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The Impact of Intraoperative Donor Blood on Packed Red Blood Cell Transfusion During Deceased Donor Liver Transplantation: A Retrospective Cohort Study

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Background. Blood from deceased organ donors, also known as donor blood (DB), has the potential to reduce the need for packed red blood cells (PRBCs) during liver transplantation (LT). We hypothesized that DB removed during organ procurement is a viable resource that could reduce the need for PRBCs during LT. **Methods.** We retrospectively examined data on LT recipients aged over 18 y who underwent a deceased donor LT. The primary aim was to compare the incidence of PRBC transfusion in LT patients who received intraoperative DB (the DB group) to those who did not (the nondonor blood [NDB] group). **Results.** After a propensity score matching process, 175 patients received DB and 175 did not. The median (first–third quartile) volume of DB transfused was 690.0 mL (500.0–900.0), equivalent to a median of 3.1 units (2.3–4.1). More patients in the NDB group received an intraoperative PRBC transfusion than in the DB group: 74.3% (95% confidence intervals, 67.8-80.8) compared with 60% (95% confidence intervals, 52.7-67.3); $P = 0.004$. The median number of PRBCs transfused intraoperatively was higher in the NDB group compared with the DB group: 3 units (0–6) compared with 2 units (0–4); $P = 0.004$. There were no significant differences observed in the secondary outcomes. **Conclusions.** Use of DB removed during organ procurement and reinfused to the recipient is a viable resource for reducing the requirements for PRBCs during LT. Use of DB minimizes the exposure of the recipient to multiple donor sources.

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INTRODUCTION

Transfusion of packed red blood cells (PRBCs) during liver transplantation (LT) has been associated with increased morbidity and mortality.[1-5] Clinical studies have shown that transfusion of PRBCs during kidney transplantation is associated with delayed graft function.[6] Reducing PRBC transfusion during LT has been reported to decrease the frequency of acute cellular rejection by inducing immunological tolerance to the liver allografts.[7-11] Use of donor blood (DB) during LT could reduce the requirements for PRBCs and minimize exposure of the recipient to multiple donor sources. There is experimental and clinical evidence of the potential for induction of tolerance to liver allografts by DB transfusion.[7,10,12]

In contrast to the use of PRBCs, DB transfusion may positively affect graft survival.[7] DB is the use of blood from the deceased organ donor for subsequent transfusion into the organ recipient. Although the transfusion of DB and PRBCs are considered as an allogeneic transfusion, the storage of PRBCs is not a benign process and differs fundamentally from DB in numerous regards. Storage of PRBCs decreases the amount of 2,3 diphosphoglycerate

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(DPG),[13] which normally promotes the release of oxygen in deoxygenated tissues.[13] Likewise, there is a reduction in red blood cell–mediated vasodilation, which can adversely affect blood flow to hypoxic tissues. Massive PRBC transfusion also exposes the recipient to multiple donor sources. In contrast, red blood cells that are collected by cell salvage during surgery (ie, autologous transfusion) do not suffer similar decreases in the amount of DPG.[14] This results in better oxygen-carrying capacity and increased hemoglobin-oxygen affinity, compared with PRBCs.[15] Following transfusion of PRBCs in vivo, levels of DPG decrease; this does not happen after transfusion of blood collected via cell salvage.[16]

To date, no study has investigated the use of DB in the setting of deceased donor LT. In our hospital, in preference to PRBC transfusion, DB is collected from all deceased liver donors and transfused into LT recipients as part of standard transfusion practice. Accordingly, LT recipients only receive PRBCs when the available DB has been administered, and there is an ongoing need for red cell transfusion.

No formal analysis of this unique DB transfusion practice has been undertaken. Therefore, we hypothesized that the use of DB removed during organ procurement is a viable resource for reducing the requirements of PRBCs during LT. We conducted a propensity-matched cohort study of patients undergoing deceased donor liver LT, comparing PRBC requirements in LT patients who received DB to those who did not.

MATERIALS AND METHODS

The study was conducted at Austin Health, a university teaching hospital based in Melbourne, Australia, which is home to the Victorian Liver Transplant Unit. The unit is a collaborative service between Austin Health and Melbourne's Royal Children's Hospital. To date, >1200 transplants have been undertaken by a multidisciplinary team of 5 transplant surgeons and 9 anesthesiologists.

The unit is part of a nationally coordinated system for organ and tissue donation for transplantation. Our team undertakes organ retrievals nationally. Austin Health is the site for all LT for the Australian states of Victoria and Tasmania. We have used DB for all in-state recipients since our first LT in 1993.

The study was approved as a quality improvement project by the Austin Health Human Research Ethics Committee (Approval number LNR/18/Austin/250). Because of the noninterventional and retrospective study design, the need for informed written consent from participants was waived. The study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR no: 12619000222145).

Study Aims and Objectives

The primary aim was to compare the PRBC transfusion incidence in LT patients who received intraoperative DB (the DB group) to those who did not (the nondonor blood [NDB] group). Secondary outcomes investigated were differences between the groups in the transfusion of other blood and coagulation products, reoperation rates, hepatic or portal vein thrombosis within 30 postoperative days, primary graft nonfunction, intensive care unit (ICU) and hospital length of stay, and long-term graft failure. Primary graft nonfunction was defined as poor graft condition requiring transplantation or progressing to patient death within the first 30 d of surgery in the absence of vascular conditions, such as hepatic artery and portal vein thrombosis.[17] Long-term graft failure was defined as the need for retransplantation after 30 postoperative days.

Patient Selection

We examined data on all LT recipients over the age of 18 years who underwent a deceased donor LT at Austin Health between November 2009 and November 2018. Excluded were patients who underwent living-related LT (DB not administered), multiorgan and redo LT, and those requiring venous–venous bypass.

During this period, all patients underwent a multidisciplinary protocolized preoperative workup that included optimization of medical comorbidities, nutrition, hemoglobin, and glycemic control. Blood and blood products were administered according to standard hospital guidelines as clinically indicated and in accordance with Australian patient blood management guidelines for critical bleeding and massive transfusion.[18] There were no changes to surgical or anesthesia techniques.

Deidentified patient data were entered into an electronic database. Data were collected through Austin Health's Data Analytics Research and Evaluation Centre and were crosschecked with blood bank and medical records by 2 independent authors. Austin Health utilizes Cerner electronic medical records, which allowed comprehensive electronic data capture and access to patient health information in the perioperative setting.

Donor Blood Collection Protocol at the Time of Organ Procurement

Immediately before skin incision, the donor medical records were checked for any contraindications to collection of DB. We collected DB for all liver organ procurements unless (1) the donor organ was being transported to an interstate transplant unit, (2) the donor and recipient ABO grouping were nonidentical, (3) the donor was rhesus positive and the recipient rhesus negative, or (4) the donor was cytomegalovirus positive and the recipient cytomegalovirus negative.

In the absence of any contraindications, 10 mL of DB was placed into a K3-ethylenediaminetetraacetic acid blood tube and labeled with the donor number, donor date of birth, and donor hospital. This blood was sent to the Austin Health blood bank for formal crosschecking of blood from the recipient.

During the organ procurement, immediately before surgical incision, the donor received a broad-spectrum intravenous antibiotic. A dedicated perfusion technician set up a 3-L cell saver collection reservoir (Haemonetics, Braintree, MA) with a 150-μm raised filter. Sterile suction tubing was connected to the reservoir suction port and suction tap. The suction tube was clamped to prevent unplanned drainage of blood. After the donor was administered 25 000 units of intravenous heparin, in most cases, the abdominal aorta was cannulated with a 22-French arterial cannula (Medtronic, Dublin, Ireland); in some cases, the portal vein was also cannulated through the inferior mesenteric vein. A 32-French catheter with side holes (Portex Limited,

Hythe, Kent, United Kingdom) was aseptically connected to the 3-L cell saver reservoir. The inferior vena cava was then ligated superior to the confluence of the common iliac veins and cannulated with the catheter, with the tip of the catheter placed at the level of the insertion of the hepatic veins into the inferior vena cava. Suction was then applied to the reservoir.

Commencement of organ perfusion occurred immediately after the release of the clamp on the tubing connected to the inferior vena cava catheter and at the time of crossclamping of the supracoeliac aorta. The liver was preserved with Belzer UW cold storage solution cooled to 2°C–6°C (36°F–43°F). The physiochemical components of the cold storage solution included sodium (29 mEq/L), a potassium (125 mEq/L), and pH of approximately 7.4 at 20°C (calculated osmolarity of 320 mOsm).

Immediately before, or at the time of aortic crossclamp, the perfusion technician released the clamp on the suction tube and ensured a good flow of DB into the cell saver reservoir. Once the cell saver reservoir was full (3-L maximum capacity), the perfusion technician labeled the reservoir with the donor details, disconnected the suction tubing, secured the ports on the reservoir, placed the reservoir into a sterile plastic bag to create an additional fluid barrier from the ice, and placed the reservoir into a liver cooler transport container, with an adequate cover of ice. The DB was transported with the donor liver to our hospital for implantation.

Donor Blood Collection Protocol for the Liver Transplantation

At the time of surgical time-out for the LT recipient site, the Austin Health blood bank confirmed compatibility of the DB with the recipient's blood. If compatible, the recipient perfusion technician removed the reservoir containing the DB and processed/washed the DB through a Cell Saver Elite system (Haemonetics), removing undesirable components, including the preservation solution. DB was concentrated using a 225-mL cell saver processing set. This resulted in a total of 900 mL of concentrated red blood cells (approximately 4 units of red blood cell equivalent). Once the DB was processed, the perfusion technician documented the volume of processed blood in the patient's medical records. If no DB was transfused, a volume of 0 mL was recorded.

Quality improvement initiatives at our institution between 1993 and 2004 assessed the safety of DB infused into 141 LT recipients. The quality improvement process confirmed that the concentrations of potassium, magnesium, and hemoglobin sampled after processing of the DB were safe for transfusion into LT recipients (Table S1, SDC, http://links.lww.com/TP/B976). Further, microbiological culture testing found no cases of organisms that were identified in the culture microbiology of DB to be present in the culture microbiology of the recipient blood within 1 wk of transplantation.

Standardization of Anesthesia, Surgery, and Blood Transfusion

All transplants were performed by a dedicated team of 5 transplant surgeons and 9 anesthesiologists. Most transplants were undertaken with 2 transplant surgeons in attendance. All patients received a "reverse -L" surgical incision and received a standard piggyback transplant technique. Anesthesia management was standardized, and routine hemodynamic monitoring included 2 arterial lines (right femoral arterial for continuous blood monitoring and a radial arterial line for dedicated blood sampling), a multilumen central venous catheter, and a pulmonary artery catheter for measurements of continuous cardiac output and mixed venous saturations. Management of coagulopathy was strictly protocolized with hourly thromboelastography to guide the rational use of coagulation factors.

Transfusion triggers for red blood cells were guided by the Australian patient blood management guidelines for critical bleeding and massive transfusion.[18] They included a hemoglobin level of ≤7 g/dL in the presence of hemodynamic stability and the absence of bleeding, or ≤8 g/dL in the presence of unpredictable and ongoing bleeding; evidence of inadequate oxygen delivery to the tissues (ie, mixed venous oxygen saturation <65%), or myocardial ischemia, defined as new ST-segment elevation/depression >0.2 mV for >1 min and new wall motion abnormalities as detected by transesophageal echocardiography or patients with impaired myocardial contractility. In these situations, a blood transfusion was considered to achieve a target hemoglobin of >8–9 g/dL. If DB was present, this was used as first-line treatment for anemia. Once all the DB was administered, PRBCs were transfused if required.

Variables Collected

Data collected included baseline patient characteristics including age at transplant, modified end-stage liver disease (MELD) score, total cold ischemic time (min), total warm ischemic time (min), international normalized ratio (INR), prothrombin time (PT) (s), albumin (g/L), creatinine (g/L), bilirubin (g/L), hemoglobin concentration (g/L), and platelet count ($\times 10^3/\mu L$). Intraoperative parameters collected included units of allogeneic transfusion requirements (PRBC, fresh frozen plasma [FFP], cryoprecipitate), minimum intraoperative temperature (°C), lowest intraoperative pH, volume of Plasma-Lyte infused (mL), volume of albumin infused (mL), volume of cell saver blood infused (mL), volume of DB transfused (mL), and the total volume of intraoperative fluids transfused (mL). We collected data on postoperative ICU stay (h) and postoperative hospital stay (d); the number of returns to the operating theater due to bleeding, infection, or other reasons, hepatic artery or inferior vena cava thrombosis requiring treatment within the first 30 d, primary graft nonfunction, and long-term graft failure.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23, and R software 3.5.2. We grouped patients into 2 groups: NDB group and DB group. Before statistical analysis, missing data analysis was performed, which confirmed that all variables had <10% missing values. Variables of the top 3 missing data rates were intraoperative lowest core temperature (5.7%), preoperative bilirubin level (4.1%), and intraoperatively administrated Plasma-Lyte volume (4.1%). All continuous variables were tested for normality using the Shapiro–Wilk

test. Nonparametric statistical methods were applied when the normality was violated. Variables that violated the normality assumption included total warm ischemic time, INR, PT, platelet counts, creatinine level, bilirubin level, intraoperative albumin, and intraoperative Plasma-Lyte. Following log-transformation and nonparametric statistical analysis, the following variables continued to violate normality—units of intraoperative packed red cells, FFPs, cryoprecipitate, platelet, and autologous cell saver volumes.

The propensity score matching method was adopted to decrease unknown biases. Propensity scores were estimated with demographic variables by multiple regression analysis and estimated with the demographic variables including age, sex, MELD score, total cold and warm ischemic times, preoperative albumin level, platelet counts, and hemoglobin level. Given that the MELD score formula includes serum bilirubin, INR, and serum creatinine, we excluded preoperative bilirubin and creatinine, PT, and INR for propensity score estimation.

Several matching processes were evaluated including optimal, nearest neighborhood, and inverse propensity treatment weighting methods. For the nearest neighborhood method, logistic regression was used to estimate the distance measure. Inverse propensity treatment weighting was applied to each case if 1 case belonged to the NDB group, and the weight was calculated by the inverse value of its propensity score. If 1 case belonged to the DB group, the weight was calculated by the inverse value of 1—propensity score.[19] R packages "MatchIt"[20] and "optmatch"[21] were used for the matching process. The most balanced model was selected based on the standardized difference (<0.1) and a visual check of propensity score distributions and standardized differences histograms.

The Student *t* test, *z* test, correlation analysis, Wilcoxon signed-rank test, and chi-squared test were used for the unmatched data according to the characteristics of variables. For the matched data, paired *t* test, *z* test, correlation analysis, Mann–Whitney test, and chi-squared test were used. All data were presented with mean ± SD, number (percentile), or median (first–third quartiles). The statistically inferred values were expressed as mean (95% confidence intervals [CIs]) with corresponding effect sizes, *P*. A 2-tailed *P* of <0.050 was considered statistically significant. The study was reported according to the STrengthening the Reporting of OBservational studies in Epidemiology statement for observational research.[22]

RESULTS

Between November 2009 and November 2018, a total of 543 adult patients underwent LT. Nineteen patients were excluded (combined liver-cardiac transplantation, n = 1; combined liver-small bowel transplantation, n = 2; combined liver-pancreas transplantation, n = 2; combined liver-kidney transplant, n = 8; redo LT, n = 6). A total of 524 LT recipients were included in the statistical analysis. There were no missing data.

Among the 4 results of the propensity score matching process, optimal 1:1 matching result showed the most balanced demographic data. Accordingly, 350 LT recipients were included in the propensity score matching process: 175 from the DB group and 175 from the NDB group. The median (first–third quartile) volume of DB transfused was 690.0 mL (500.0–900.0 mL), equivalent to a median of 3.1 units (2.3–4.1 units). Baseline patient characteristics of matched data are presented in Table 1.

Primary Outcome

After matching, more patients in the NDB group received an intraoperative PRBC transfusion than in the DB group: 74.3% (95% CI, 80.8-67.8) compared with 60% (95% CI, 67.3-52.7); $P = 0.004$, Cohen's $h = 0.31$. The

TABLE 1.

Baseline liver transplant recipient characteristics

	Matched data (N = 350)				
	NDB (N = 175)	DB (N = 175)	Mean difference (95% CI)[c]	*P*	Standardized difference[a]
Age (y)	54.1 ± 10.3	54.3 ± 11.2	–0.2 (–2.4 to 2.0)	0.847	0.020
Sex, female (%)	59 (33.7)	60 (34.3)	–	>0.999	0.012
MELD score	18.1 ± 8.8	18.8 ± 8.5	–0.7 (–2.6 to 1.3)	0.511	0.075
Total cold ischemic time (min)	360.7 ± 107.4	358.9 ± 111.3	1.8 (–8.3 to 11.9)	0.725	0.016
Total warm ischemic time (min)[b]	45 (40–53)	43 (38–50)	1.01 (0.94 to 1.09)	0.749	0.030
INR[b]	1.6 (1.3–2.1)	1.6 (1.3–2.1)	0.98 (0.91 to 1.07)	0.673	0.045
PT (s)[b]	17 (14–23)	18 (14 – 23)	0.99 (0.91 to 1.07)	0.720	0.038
Albumin (g/L)	30.6 (6.7)	30.0 (6.6)	0.6 (–0.8 to 2.0)	0.388	0.093
Creatinine (g/L)[b]	88.0 (67.0–114.0)	90.0 (68.0–127.0)	0.98 (0.89 to 1.09)	0.743	0.037
Bilirubin (g/L)[b]	91.0 (30.0–203.0)	85 (34–274)	0.89 (0.66 to 1.18)	0.414	0.091
Hemoglobin concentration (g/L)	104.6 (24.2)	102.7 (24.7)	1.9 (–3.2 to 7.0)	0.472	0.076
Platelet count ($\times 10^3/\mu\ell$)[b]	82 (55–117)	78 (53–127)	1.03 (0.89 to 1.18)	0.719	0.038

Data are presented as mean ± SD, number (percentile), or median (first–third quartiles). Mean difference is presented with 95% confidence intervals (CIs). Matching process using propensity scores produced data with balanced demographic variables, see details in the description of statistical analysis.

[a]Standardized difference >0.1, indicates an imbalanced variable of comparing groups.

[b]Log transformed variables during statistical inferences, presented as median (first–third quartiles) of original scale.

[c]Mean difference of log transformed variables presented as ratio of NDB over DB as original scale.

DB, donor blood transfused group; INR, international normalized ratio; MELD score, modified end-stage liver disease score; NDB, nontransfused donor blood group; PT, prothrombin time.

median (first–third quartile) number of PRBCs transfused intraoperatively was higher in the NDB group compared with the DB group: 3 units (0–6 units) compared with 2 units (0–4 units); $P = 0.004$, effect size $r = 0.22$. The relative risk of requiring a PRBC transfusion for patients receiving DB compared with those who did not was 1.41 (95% CI, 1.11-1.85). The number of patients needed to treat with DB to prevent a PRBC transfusion was 6.12 (95% CI, 3.68-21.92).

Secondary Outcomes

The median (first–third quartile) total number of units of blood transfused was 8.0 units (4.0–13.1 units) in the NDB group compared with 10.8 units (6.1–19.0 units) in the DB group ($P < 0.001$, effect size 0.23 units). The median (first–third quartile) estimated blood loss was higher in the DB group compared with the NDB group: 6.75 L (3.84–11.88 L) compared with 5.0 L (2.50–8.19 L); $P = 0.001$.

There were no observed differences between the groups in the number of patients who received FFP, cryoprecipitate, platelets, or autologous cell saved blood. Likewise, the volume of blood and blood product transfused were similar (see Table 2). Correlation analysis revealed that PRBC transfusion correlated with DB transfusion, MELD score, total cold ischemic time, preoperative INR, PT, hemoglobin, creatinine, and bilirubin (see Table 3). Partial correlation analysis, controlled with MELD, total cold ischemic time, and preoperative hemoglobin, found that DB transfusion was negatively correlated with intraoperative PRBC transfusion. Intraoperative fluid administration, arterial pH, and core temperature were similar between the groups (see Table 4). Postoperative outcomes were also similar, and effect sizes were small (see Table 5). There was no association with postoperative outcomes and DB transfusion (see Table 6).

TABLE 3.

Correlation analysis with intraoperative packed red blood cell transfusion

	Matched (N = 350)	
	Correlation coefficient	*P*
Correlation analysis		
Donor blood transfusion[b]	–0.166	0.002[a]
Sex[b]	0.069	0.201
Age	–0.033	0.540
MELD score	0.226	<0.001[a]
Total cold ischemic time	0.086	0.108
Total warm ischemic time	0.024	0.650
INR	0.208	<0.001[a]
PT	0.206	<0.001[a]
Preoperative serum albumin	–0.02	0.711
Preoperative platelet count	–0.064	0.235
Preoperative hemoglobin level	–0.376	<0.001[a]
Preoperative serum creatinine	0.206	<0.001[a]
Preoperative serum bilirubin	0.241	<0.001[a]
Partial correlation analysis		
Donor blood transfusion[b]	–0.159	0.003[a]

[a]$P < 0.050$ with correlation analysis.
[b]Spearman's rho Correlation Coefficient.
INR, international normalized ratio; MELD score, modified end-stage liver disease score; PT, prothrombin time.

DISCUSSION

We performed a propensity-matched analysis of adult patients undergoing deceased donor LT who received DB during their transplant. An analysis of 350 patients (175 in each arm) with similar baseline characteristics showed that fewer patients in the DB group required a PRBC transfusion, and the number of units of transfused PRBCs was lower in the DB group. Our findings support the use

TABLE 2.

Intraoperatively administered blood products

	Matched (N = 350)			
	NDB (N = 175)	DB (N = 175)	*P*	Effect size
Number of administered blood products				
PRBC (units)	3 (0–6)	2 (0–4)	0.004[a]	0.22
Fresh frozen plasma (units)	0 (0–3)	1 (0–4)	0.659	0.03
Cryoprecipitate (units)	0 (0–8)	0 (0–8)	0.799	0.02
Platelet (pooled adult units)	0 (0–2)	0 (0–2)	0.799	0.02
Autologous cell saver (mL)	930.0 (450.0–1900.0)	1150.0 (500.0–2475.0)	0.079	0.09
DB (units)	–	3.1 (2.3–4.1)	–	–
Total blood administered (units)	8.0 (4.0–13.1)	10.8 (6.1–19.0)	0.001[a]	0.23
Estimated total blood loss (L)	5.0 (2.50–8.19)	6.75 (3.84–11.88)	0.001[a]	0.28
Number of patients who received corresponding blood products				
PRBC	130 (74.3%)	105 (60%)	0.004[a]	0.306
Fresh frozen plasma	87 (50%)	91 (52.3%)	0.667	0.046
Cryoprecipitate	72 (41.4%)	75 (43.1%)	0.741	0.035
Platelet	80 (46%)	81 (46.6%)	0.912	0.012
Autologous cell saver	156 (89.7%)	166 (95.4%)	0.041[a]	0.223

Data are presented with median (first–third quartile) or number (proportion).
[a]$P < 0.05$ under Mann-Whitney *U* test, Wilcoxon signed-ranks test, or Z test. Common effect size *r* for ranked data comparisons and Cohen's *h* for rate comparison.
DB, donor blood transfused group; NDB, not transfused donor blood group; PRBC, packed red blood cell.

TABLE 4.
Intraoperative parameters

	Matched (N = 350)				
	NDB (N = 175)	DB (N = 175)	Mean difference[b] (95% CI)	P	Effect size
Total volume infused with the fluid management system (mL)[a]	7013.0 (4343.0–9550.0)	7140.0 (5188.0–11443.0)	0.87 (0.76 to 1)	0.053	0.21
Intraoperative Plasma-Lyte (mL)[a]	4000.0 (3000.0–6000.0)	4000.0 (3000.0–6000.0)	0.95 (0.83 to 1.09)	0.488	0.08
Intraoperative 20% albumin (mL)[a]	800.0 (500.0–1100.0)	800.0 (500.0–1200.0)	0.93 (0.81 to 1.08)	0.351	0.10
Intraoperative event	12 (6.9%)	15 (8.6%)	–	0.689	0.03
Lowest pH of arterial blood	7.291 ± 0.0704	7.287 ± 0.068	0.004 (–0.011 to 0.019)	0.610	0.06
Lowest core temperature (ºC)	35.51 ± 0.85	35.53 ± 0.75	–0.02 (–0.20 to 0.16)	0.818	0.03

Data are presented as mean ± SD, number (percentile), or median (first–third quartile). Effect sizes were Cohen's *d* or Cremér's V for t test, paired t test, or chi-squared test, respectively.
[a]Log transformed variables during statistical inferences, presented as median (first–third quartile) of original scale.
[b]Mean difference of log transformed variables presented as ratio of NDB over DB as original scale.
CI, confidence interval; DB, donor blood transfused group; NDB, not transfused donor blood group.

TABLE 5.
Postoperative outcomes

	Matched (N = 350)				
	NDB (N = 175)	DB (N = 175)	Mean difference[b] (95% CI)	P	Effect size
Returns to the theater	38 (21.7)	33 (18.9)	–	0.595	0.04
Reoperations for bleeding control	15 (8.6)	17 (9.7)	–	0.853	0.02
Reoperations for infection	8 (4.6)	6 (3.4)	–	0.786	0.03
Hepatic artery or portal vein thrombosis	11 (6.3)	10 (5.7)	–	>0.999	0.01
Primary graft nonfunction (retransplantation within 30 postoperative d)	6 (3.4)	4 (2.3)	–	0.75	0.03
Long-term graft failure (retransplantation after 30 postoperative d)	3 (1.7)	5 (2.9)	–	0.723	0.04
ICU stay duration (h)[a]	85.0 (44.0–155.0)	70.0 (57.0–132.0)	0.03 (–0.08 to 0.14)	0.590	0.06
Postoperative hospital stays (d)[a]	355.0 (256.0–757.0)	399.0 (262.0–693.0)	0.05 (–0.06 to 0.17)	0.352	0.10

Data are presented with the number (percentile) or median (first–third quartile). Effect sizes are Cremér's V or Cohen's *d* according to the statistical method, Chi-squared test, *t* test, or paired *t* test.
[a]Log transformed variables during statistical inferences, presented as median (interquartile range) of original scale,
[b]Mean difference of log transformed variables presented as ratio of NDB over DB as original scale.
CI, confidence interval; DB, donor blood transfused group; ICU, Intensive care unit; NDB, not transfused donor blood group.

TABLE 6.
Correlation between donor blood transfusion or not, and outcomes (partial correlation controlled by packed red blood cell transfusion)

	Matched (N = 350)	
	Correlation coefficient	P
Returns to theater	0.015	0.777
Returns for bleeding	–0.04	0.451
Returns due to infection	0.019	0.717
Hepatic artery or portal vein thrombosis	0.009	0.868
Primary graft nonfunction	0.016	0.773
Postoperative ICU	–0.067	0.215
Postoperative hospital stay	–0.078	0.147

ICU, intensive care unit.

of DB being removed during organ procurement as a viable resource for reducing the requirements for PRBCs during LT. Further, our findings imply that the use of DB minimizes the exposure of the recipient to multiple donor sources.

Relationship to Previous Studies

The association between PRBC transfusion and adverse outcomes in LT is well known.[23-25] PRBC transfusion has been found to be an independent risk factor for 1- and 5-y mortality.[25-27] Azevedo et al[28] found that for each unit of PRBCs transfused, there was a 13% increase in the relative risk of 30-d mortality. Most recently, Danforth et al[29] identified preoperative risk factors associated perioperative complications that contribute to perioperative mortality. Preoperative anemia was a significant factor associated with massive transfusion (>10 units PRBC).

PRBCs have been implicated as a risk factor for surgical site infections following LT, with an associated mortality of around 10%–25%.[2,30,31] PRBCs have multiple immunosuppressive effects, including the effects of storage resulting in cell breakdown and exposure to donor lymphocytes.[32] Alloimmunization following PRBC transfusion in LT is cited as occurring in 8%–23% of patients.[33,34] PRBC

transfusions have also been associated with new-onset acute and chronic renal failure and postoperative delirium in the ICU.[35-38] Both effects are associated with increased morbidity and mortality, as well as increased healthcare costs. As a result, many studies have focused on practical strategies to reduce transfusion, such as autologous cell salvage[32] and intraoperative phlebotomy,[24,38,39] both of which have been shown to reduce PRBC transfusion.

Clinical Implications of Our Findings

The use of DB offers a pragmatic solution to reduce intraoperative transfusion of PRBCs. DB is a resource that would otherwise be discarded, whereas PRBCs are a limited resource whose supply depends on donors. Given that this is a finite resource, cost is an important consideration. Two units of PRBC are estimated to cost between US$1270.49 and US$2458.77 in the United States, approximately €877.69 in Europe,[32] and A$800 in Australia. The direct cost of DB relates to the cost saver reservoir needed to collect the DB (A$80), and the cost of compatibility testing, which are considerably less than the cost of a single unit of PRBCs.

DB forms an essential component of normothermic machine perfusion for cardiac grafts, so much so that they are unable to reanimate the grafts satisfactorily using PRBCs.[40,41] In LT, common practice for normothermic machine perfusion is to add 3–4 units of PRBCs to the priming volume.[42] The use of DB in centers that use normothermic machine perfusion for liver transplants could have an even greater impact in reducing the amount of PRBCs used during the entire transplant process.

Strengths and Limitations

There are several limitations to this study. Ours is a single center, which limits the external validity of our findings; however, our hospital has similar characteristics to many other LT centers, nationally and internationally. We only included adult patients undergoing deceased donor LT, which limits the broad application of our findings to deceased donor pediatric LT recipients. Our findings are not generalizable for other deceased donor organ transplants; however, the use of DB in cardiac transplantation may confer similar benefits in reducing the number of PRBCs transfused. As this was a retrospective study, we were not able to validate the microbiological safety data previously undertaken.

Although the volume of estimated blood loss was higher in the NDB group, the ability of clinicians to correctly estimate blood loss is poor,[43-46] limiting the accuracy of these findings. Rather, we used objective metrics and variables, which were not amenable to clinician error. We did not record patient factors associated with increased intraoperative bleeding such as the use of aortic conduits, as such techniques are not undertaken in our center. We did not examine for other complications of PRBC transfusion, such as transfusion-related lung injury and postoperative renal injury; neither did we perform a cost evaluation of this intervention. Finally, our sample population was not large enough to investigate the association of DB with long-term immunological outcomes. Our findings provide valuable data for sample size estimations for future studies on the use of DB in LT recipients.

Our study has several strengths. To date, this is the largest review of the use of DB in the context of LT and provides a comprehensive evaluation of the use of DB in reducing intraoperative transfusion requirements. As there was no random assignment of DB to patients, we used propensity score matching, which allowed separation of confounding factors adjustment, and analysis of the treatment effect. Further, propensity matching eliminated a greater portion of bias, allowing a more precise treatment effect of DB on PRBC transfusion to be estimated. By reporting the reduced rate of PRBC transfusion in LT patients who receive DB, we have defined a need for further research in this area.

CONCLUSION

The use of DB was associated with a lower number of total PRBCs being transfused intraoperatively. Our findings support the use of DB being removed during organ procurement as viable resource for reducing the requirements for PRBCs during LT. The use of DB minimizes recipients' exposure to multiple donor sources. Further study is needed to determine whether this could also decrease the frequency of acute cellular rejection by inducing immunological tolerance to the liver allografts. This is an exciting area of study with important potential for improving survival following LT.

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