to its conditional median on sex, whereas creatinine level was imputed to its conditional median on dialysis.

Indicator variables were used to model missing smoking status (21% missing) and left main coronary artery disease (10% missing).

The study population was randomly divided into a 70% development sample (14,264 patients) and a 30% validation sample (6,113 patients). The development sample was used to identify predictor variables and develop a multivariable model. The validation samples were used to assess model fit and discrimination. After we chose variables and assessed model fit, the development and validation samples were combined, and the final model coefficients were estimated using the combined (development plus validation) data.

We considered preoperative variables known to be important risk factors [7–10, 12] in the univariate analysis (Table 1). Continuous variables including body surface area (BSA), albumin level, ejection fraction, platelet count, international normalized ratio (INR), and creatinine level were categorized based on clinical input. Patients' age, time (number of years since 2011), and last preoperative Hct were modeled continuously. X^2 tests were performed for categorical variables, and Wilcoxon rank-sum tests were performed for continuous variables. We used a threshold of $p < 0.01$ for a variable to enter into a multivariable logistic regression.

The final list of variables was selected from a supervised backward selection process, using a threshold of $p < 0.001$. The functional form of continuous variables was further evaluated. The interaction between sex and Hct was investigated but removed from the model because of lack of significance. Preoperative Hct was modeled using linear splines with knots at 36, 39, and 43; these cut points were informed by nonlinear effect and clinical input. To account for the clustering of patients within medical centers, a generalized linear mixed model with a random intercept for center effect was used as the final model. The coefficients of fixed effects predictors were estimated, and the predictive probability of transfusion was calculated from the subject-specific fixed effect.

The model's calibration was assessed as a function of the correlation (Pearson's correlation coefficient) between the observed and expected (as predicted by subject-specific fixed effect from the mixed model) transfusion rates.

Sensitivity analyses by clinically important subgroups of age, sex, operative status, preoperative Hct and medical center were performed to evaluate the model's