# Predictors of massive transfusion with thoracic aortic procedures involving deep hypothermic circulatory arrest

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**Objective:** Massive perioperative blood product transfusion may be required with thoracic aortic operations and is associated with poor outcomes. We analyzed independent predictors of massive transfusion in thoracic aortic surgical patients undergoing deep hypothermic circulatory arrest.

**Methods:** The study consisted of 168 consecutive patients undergoing open thoracic aortic procedures involving deep hypothermic circulatory arrest between July 2005 and August 2008. We identified 26 preoperative and procedural variables as potentially related to blood product use, tested for association with total blood products transfused by multivariate linear regression model, and constructed logistic regression model for massive transfusion (requiring $\geq$5 units of transfused packed red blood cells between incision and 48 postoperative hours).

**Results:** Multivariate linear regression determined that 6 significant variables accounted for 42% of variation in total blood products transfused: age ($P = .008$), preoperative hemoglobin ($P = .04$), weight ($P = .02$), cardiopulmonary bypass time ($P < .0001$), emergency status ($P < .0001$), and resternotomy ($P < .0001$). Final predictive logistic regression model included 1-g/dL increase in preoperative hemoglobin (odds ratio, 0.54; 95% confidence interval, 0.43–0.69; $P < .0001$), 10-minute increase in cardiopulmonary bypass time (odds ratio, 1.15; 95% confidence interval, 1.05–1.26; $P = .0026$), and emergency status (odds ratio, 4.02; 95% confidence interval, 1.53–10.55; $P = .0047$.

**Conclusions:** Cardiopulmonary bypass time, emergency status, and preoperative hemoglobin were independent predictors of massive transfusion. These variables, along with weight, age, and resternotomy, were associated with total blood product use in thoracic aortic operations involving deep hypothermic circulatory arrest. (J Thorac Cardiovasc Surg 2011;141:1283-8)

Massive perioperative transfusion may occur with thoracic aortic operations. Although there is certainly no substitute for meticulous surgical technique, the etiology of unusually high transfusion requirement is often multifactorial. Hemostatic derangements in aortic surgery are caused by a multitude of interrelated factors, including interference with the vascular integrity, surgical dissection, deep hypothermic circulatory arrest (DHCA), ischemia and reperfusion, dilution of coagulation factors from large-volume fluid resuscitation, transient need for heparinization, and the use of cardiopulmonary bypass (CPB).[1] Patient-level factors include age, sex, diabetes, preoperative hemoglobin, platelets, prothrombin time, and partial thromboplastin time.[2-4]

There are few clinical data addressing predictors of massive transfusion specific to operations for disease of the thoracic aorta, particularly those involving DHCA.[5,6] The DHCA used for neuroprotection in thoracic aortic surgery slows coagulation cascade activity, reduces coagulation factor synthesis, increases fibrinolysis, decreases platelet count, and impairs platelet function.[7] The prosthetic grafts used for aortic repair consume platelets and other factors.[8] Aortic disease itself may also predispose toward coagulopathy through the exposure of tissue factor and other mechanisms.[9,10]

Adverse outcomes attributable to the sequelae of massive perioperative transfusion are well recognized in the cardiac surgical literature, including a strong independent association with mortality.[11,12] Identification of patients at high risk for requiring massive transfusion not only will allow improved risk stratification and preoperative counseling but also may create an opportunity for therapeutic modalities targeted toward individual patients in the perioperative period. Our objective was to determine the predictors of massive perioperative transfusion with open thoracic aortic procedures involving DHCA. We therefore tested the hypothesis that patient and procedural

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**Abbreviations and Acronyms**
CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest
IQR = interquartile range
PRBCs = packed red blood cells

characteristics could be used to model the need for transfusion with thoracic aortic surgery.

## MATERIALS AND METHODS

### Data Source

The Duke Thoracic Aortic Surgery Database is a prospectively maintained, comprehensive clinical registry of all patients who have undergone any thoracic aortic procedure at Duke University Medical Center (Durham, NC) since 2005. This study included all patients who underwent a thoracic aortic procedure with DHCA between July 2005 and August 2008, excluding only patients who underwent a separate procedure in the perioperative period that resulted in massive transfusion. All procedures were performed by a single surgeon (G.C.H.), thus minimizing the contribution of variation in surgical technique to the findings. This study was approved by the Duke University institutional review board, which waived the need for individual patient consent. The Duke Thoracic Aortic Surgery Database provided baseline characteristics, clinical variables, and surgical procedure details. Review of individual medical records was undertaken to complete any missing clinical data points, and blood bank records provided precise information regarding amounts of blood products administered.

### Conduct of Procedures and Anesthesia

Nonpulsatile CPB was conducted for each case with a membrane oxygenator after a crystalloid and mannitol prime and with an arterial line filter. Porcine heparin was administered as a bolus of 300 U/kg and supplemented to maintain an activated clotting time longer than 480 seconds. A 5000-unit bolus of heparin was given before circulatory arrest. During CPB, temperature-adjusted flow rates of 2.5 L/(min · $m^2$) were used, and mean arterial pressure was generally maintained between 50 and 70 mm Hg. Anesthesia was maintained with isoflurane (0.5%–1.0%) by the oxygenator. Alpha stat management was used for maintenance of normal pH, $Po_2$, and $Pco_2$ values. Antegrade and retrograde cold blood cardioplegic solutions were used for myocardial protection. Our institutional preference is to perform open thoracoabdominal (extent I–III) and descending aortic aneurysm repairs with DHCA.

Before the portion of the aortic reconstruction requiring DHCA, the patient was cooled on CPB until electrocerebral inactivity was detected by electroencephalography by previously described techniques[13]; electrocerebral inactivity was usually reached at a nasopharyngeal temperature between 14°C and 18°C. Once electrocerebral inactivity was achieved through hypothermia, the circulation was stopped. Antegrade cerebral perfusion (5–15 mL/[kg · min]) was typically used for adjunct cerebral perfusion during the period of systemic DHCA. After aortic reconstruction, CPB was reinstituted, and the patient was gradually rewarmed to a normal temperature after a 5-minute period of cold reperfusion for free radical washout. Four units of fresh-frozen plasma were typically added to the circuit to ensure adequate anticoagulant factors during DHCA. A hematocrit of 0.18 to 0.20 was generally acceptable during CPB, although this was increased to more than 0.20 for separation from CPB. Protamine sulfate was administered after separation from CPB to reverse heparin anticoagulation until the activated clotting time returned to baseline or the ratio of 1 mg to 100 units of heparin was reached. We maintained a general approach of avoiding unnecessary use of blood products, which were not administered unless bleeding or anemia was observed. After separation from CPB, red blood cells were transfused according to the patient's preoperative condition, volume status, and hemoglobin concentration.

Standard practice included intraoperative administration of an antifibrinolytic therapy. Before its withdrawal from the US market, aprotinin (Bayer Corporation, West Haven, Conn) was used (2-MKIU bolus and 0.5-MKIU/h infusion until bleeding cessation). Subsequently, $\epsilon$-aminocaproic acid was administered as a 10-g bolus followed by a 1-g/h infusion, with an additional 5-g bolus before separation from CPB to account for that lost during hemofiltration, which was performed in all cases to remove excess crystalloid before separation from CPB. The return of washed, shed red blood cells (BRAT II blood cell salvage machine; Cobe Cardiovascular Inc, Arvada, Colo) to the patient was routine. Transfusion decisions in the perioperative period were aided by local guidelines and use of chest tube output, activated clotting time, platelet count, fibrinogen level, thromboelastography, prothrombin time, and partial thromboplastin time, as recommended by the American Society of Anesthesiologists published guidelines.[14] Clopidogrel and other $P2Y_{12}$ inhibitors, regardless of dose, were withheld 7 days before the operation. Aspirin (325 mg) was withheld 5 days before the operation. Aspirin (81 mg) was not withheld before the operation. All antiplatelet agents were restarted at preoperative dosages on postoperative day 1 unless active bleeding was present.

### Outcome Measures

The 26 candidate variables for the analysis included age, sex, race, American Society of Anesthesiologists grade, diabetes, preoperative creatinine level, warfarin (Coumadin) use, partial thromboplastin time, platelet count, international normalized ratio, hemoglobin concentration, weight, height, body surface area, blood pressure, aprotinin use, previous cardiac surgical procedure, emergency status, concomitant cardiac procedure, total arch versus hemiarch repair, thoracoabdominal aortic aneurysm type, aortic crossclamp time, cerebral circulatory arrest time (period when brain was receiving less than 100% of normal cerebral blood flow, including antegrade or retrograde cerebral perfusion), systemic circulatory arrest time (period during which lower body was not perfused, longer than cerebral circulatory arrest time for total arch replacement and open descending or thoracoabdominal aortic repairs and equal to cerebral circulatory arrest time for hemiarch repairs), and CPB time. Allogeneic blood product use included all products given from the time of incision through postoperative days 0, 1, and 2, including any given at the time of return to the operating room for bleeding. Volume of intraoperative blood cell salvage machine transfusion was not included in this calculation, because this blood is not allogeneic. Considering the need for massive transfusion as a dichotomous outcome, we used a previously described definition of massive transfusion.[11] Patients who received at least 5 units of packed red blood cells (PRBCs) were defined as having had massive transfusion.

### Statistical Analysis

Patient and operative characteristics are summarized according to presence or absence of massive transfusion. Table 1 presents categoric variables as percentages; continuous variables are presented as mean ± SD unless otherwise stated. For comparisons, the Wilcoxon rank sum test was used for continuous variables, and the $\chi^2$ test was used for categoric variables, with an alternative hypothesis that the rates across columns were not equal.

We evaluated the association of patient and procedural characteristics with the need for transfusion in 2 ways. Primarily, a linear regression model was developed with total blood products transfused as the outcome variable. Total blood products included all allogeneic products from the case start time through 48 postoperative hours. Because blood product use was not normally distributed, a log transform was performed before

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