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Original Article

Development of a Predictive Model for Blood Transfusions and Bleeding During Liver Transplantation: An Observational Cohort Study

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Objective: Orthotopic liver transplantation (OLT) frequently is associated with major blood loss and considerable transfusion requirements. The goal of this study was to define the risk factors for multiple transfusions and major bleeding during OLT and to help identify higher risk patients that could benefit from targeted interventions.

Design: OLTs were studied for this observational cohort study.

Setting: Community hospital.

Participants: A total of 800 consecutive OLTs were studied.

Intervention: No intervention.

Measurements and Main Results: Baseline and intraoperative data were gathered. Multivariate logistic regression analyses were performed to find variables associated with 2 outcomes: transfusion of more than 2 units of red blood cells (RBC) and bleeding $\geq$ 900 mL. Two nomograms were developed to predict individual risks. The overall intraoperative RBC transfusion was 0.6 $\pm$ 1.4 units on average, and 61 surgeries (7.6%) received more than 2 units of RBC (4.5 $\pm$ 1.9). Some variables were associated with the outcomes: 5 were associated with transfusion of more than 2 units of RBC (patient's height, starting hemoglobin concentration, starting bilirubin value, the use of a phlebotomy, and central venous pressure [CVP] at the time of vena cava clamping) and 3 with blood loss of $\geq$ 900 mL (starting hemoglobin value, Child-Turcotte-Pugh score, and CVP at the time of vena cava clamping). Preclamping CVP showed the strongest association with both outcomes. Nomograms were developed to predict the individual OLT recipients' risk of requiring more than 2 units RBC and suffering from major bleeding. Among the variables associated with multiple RBC transfusions and major bleeding, 3 can lead to interventions: baseline hemoglobin value, the use of a phlebotomy, and the preclamping CVP.

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Conclusion: Some variables were able to predict the risk of multiple transfusions and major bleeding in this low bleeding liver transplantation population. Further studies based on these variables should be done to better define the role of targeted interventions in higher risk liver transplant recipients.

Key Words: liver transplantation; bleeding; transfusion; coagulation

ORTHOTOPIC LIVER TRANSPLANTATION (OLT) often is associated with major blood loss and a need for massive blood product transfusions.[1] During the past 2 decades, a significant decrease in perioperative blood loss and blood product requirements has been observed during OLT.[2] Although some centers used very limited amount of transfusions, major intraoperative bleeding was still common in many other programs.[3–5]

Hemostasis in cirrhotic patients is a complex state characterized by a reduced level of both pro- and anticoagulant proteins. A low platelet count counterbalanced by an elevated von Willebrand factor and a low plasma levels of ADAMST13 (a von Willebrand factor cleaving protease) are other characteristics of this state.[6,7] Hyperfibrinolysis also is very common.[6,7] With such an understanding of these hemostatic characteristics, some clinicians adopted a wait-and-see approach instead of a prophylactic one, using transfusion of blood products only when active, nonsurgical bleeding occurs rather than to "correct" abnormal hemostasis laboratory values.[8,9] Such an approach likely has contributed to the observed decrease in the volume of blood transfusions associated with OLT today.[2,8] However, some studies still report populations with high amounts of RBC transfusions (mean ≥ 6 RBC units, ≥ 8 RBC units, or 20-30 RBC units) and have tried to predict transfusions with different models based on cohorts between 150 and 800 OLTs.[3–5] They obtained conflicting results for many potential predictive variables (age, starting hemoglobin value, international normalized ratio [INR], platelets count, creatinine, albumin, and second OLT).

A substantial and growing body of evidence suggests that the excessive use of blood products is associated with an increased morbidity and mortality during OLT.[9–16] Because it is likely that decreased blood loss could prevent the deleterious effects of transfusions and affect outcomes, interventions to reduce bleeding in liver transplant recipients are needed. However, few high-quality evidence supports interventions that decrease blood product exposure and improve outcomes in this population, except the use of antifibrinolytic drugs.[17–20]

To help target interventions that reduce OLT patients' exposure to blood products, predictive models to identify higher risk patients for bleeding and transfusions should be developed. Previous studies suggested that it is possible to develop such predictive models, even in a liver transplantation center with a low transfusion rate.[2,21] Therefore, the authors completed a longitudinal observational cohort study to further define the risk factors for major bleeding and multiple transfusions in their OLT population and to help identify higher risk patients. The primary objectives of this study were to describe the authors' OLT population further with a large cohort study and to develop a model that could predict the risk of using > 2 units RBC and major intraoperative bleeding based on baseline and intraoperative characteristics. The secondary objective was to develop a logistic regression-based nomogram that predicts the individual risk of these outcomes.

Patients and Methods

This is a nonexperimental observational cohort study. The authors report it according to the STROBE statement guidelines for observational studies.[22] This study was undertaken at the Centre Hospitalier de l'Université de Montréal (CHUM) (registered on Clinical Trial.gov, NCT: 02548130). After approval by the review ethics board (REB approval #15.113), all consecutive OLTs in adults that took place in the authors' center between October 2002 and February 2016 were included. No exclusion criteria were applied.

Data Collection and Management

Baseline population characteristics, including baseline laboratory values, as well as intraoperative data were collected prospectively with a standardized data report form during and after each OLT. Collected intraoperative data included duration of surgery, baseline and preanhepatic CVP, volume of fluid resuscitation, type of fluid used, volume of phlebotomy performed, blood products transfused, volume of cell saver reinfused, total bleeding, and total intraoperative diuresis. Postoperative hemoglobin, creatinine, and INR values, as well as mortality up to 1 year, also were collected. Data were kept in a secured database. Because all OLTs were included, no selection bias was expected.

Outcomes

The authors' outcomes of interest were the number of RBC units transfused and the total intraoperative blood lost. Intraoperative blood lost was measured from the blood suctioned through the cell saver minus the irrigating fluid put in the surgical field.

Intraoperative Management Protocol

A standard monitoring and anesthesia technique were used in all patients, as previously described.[2,8,18] All grafts were harvested from cadaveric donors and were transplanted using a total cross-clamping technique with vena cava replacement. The transfusion of procoagulant blood products was based on a "wait and see," approach and all blood products were