Risk Factors Related to Transfusion Requirements in Patients Undergoing Implantation of Ventricular Assist Devices

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Objective: **The identification of transfusion risk factors in patients receiving left ventricular assist devices to allow for targeted use of blood conservation strategies and improved blood utilization.**

Design: **This is a retrospective analysis of prospectively collected data between April 2009 and June 2012. Linear regression was used to determine factors associated with increased transfusion. Logistic regression was used to determine factors that were associated with more than the median number of units transfused.**

Setting: **Single center, university hospital.**

Participants: **Patients (n = 144) who underwent left ventricular assist device implantation.**

Intervention: **Transfused blood product data for the day of surgery and for 3 days after were obtained from the blood bank.**

Measurements and Main Results: **Beta-blockers were associated with 1.7 ± 0.65 fewer red blood cell (RBC) units and 2.2 ± 0.7 fewer fresh frozen plasma units transfused. Each year of older age was associated with 0.113 ± 0.023 units of RBC, 0.543 ± 0.101 platelet, and 0.098 ± 0.017 plasma units transfused. International normalized ratio was associated with more platelet transfusion (20.813 ± 5.757 units per 1.0 increase), but not with plasma or RBC transfusion. Lower platelet counts were associated with both platelet (-0.045 ± 0.019 units per 10,000 μL^{-1}) and plasma transfusions (-0.011 ± 0.004). Myocardial infarction was associated with increased RBC and plasma transfusion, and cardiogenic shock was associated with increased platelet transfusions, but nitrate use was associated with reduced platelet transfusion.**

Conclusion: **Beta-blockers may be a modifiable factor to decrease transfusions. The association between international normalized ratio and platelet transfusions suggests that better determination of the type of coagulopathy may promote more appropriate transfusions.**

KEY WORDS: circulatory assist devices, ventricular assist devices, VADs, transfusion, bleeding

HEMORRHAGE IS a common complication associated with placement of ventricular assist devices (VAD).[1,2] Hemorrhage can lead to hypoperfusion and multiorgan failure and is treated frequently with transfusion, both to replenish red blood cells (RBC) and to promote hemostasis. Transfusion of RBC has been associated with postoperative complications, such as sepsis, late mortality, and right ventricular failure in patients receiving VAD.[3–5] Perioperative hemorrhage can have many causes, including preoperative coagulopathy from hepatic dysfunction, poor nutritional status, preoperative anticoagulants, and antiplatelet agents; cardiopulmonary-bypass–induced thrombocytopenia and platelet dysfunction; and the extensive nature of the surgery, which requires median sternotomy, cardiac mobilization (often in patients who have had previous cardiac surgery), and extensive dissection to create a pocket for the pump.

Although transfusion is common, there have been few studies to determine the risk factors for transfusion and none for the individual blood components.[6] Studies in patients undergoing coronary artery bypass grafting have shown that patient variables can predict transfusion risk.[7] The identification of such risk factors in VAD patients may allow for targeted use of blood conservation strategies, improved efficiency in blood utilization, and education of patients regarding the risk of transfusion.[8–10] It also may allow for further research into individual risk factors to better understand the pathophysiology of bleeding in this unique surgical population. The purpose of this study was to determine the factors associated with transfusion of RBC, platelets (PLT), and fresh frozen plasma (FFP) in patients receiving elective left VAD.

METHODS

Using prospectively collected data, a retrospective cohort study was undertaken that was approved by the institutional review board, which waived informed consent given the use of deidentified data. All patients who underwent a left ventricular assist device (VAD) procedure between April 2009 and June 2012 were included. Transfused blood (RBC, PLT, and FFP) data for the day of surgery and for 3 days after were obtained from the blood bank and included in all totals. All other data were obtained from the Department of Cardiac Surgery database, which records demographic characteristics, comorbidities, preoperative medicine usage, and perioperative processes of care.

University of Michigan is home to one of the largest VAD programs in the United States and one of only two in Michigan. It receives referrals from throughout Michigan and northwestern Ohio. Since the program began in the late 1990s, more than 580 long-term devices have been implanted. In 2012, 63 VADs were implanted.

April 2009 was chosen as the start date, because institutional perioperative protocols and management changed then in an attempt to decrease hemorrhage and transfusion.

Patients were monitored with an arterial catheter, pulmonary artery catheter, and transesophageal echocardiography. After anesthesia induction, all patients received aminocaproic acid with a loading dose of 70 mg/kg, followed by an infusion of 30 mg/kg/h. A second 70 mg/kg load was given after successful separation from bypass. Patients also received an infusion of vitamin K at 1 mg/h. If initial hematocrit >30%, autologous blood, 2 units of 400-500 mL, were removed into citrate-phosphate-dextrose sterile collection bags for later reinfusion. If needed, hypotension was treated with phenylephrine or norepinephrine.

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After positioning, sterile preparation, and draping, a midline incision was made from the sternal notch to just below the xiphoid process. The sternum was divided and the pericardium suspended. A preperitoneal space was created in the left upper quadrant and the device positioned there. The inlet cannula was positioned across the diaphragm along the costal margin to the apex of the left ventricle (this step was eliminated for VADs placed intrapericardially). The driveline was tunneled and exited the right upper quadrant below the costal margin in the midclavicular line. Heparin (300 units/kg) was administered with a goal activated coagulation time of 450 seconds. Standard cannulation was performed using the ascending aorta for arterial inflow and bicaval drainage for venous return. Cardiopulmonary bypass circuits were Xcoating (Terumo, Inc, Tokyo, Japan), and the oxygenator was CAPIOX RX (Terumo, Inc, Tokyo, Japan). Once on cardiopulmonary bypass, an apical core of left ventricular muscle was removed and the apical connector of the VAD (DuraHeart, Terumo Heart Inc, Ann Arbor, MI), HeartWare (HeartWare, Framingham, MA), or HeartMate II (Thoratec Corporation, Pleasanton, CA)) was sewn to the apex of the left ventricle with 2-0 Ethibond using an interrupted, pledgetted mattress stitch. The inlet cannula of the VAD then was positioned within the apical connector and secured. A side-biting vascular clamp was placed on the ascending aorta and an aortotomy sized to the outflow graft was made. The outflow graft then was sewn to the ascending aorta using 4-0 prolene sutures in a running fashion. A needle vent was placed in the ascending aorta above the level of the outflow graft. After resumption of mechanical ventilation and deairing, the outflow cannula was connected to the outflow graft valve housing with partial release of the clamp on the aortic graft to facilitate further deairing. The VAD then was actuated electrically at low speed during weaning from cardiopulmonary bypass. The goal hematocrit for weaning from cardiopulmonary bypass was $\geq 23\%$. Nitric oxide was used for pulmonary vasodilation and right ventricular afterload reduction. Dobutamine was used for inotropy. Cannulae were removed and protamine administered. Autologous blood then was returned to the patient. If necessary, residual coagulopathy as determined by surgical discretion was corrected by transfusion of 4 units of FFP to one 5-pack of PLT. Chest tubes were placed in the mediastinum. The pericardium and the chest then were closed.

Because the study focused on both the absolute quantity of blood transfused and the massive transfusion, data were analyzed separately for the absolute quantity of blood transfused and for massive transfusion. To determine the factors (Table 1) associated with increasing units of transfused blood, linear regression was used. First, all factors were analyzed using univariate linear regressions with number of transfused units as the outcome. Then, factors with univariate p values <0.2 were used to construct multivariate linear regression models for each outcome to find independent predictors of quantity of blood products given; p-values <0.05 denoted statistical significance. Predictive accuracy of the linear regression was assessed as Pearson's correlation (r^2) between predicted and actual number of transfused units.

To determine the factors associated with large transfusion, the median number of transfused units was found first. Univariate factors were compared between those who received fewer than the median number of units and those who received more. Student's *t* test, Mann-Whitney U test, Fisher's exact test, and chi-square test were used for comparisons, as appropriate. Factors with p values <0.2 were used to construct multivariate logistic regression models to find independent predictors of receiving the median number of units or more of each blood product; p values <0.05 and 95% confidence intervals that excluded 1 denoted statistical significance. Discrimination of the logistic regression models was assessed as the area under the receiver operator characteristic curve (c-statistic).

Models for both number of transfused units and massive transfusion were created separately for each of RBC, FFP, and PLT. Statistics were done using R version 3.0.2 (R Foundation, Vienna, Austria).

Table 1. Patient Characteristics (n = 144)

Characteristics	Yes	%	
Demographic characteristics			
Race African American	25	17	
Race Caucasian	114	79	
Race Other	5	3	
Male	114	79	
Morbidities			
Smoker	25	17	
Diabetes	49	34	
Hypercholesterolemia	79	55	
Hypertension	71	49	
Chronic lung disease	51	35	
Peripheral vascular disease	7	5	
Cerebrovascular disease	16	11	
Cardiogenic shock	42	29	
Resuscitation	5	4	
Myocardial infarction	63	44	
Previous coronary intervention	131	91	
Status (emergent)	17	12	
Preoperative medication			
Beta-blocker	51	35	
ACE inhibitor	19	13	
Nitrates	18	13	
Anticoagulation	99	69	
Inotrope	116	81	
Aspirin	53	37	
Lipid-lowering medication	79	55	
Type	**Median**	**25th%**	**75th%**
Demographic characteristics			
Age (years)	58	48	64
Height (cm)	177	170	180
Weight (kg)	82	72	98.2
Body surface area (m^2)	2	1.9	2.2
Body mass index (kg/m^2)	27	23	32
Ejection fraction	10	10	15
Preoperative laboratory tests			
White blood cells (K/uL)	8.2	6.4	10.2
Hematocrit (%)	33.6	30.2	36.6
Hemoglobin (g/dL)	11.2	10.1	12.6
Platelets (K/uL)	171	128	225
Sodium (mmol/L)	134	131	137
Potassium (mmol/L)	4.1	3.9	4.4
Chloride (mmol/L)	99	96	103
Bicarbonate (mmol/L)	28.5	26	30
Blood urea nitrogen (mg/dL)	28	20	38
Creatinine (mg/dL)	1.2	1	1.5
Glucose (mg/dL)	120	104	143
Calcium (mg/dL)	9	8.6	9.3
Phosphorus (mg/dL)	3.8	3.4	4.4
Total protein (g/dL)	6.4	5.8	7
Albumin (g/dL)	3.7	3.4	4
Alanine aminotransferase (IU/L)	34	22	57
Aspartate aminotransferase (IU/L)	32	26	46
Lactate dehydrogenase (IU/L)	270	207	331
Alkaline phosphatase (IU/L)	86	70	113
Total bilirubin (mg/dL)	0.9	0.7	1.4
Prothrombin time (sec)	11.5	10.9	12.2
International normalized ratio	1.1	1	1.2
Partial thromboplastin time (sec)	27.9	25.6	38.3
MELD score	11	9	12

NOTE. 4 patients were missing ejection fraction and 1 was missing lactate dehydrogenase value.

Abbreviations: ACE, angiotensin-converting enzyme; MELD score, model for end-stage liver disease score.