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Bloodless living donor liver transplantation
Risk factors, outcomes, and diagnostic predictors

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Abstract

Massive bleeding is often unavoidable during liver transplantation (LT). However, blood transfusions are associated with risks and should be avoided whenever possible. This study compares preoperative factors and outcomes between non-transfusion and transfusion groups to identify variables that could be used to predict bloodless surgery in living donor liver transplantation (LDLT) patients.

We conducted a retrospective study of 87 LDLT patients. The group of patients who did not require packed red blood cell (PRBC) transfusion (non-PRBC group, n = 44) was compared with those who did (PRBC group, n = 43). We compared risk factors, fluid management, and outcomes between the groups and identified variables for prediction of transfusion during LDLT.

Compared with the PRBC group, the non-PRBC group had a lower model for end-stage liver disease (MELD) score (8.1 ± 1.1 vs 18.2 ± 8.8), international normalized ratio (INR) (1.16 ± 0.1 vs 1.80 ± 0.94), and partial thromboplastin time (PTT) (37.1 ± 6.3 vs 54.1 ± 24.0), but higher hemoglobin (Hb) (13.6 ± 1.6 vs 11.5 ± 2.2) and hematocrit (HCT) (39.1 ± 4.4 vs 32.6 ± 6.0). The non-PRBC group were more likely to receive colloid and albumin but had shorter intensive care unit (ICU) and hospital length of stay. The area under the receiver operative characteristic (ROC) curve of the MELD score was the highest (91%) using a cutoff value of 10.5.

Patients without PRBC transfusion during LDLT were in better condition preoperatively and had better outcomes. The MELD score is a significant predictor for PRBC transfusion.

Abbreviations: BIS = bispectral index, DDLT = deceased living donor liver transplantation, ECG = electrocardiography, Hb = hemoglobin, HCT = hematocrit, ICU = intensive care unit, INR = international normalized ratio, LDLT = living donor liver transplantation, LT = liver transplantation, MELD = Model for End-Stage Liver Disease, PRBC = packed red blood cell, PTT = partial thromboplastin time, ROC = receiver operating characteristic, TB = total bilirubin.

Keywords: blood transfusion, liver transplantation, living donor, predictor, red blood cell, risk factor

1. Introduction

The requirement for blood transfusion during liver transplantation (LT) following massive bleeding has been of significant concern since LT was first performed by Starzl et al in 1963. In addition to the risks posed by bleeding itself, patients requiring transfusion have more septic episodes, worse graft survival, and longer intensive care unit (ICU) and hospital stays.[1] Transfusion itself is associated with a variety of complications: hemolytic and allergic reactions, transfusion-related acute lung injury, risk of infection, graft versus host disease, and immune sensitization.

Several studies have described anesthetic and surgical techniques that can be used to reduce the need for transfusion.[2–4] However, bloodless LT remains uncommon and minimizing the need for blood transfusion during transplantation is an ongoing challenge.

Previous reports have identified a number of preoperative variables associated with increased risk of intraoperative hemorrhage during deceased donor liver transplantation (DDLT) and a consequent requirement for blood transfusion, including primary diagnosis, preoperative coagulation test results, and biochemical parameters.[5–7] In contrast, no study has evaluated factors associated with requirements for blood transfusion during living donor liver transplantation (LDLT). Therefore, we investigated patients' clinical and laboratory factors, outcomes, and diagnostic predictors associated with the need for blood transfusion in LDLT.

This study has 2 aims: first, to compare clinical factors and outcomes between LDLT patients who underwent PRBC transfusion and those who did not; and second, to determine factors that can be used to predict bloodless LDLT.

2. Methods

With the approval of the institutional review board of Pusan National University Yangsan Hospital (ID 05–2015-097), we retrospectively reviewed data from clinical records of 87 patients who underwent LDLT at Pusan National University Yangsan Hospital, during a 3-year period from December 14, 2011 to December 23, 2014.

Preoperative demographics and risk factors.

	Entire group (n=87)	Non-PRBC group (n=44)	PRBC group (n=43)	P value
Age (yr)	50.7±11.6	53.3±5.4	50.5±11.7	.077
Gender (Male/Female, %)	66/21 (76/24)	37/7 (84/16)	29/14 (67/33)	.070
MELD score	13.1±8.0	8.1±1.1*	18.2±8.8	<.001
Previous abdominal surgery	21 (24)	9 (20)	12 (28)	.574
Preoperative Hb	12.5±2.2	13.6±1.6*	11.5±2.2	<.001
Hematocrit (%)	35.9±6.2	39.1±4.4*	32.6±6.0	<.001
Platelet (×10³/μL)	99.3±59.6	106.5±48.7	91.9±68.8	.257
INR	1.47±0.7	1.16±0.1*	1.80±0.94	<.001
PTT (sec)	45.5±19.4	37.1±6.3*	54.1±24.0	<.001
Serum creatinine (mg/dL)	0.87±0.4	0.78±0.2	0.96±0.58	.066

All measured values are presented as mean ± standard deviation or numbers of patients (%).

Hb = score, hemoglobin, INR = international normalized ratio of prothrombin time, MELD = model for end-stage liver disease, PTT = partial thromboplastin time.

* $P < .05$ compared with the PRBC group.

At our hospital, anesthetic management during LT is performed using a standardized protocol developed by consensus between all anesthesiologist groups. The anesthetic protocol used during the study period was similar to the protocol that is currently used. The protocol included induction with etomidate or propofol, muscle relaxation with cisatracurium, positive pressure ventilation with an oxygen/air mixture, and anesthesia maintenance with remifentanil and low end-tidal concentrations of desflurane titrated to optimal bispectral index (BIS, XP version 4.1; Aspect Medical Systems, Newton, MA, USA). All hemodynamic monitoring parameters were recorded at five-minute intervals.

Radial arterial pressure, capnography, bispectral index, central venous pressure, femoral venous pressure, pulmonary arterial pressure, body temperature, electrocardiography (ECG), oxygen saturation, and cerebral oximetry (INVOS 5100; Somanetics Corp., Troy, Michigan, USA) were continuously monitored throughout the surgery. Cardiac output and stroke volume variation were measured using the Vigileo/FloTrac (Edwards Lifesciences Corp, Irvine, California, USA). Arterial blood gas analysis and lactate and blood glucose level measurements were performed every hour. PRBC transfusion was administered for patients with a hemoglobin (Hb) level of less than 7 mg/dL and a lactate level greater than 5 mmol/L. All surgical procedures were performed by a single experienced surgical team throughout the study period.[8]

Patients treated with PRBC transfusion were classified as the "PRBC group" and those who were not as the "non-PRBC group." Preoperative demographics, risk factors, intraoperative fluid management, and postoperative outcomes were compared between the 2 groups. Preoperative clinical variables included age, gender, model for end-stage liver disease (MELD) score, and previous history of abdominal surgery. Laboratory test variables included Hb, hematocrit (HCT), platelet count, international normalized ratio of prothrombin time (INR), partial thromboplastin time (PTT), and serum creatinine level. The MELD score included 3 objective parameters: serum total bilirubin (TB), INR, and creatinine (MELD = $3.78 \times \ln$ [serum bilirubin (mg/dL)] + $11.2 \times \ln$ [INR] + $9.57 \times \ln$ [serum creatinine (mg/dL)] + 6.43; where ln = natural log). Intraoperative fluid management variables included volume of administered blood components, colloid, and albumin. Postoperative outcomes included length of stay in the ICU, length of stay in hospital, postoperative mortality, and postoperative surgical procedures.

2.1. Statistical analysis

Statistical calculations were performed using SPSS 13.0 (IBM Corp., Armonk, New York, USA). Categorical variables were analyzed using Pearson Chi-squared test. Parametrically distributed data were compared using unpaired Student t tests and non-parametrically distributed data were compared using the Mann–Whitney U test. A P value of less than .05 was defined as significant. The discriminatory power of preoperative risk factors for predicting a requirement for transfusion was assessed by the area under the receiver operating characteristic (ROC) curve. To identify variables that could predict the need for PRBC transfusion, a multiple logistic regression model was used.

3. Results

3.1. Preoperative risk factors

Preoperative patient demographics and clinical and laboratory variables for the entire group and the non-PRBC and PRBC groups are listed in Table 1. The non-PRBC group had a lower preoperative MELD score (8.1±1.1 vs 18.2±8.8), INR (1.16± 0.1 vs 1.80±0.94), and PTT (37.1±6.3 vs 54.1±24.0), but higher Hb (13.6±1.6 vs 11.5±2.2) and HCT (39.1±4.4 vs 32.6 ±6.0) compared with the PRBC group.

3.2. Intraoperative fluid management

A mean of 3.5 units (± 5.5 units) of PRBCs were transfused across the whole group. Forty-four patients (51%) did not receive PRBCs; the remaining 43 patients received a mean of 7.1 units (± 6.0 units) of PRBCs. However, the non-PRBC group received greater amounts of colloid and albumin (Table 2).

3.3. Influence of PRBC transfusion on patient outcome

The PRBC group had an increased requirement for ICU care ($P < .001$) and an increased duration of hospital stay ($P < .001$). There were no statistically significant differences observed between the non-PRBC group and PRBC group for other patient outcomes (Table 3).

3.4. Factors predicting the need for PRBC transfusion

Among the preoperative risk factors, the MELD score, Hb, HCT, and INR had discriminatory power between the non-PRBC and

Table 2

Intraoperative transfusion of blood components and fluid management.

	Entire group (n=87)	Non-PRBC group (n=44)	PRBC group (n=43)	*P* value
PRBC (units)	3.5±5.5	0*	7.1±6.0	<.001
FFP (units)	3.1±4.7	0*	6.3±4.9	<.001
Platelet (pheresis, units)	1.4±3.3	0*	2.7±4.2	<.001
Colloid (mL)	195.4±298.8	272.7±331.6*	116.3±240	.0138
Albumin (20%, mL)	327.8±224.2	234.1±155.4*	423.7±244	<.001

All measured values are presented as mean±standard deviation.
FFP=fresh frozen plasma, PRBC=packed red blood cell.
* *P*<.05 compared with the PRBC group.

Table 3

Postoperative outcomes.

	Entire group (n=87)	Non-PRBC group (n=44)	PRBC group (n=43)	*P* value
ICU stay (days)	9.6±6.7	7.3±3.2*	12.0±8.4	<.001
Hospital stay (days)	31.6±21.6	27.5±14.7*	35.8±26.4	<.001
Postoperative mortality	4 (4.6)	0 (0)	4 (9.3)	.1305
Postoperative surgical precedures				
Re-procedure	6 (6.9)	1 (2.3)	5 (11.6)	.2149
Bleeding control	9 (10.3)	4 (9.0)	5 (11.6)	1

All measured values are presented as mean±standard deviation.
ICU=intensive care unit, PRBC=packed red blood cell.
* *P*<.05 compared with the PRBC group.

PRBC groups using ROC curve analysis. For the MELD score, the area under the ROC curve was the highest (91%) using a cutoff value of 10.5 (Fig. 1, Table 4). In the multiple logistic regression analysis with forward selection, the variables included in the final predictive model were MELD score, platelet count, sex, and creatinine. However, only the MELD score was found to be a statistically significant predictor of PRBC transfusion (*P*<.001) (Table 5).

4. Discussion

This study demonstrated a remarkable rate of bloodless LDLT (50.6%) achieved through the coordinated efforts of the anesthesiologist and surgeon over the last 3 years. We had well-defined criteria for PRBC transfusion and strictly adhered to them. Our PRBC transfusion criteria were not associated with adverse effects.
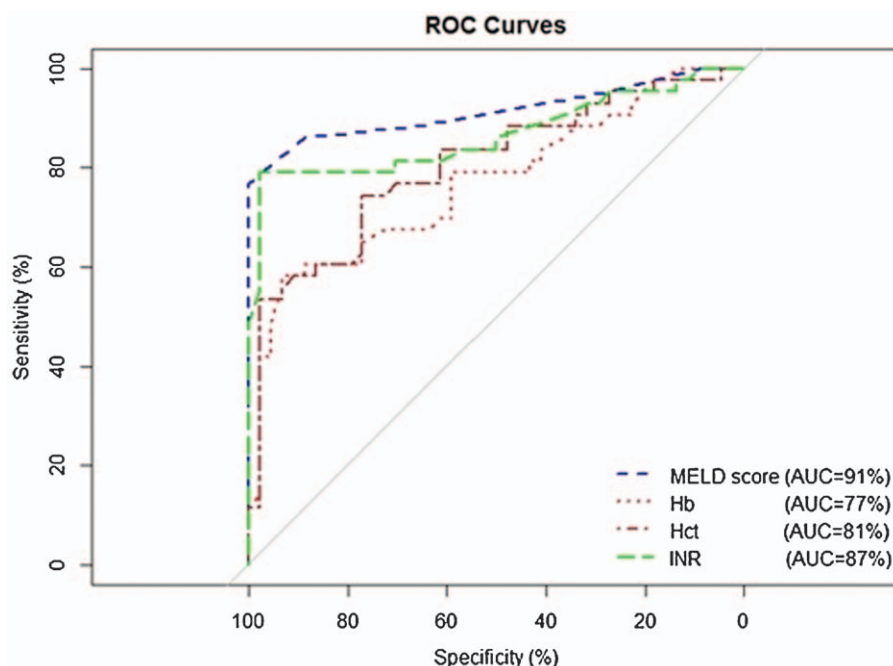

Figure 1. Area under the receiver operating characteristic curve was used to identify the discriminatory power between the two groups. Hb=hemoglobin, HCT=hematocrit, INR=international normalized ratio of prothrombin time, MELD=model for end-stage liver disease.

Table 4

Results of receiver operating characteristic curve to identify the discriminatory power between two groups.

	Cut off value	Specificity	Sensitivity
MELD score	10.5	100.0	76.7
Hb	11.5	93.2	58.1
Hct	36.6	77.3	74.4
INR	1.31	97.7	79.1

Hb = score, hemoglobin, Hct = hematocrit, INR = international normalized ratio of prothrombin time, MELD = model for end-stage liver disease.

This retrospective study was conducted to analyze outcomes associated with a high rate of bloodless LDLT in patients undergoing LDLT. In addition, this study may have important implications as previous studies have analyzed factors associated with PRBC transfusion during DDLT, rather than LDLT.[9,10]

In an analysis of preoperative factors associated with the need for PRBC transfusion, we found that patients in the non-PRBC group were in a better condition preoperatively than those in the PRBC group, similar to results from other studies.[4,11] The non-PRBC group had a decreased requirement for ICU care and hospitalization. A limitation of this study is that we could not demonstrate the independent effects of PRBC transfusion on patient outcome.

Several reports[3,4] emphasize the difficulties in identifying generally applicable preoperative factors that can reliably predict the need for PRBC transfusion during DDLT. The results of these studies may be influenced by variability in surgical procedures and anesthetic protocols. In contrast, in our study of LDLT, the patients received the same anesthetic management and surgical treatment.

One of the main purposes of our study was to identify predictive preoperative factors for bloodless LDLT using strict PRBC transfusion criteria. First, our findings using ROC curve analysis suggested a positive point that can be used as a standard to determine the need for PRBC transfusion (MELD score, Hb, HCT and PTT/INR) (Fig. 1). Second, we demonstrated that the MELD score is a powerful predictive factor for PRBC transfusion requirements using multiple logistical regression analysis. This result is important because previous studies[3,11] have not been able to determine statistically significant predictors for PRBC transfusion requirements using multiple logistical regression analysis. A study by Massicotte et al. confirmed that the MELD score could not predict blood loss and PRBC transfusion during DDLT.[12] However, they examined PRBC transfusion rates of patients with higher levels of MELD than those in our study. Moreover, there has been a lack of interest in determining predictive factors for PRBC transfusion requirements in LDLT.

Table 5

Results of logistic regression analysis with forward selection to detect predictors.

	Estimate	Standard Error	Odds ratio	P value
MELD score	1.173	0.322	3.232	<<.001
Platelet	0.014	0.008	1.014	.072
Sex (based on a men)	−2.050	1.019	0.129	.044
Creatinine	2.267	2.305	9.554	.156

MELD = model for end-stage liver disease score.

This study has important limitations; however, most of these stems from the selection of preoperative clinical variables and the small sample size. For effective clinical recommendation to be made based on the results of study, future studies should be performed that include larger samples and a greater number of risk factors.

The aim of the present study was to compare factors between patients treated with and without PRBC transfusion, and to identify significant predictors associated with requirements for PRBC transfusion, in patients treated using well-defined criteria for transfusion.

In conclusion, patients in the non-PRBC group were in a better condition preoperatively. A requirement for PRBC transfusion was associated with an increased need for ICU care and longer hospital stays. We also found that the MELD score was a significant predictive factor of the requirement for PRBC transfusion. Many studies report that blood transfusion can cause serious complications.[13] Reducing the need for blood transfusion is important in LDLT patients, who often have unstable hemodynamics and an imbalance in electrolytes during the operation. We were able to avoid PRBC transfusion in 50% of LDLT patients using strict criteria for PRBC transfusion. We hope that our findings are useful to other physicians who plan to attempt bloodless LDLT. Further large studies should be performed at multiple organizations, based on the findings of this study, to attempt to reduce blood transfusions during LT.

Author contributions

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