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A quantitative model to predict blood use in adult orthotopic liver transplantation

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ABSTRACT

To identify preoperative predictors for the use of any blood component during and after orthotopic liver transplantation (OLT), we performed a retrospective analysis on 602 OLT patients who were randomly split into a training set (n = 482) and a validation set (n = 120). Hemoglobin and calculated MELD score were identified as independent predictors for blood use using bootstrap aggregation. A logistic regression model constructed using both variables showed comparable performance in the training and validation sets. Predictive scores can be obtained from a nomogram, and a score above –2.328 predicted transfusion of any blood component with a positive predictive value of 97% and 96% in the training and validation sets, respectively.

1. Introduction

Blood transfusion has played an important role in orthotopic liver transplantation (OLT) since the first successful procedure in 1967. With the improvement of surgical techniques and anesthesia practices, the amount of blood transfused has been dramatically reduced [1–3]. Some centers achieved avoidance of RBC transfusion in up to 40% of liver recipients [4–7], and bloodless OLT has been reported in single cases and case series [8–16]. Also contributing to this trend is the increasing awareness of the hazards associated with blood transfusion in OLT [4,17,18], which have been observed in patients receiving red blood cells, platelets and plasma products [17,19,20]. Even a moderate number of blood components has been associated with longer hospitalization and shortened survival [4]. These factors make it desirable to perform OLT with as little blood transfusion as tolerated. However, most patients still require transfusion support during and after OLT, and preoperative predictors for such requirement can prepare the blood bank for timely provision of life-saving blood.

Prediction of blood use will serve additional purposes in some extreme cases when blood transfusion is unacceptable to an individual or compatible products are not easily available. The former presents a unique ethical dilemma in Jehovah's Witnesses patients, who on the basis of religious beliefs refuse transfusion of blood products [8–16,21]. The reliance on blood transfusion may also delay OLT in patients with numerous red blood cell alloantibodies or with deficiencies in IgA or haptoglobin [22,23]. Therefore, it is beneficial to have a clinical tool to aid decision making and pretransplant counseling about whether OLT can be offered to patients with religious or biological barriers to blood transfusion. The goal of this study was to identify preoperative predictors for the use of any blood

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products, including red blood cells, platelets, plasma products, and cryoprecipitates, in an individual during and immediately after OLT. We also aimed at constructing a quantitative model to predict the probability of blood use in this clinical context.

2. Materials and methods

2.1. Study population

This is a retrospective study approved by the Human Research Protection Office of the Washington University School of Medicine. A total of 602 consecutive patients who received primary OLT between 1/1/2002 and 2/28/2011 in our institution were included. This study period was chosen because the practice of liver transplantation was relatively consistent during the interval (see the sections below on transplantation technique and transfusion protocol). Exclusion criteria include patients undergoing re-transplantation, liver–kidney transplantation, pediatric patients younger than 18 years old, and cases with extensive missing data.

2.2. Preoperative variables

Data were collected from an electronic database maintained by the Liver Transplant Division and the patients' hospital and clinic records. The demographic variables included age, body mass index (BMI), gender, and race. The primary diagnosis underlying the end stage liver disease was listed if comprising at least 5% of the study population; all others were listed under miscellaneous. The pretransplant diagnosis of HCC was coded as a separate variable. Comorbidities included diabetes, hypertension, heart disease, kidney disease and histories of cholecystectomy, transjugular intrahepatic portosystemic shunt (TIPS), and other abdominal surgeries. Presence of ascites of 5L or more, preoperative portal vein thrombosis, date of transplantation and wait-list time were also recorded. Pretransplant laboratory data included serum concentrations of sodium, albumin, creatinine and bilirubin, hemoglobin level, platelet count, International Normalized Ratio (INR), and calculated Model for End-Stage Liver Disease (cMELD) score [24]. Donor related variables included donor age, BMI, gender, procurement of the organ from local or distant facilities, cold ischemia time, and whether split liver or donation after cardiac death was used.

2.3. Primary aim

The primary aim of this study was to predict the use of one or more units of any blood component during and after OLT throughout the hospitalization. The blood components include packed red cells, single-donor platelets, plasma products (including fresh frozen plasma and thawed plasma) and cryoprecipitates.

2.4. Liver transplantation and transfusion protocol

Liver transplantations were performed by a dedicated liver transplant team during the study period. It consisted of four transplant surgeons and seven anesthesiologists who practiced under the same guideline. Standard piggy-back technique with caval preservation without the use of veno-venous bypass was practiced. Conventional coagulation parameters including prothrombin time (PT) and partial thromboplastin time (PTT), rotational thromboelastometry (ROTEM), and clinical assessment of the operative field were used to guide transfusion therapy. Red blood cells were administered to maintain the hematocrit above 20%; single donor platelets were transfused to maintain the platelet count above 25×10^9/L, or in response to signs of platelet dysfunction on ROTEM; INR was kept below 3 with plasma products. Most patients received one empiric dose of tranexamic acid (10 mg/kg). Additional antifibrinolytics and cryoprecipitate were administered based on specific ROTEM runs, including Fibtem for cryoprecipitate administration and Aptem for antifibrinolytics, although no absolute threshold values were implemented. Intraoperative use of the cell saver and isovolemic hemodilution was not part of our standard management.

2.5. Statistical analysis

Statistical analysis was performed using SPSS Statistics Version 20 (IBM, Armonk, NY), and stats and rms packages in R [25]. The study population (n = 602) was randomly split into a training set (n = 482) and a validation set (n = 120) that are non-overlapping. Standard descriptive statistics were used to describe the characteristics of the patients. Categorical variables were compared among the two groups using Chi-Square Test. Continuous variables were compared using *t* Test or Mann–Whitney *U* Test as appropriate. A two-sided p value of <0.05 was considered statistically significant.

Bootstrap aggregation was performed in the training set similarly to the work by Cywinski et al. to select independent predictors for the use of any blood product [26]. Briefly, the training set was sampled with replacement and variables with $p < 0.1$ on univariate analysis were entered into a logistic regression model using the backward stepwise method and were retained in the model if $p < 0.05$. cMELD score and its three components were analyzed separately due to strong interactions. The procedure was iterated for 1000 times, and variables that were significant in more than 50% of bootstrap analyses were deemed reliable predictors for blood use. These predictors were entered into the final logistic regression models, which were evaluated based on Nagelkerke R^2 and C index. Predictive scores were calculated by summing the products of each predictor multiplied by its corresponding regression coefficient. A nomogram was generated using an online tool [27] to determine predictive scores for patients with paired hemoglobin concentration and cMELD score. The best threshold was determined by analyzing the receiver operating characteristic (ROC) curve using the pROC package in *R*, and the positive and negative predictive values were compared between the training and validation sets.

3. Results

3.1. Patient characteristics

The demographic and clinical characteristics of the training and validation sets were largely comparable (Table 1).

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