The impact of perioperative transfusion of blood products on survival after pediatric liver transplantation


Abstract: Intraoperative transfusion of red blood cells (RBC) is associated with adverse outcome after LT in adult patients. This relationship in pediatric patients has not been studied in depth, and its analysis is the scope of this study. Forty-one variables associated with outcome, including blood product transfusions, were studied in a cohort of 243 pediatric patients undergoing a cadaveric LT between 2002 and 2009 at the General Hospital of Bergamo. Multivariate stepwise Cox proportional hazards models were adopted with adjustment by propensity scores to minimize factors associated with the use of blood products. Median age at transplant was 1.37 yr. In univariable and multivariable analyses, perioperative transfusion of FFP and RBC was an independent risk factor for predicting one-yr patient and graft survival. The effect on one-yr survival was dose-related with a hazard ratio of 3.15 for three or more units of RBC (p = 0.033) and 3.35 for three or more units of FFP (p = 0.021) when compared with 1 or no units transfused. The negative impact of RBC and FFP transfusion was confirmed by propensity score–adjusted analysis. These findings may have important implications for transfusion practice in the LT pediatric recipients.

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Key words: pediatric liver transplantation – transfusion – survival – perioperative

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A variety of donor and recipient characteristics have been identified as risk factors influencing graft and patient survival after pediatric LT (1–6) such as indication for transplantation, pretransplant morbidity, renal function, donor and recipient age, ischemia time, and type of immune suppression. Growing knowledge in this field has been important to improve post-transplant survival over the last two decades (7, 8).

In addition to these factors, several studies in adult patients have shown that intraoperative blood loss and packed red blood cell (RBC) transfusion requirement have a negative impact on outcome after LT (9–12). The risk of allogenic blood transfusion includes viral transmission, allergic reaction, alloimmunization, bacterial sepsis, TRALI, renal failure, excessive intravascular volume, and immunosuppressive effects (13, 14). Over time, improvement in surgical techniques, anesthesia, organ preservation, and
the use of intraoperative blood saver led to a significant decrease in intraoperative blood utilization (15–23).

Most of the information on blood product transfusion in critically ill pediatric patients has come from studies in adults, but the pathophysiology, developmental stage, size, blood volume, and remaining life span of pediatric patients differ from adults (24–27). Risks of RBC transfusion have been recently investigated in critically ill children (28–30), but the influence of various blood products on mortality has not been well studied in children undergoing LT (4, 31, 32).

The aim of this study was to evaluate the influence of various blood components on outcome after pediatric LT, as reflected by patient and graft survival rates.

We have attempted to limit the influence of possible confounding factors of the impact of blood transfusion on the outcome by including variables reflecting severity of disease and possibility of massive blood loss and by using propensity score–adjusted statistical analysis.

**Materials and methods**

**Patients**

Two hundred and forty-three consecutive pediatric LTs (age < 18 yr) from deceased brain-dead donors (excluding combined organ transplantation) were performed in our center between January 1, 2002 and December 31, 2009. The end of the follow-up was December 2010. Characteristics of patients, donors, transplantation, and post-transplantation course were obtained from a prospectively maintained computer database. The maximum percentage of missing data per variable was 2% (excluding cold and warm ischemia time available for 38 LTs, performed after April 1, 2008). The ethical committee of our institution approved this retrospective study.

**Surgical technique**

Seven hepato-biliary surgeons performed all the LTs with two of them involving in each procedure. ABO blood group identical or compatible grafts from deceased brain-dead donors were used for all patients. Organ procurement was performed according to standard technique (NITp). Transplants were performed using both full-size liver and split liver. They were performed with conventional techniques; biliary reconstruction was a Roux-en-Y hepatic jejunostomy and, only occasionally, a duct-to-duct Anastomosis.

**Anesthetic management and blood transfusion policy**

Fifteen anesthesiologists were involved throughout the study period.

Anesthesia was maintained with balanced technique using sufentanil, sevoflurane, cis-atracurium, and volume-controlled ventilation. Tranexamic acid was administered to all patients. Intraoperative cell salvage systems were not used. For all patients, the transfusion policy was based on weight (mL/kg), clinical blood losses, laboratory values, and hemodynamic monitoring. Blood loss was counteracted by transfusion of allogenic packed red blood cells (RBC), submitted to leukoreduction, with the aim to maintain the hematocrit between 25% and 30%. FFP was administered to correct prolonged PT or aPTT, higher than one and a half time the ranges of reference. PTls concentrates were given if the PTL count decreased under $50 \times 10^9/L$. A total body warming blanket was applied to all children.

**Postoperative management**

At the end of surgery, all patients were in the PICU, and mechanical ventilation was prolonged until necessary. Hematocrit threshold of 25% was chosen for RBC transfusion. When clinically stabilized, patients were moved to the pediatric department, until the end of hospitalization. Immune suppression was based on a double-drug regimen of tacrolimus and steroids. Doppler ultrasound was performed at the end of surgery (before the skin closure) and every 24 h for the first five postoperative days to assess patency of the liver vessels. Suspcion of arterial or portal vein thrombosis was always confirmed by angiography, CT scans, or surgical exploration. No protocol liver biopsies were performed, but any episode of clinical or laboratory suspicion of acute rejection was ruled out by a liver biopsy. The follow-up was performed at the pediatric department with out-patient visits and when necessary hospitalization.

**Analyzed variables**

The analyzed variables were selected based on a review of the literature and expected patho-physiologic mechanisms. The analyzed variables were divided into recipient’s characteristics, donor’s characteristics, transplantation’s characteristics, and complication’s characteristics. Table 1 summarizes the evaluated demographic and clinical characteristics.

Recipient’s characteristics considered were age, sex, weight, height, BMI, indication for transplantation, PELD score (33), laboratory tests, and PICU’s variables. Indication for transplantation was classified into six categories: cholestatic, metabolic, or neoplastic disease, acute liver failure, miscellaneous, and retransplantation. In this last category, eight patients, previously transplanted elsewhere, underwent retransplantation for chronic rejection at our center and were included. PELD score was calculated at the beginning of transplantation. MELD score was used if patients were 12 yr or older. Laboratory tests before LT were referred to the day of transplantation or, when not available, to the last week before LT. PICU variables are length of ventilation, length of stay, and PIM2 (34).

History of previous abdominal surgery and congenital cardiopathy were also evaluated.

Donor characteristics (age, sex, and sodium) were reported by the organ allocation center. The choice of graft size was determined by surgeons during transplantation; steatosis was quantified on the graft biopsy (35); the presence of arterial anomalies was corrected during graft preparation before transplantation. Equivalent dose of norepinephrine ($\mu g/min$) (36) was calculated as follows:

\[
\text{Equivalent dose of norepinephrine (}$\mu g/min$) = \text{norepinephrine (}$\mu g/min$) + [\text{dopamine (}$\mu g/min$/2] + \text{adrenaline (}$\mu g/min$) + [\text{phenylephrine (}$\mu g/min$/2]
\]

For all patients, the transfusion policy was based on weight (mL/kg), clinical blood losses, laboratory values, and hemodynamic monitoring. Blood loss was counteracted by transfusion of allogenic packed red blood cells (RBC), submitted to leukoreduction, with the aim to maintain the hematocrit between 25% and 30%. FFP was administered to correct prolonged PT or aPTT, higher than one and a half time the ranges of reference. PTls concentrates were given if the PTL count decreased under $50 \times 10^9/L$. A total body warming blanket was applied to all children.
Transplantation characteristics included ischemia times and blood product transusions during surgery and in the first 48 h after PICU admission.

Total ischemia time was available for all patients, instead of warm and cold ischemia time (available for 38 patients after April 1, 2008). Blood products transusions during surgery and in the first 48 h after PICU admission included RBC transfusion (1 units = 250 mL), FFP transfusion (1 units = 200 mL), and PTLs transfusion (1 units = 1 PTLs pools = 250 mL)

Complication characteristics include complications in the first year after transplantation and are defined as follows:

1. surgery complications: hemoperitoneum, peritonitis, abscesses, perforation, occlusion, and digestive hemorrhage requiring reoperation;
2. vascular thrombosis complications: hepatic artery and portal vein thrombosis, or complications involving the inferior cava vein and supra-hepatic veins;
3. biliary complications: biliary duct stenosis (leading to reoperation or radiological intervention) and biliary leakage (defined as bilirubin in the drainage doubled the value in serum);
4. infectious complications: complications satisfying the definition of sepsis, severe sepsis, and MOF (37);
5. cytomegalovirus infection or reactivation; virus isolation from tissue biopsies or secretions and antigenemia or DNAemia assay on blood samples (38);
6. post-transplant lymphoproliferative disorder: complication satisfying the WHO classification (39);
7. acute rejection (only biopsy-proven);
8. chronic rejection (only biopsy-proven).

Outcome

Primary outcome was evaluated as patient and graft survival in the first year after transplantation.

Patient survival is defined as the time period between transplantation and the end of follow-up or patient death. Graft survival is defined as the time period between transplantation and the end of follow-up or graft loss by patient death or by graft failure requiring retransplantation. If follow-up ended within one yr, patient loss was taken into account as censored data in the analysis. The same was true for the analysis of graft survival.

Statistical analysis

Continuous variables are presented as medians with ranges and categorical variables as numbers with percentages.
Kaplan–Meier product-limit estimator was used to compute cumulative survival rates. Univariate analysis with log-rank test was used to assess survival differences among variables categories. For comparison purpose, continuous variables were categorized using their median or tertiles as cutoff points. All variables with a p-value $\leq 0.1$ in the univariate analysis were included in a multivariate analysis to assess which factors influenced patient and graft survival. Cox proportional hazard regression with forward stepwise selection was used to identify main risk factors. Complications in the first year were considered in survival analysis to adjust for postoperative confounders. Effects of identified factors were presented as hazard ratios with 95% confidence interval together with their p-values. Propensity score analysis was used to adjust risk factors for selection biases in the use of blood products. Outcome for propensity score was defined as patients with overall blood components transfusion (RBC, FFP, and PTLs) above the median value (700 mL) versus patients below that threshold. All statistical tests were considered significant for p values $\leq 0.05$. The analysis was carried out using SPSS software, version 17.0 (SPSS, Chicago, IL, USA).

**Results**

**Patients characteristics**

Patient and donor characteristics as well as transplantation and post-transplantation variables for the entire group of patients are summarized in Table 1. Missing data are less than 2%. For the univariate analysis of patient and graft survival within one yr of transplant, there were 243 patients of whom 46 lost their graft, 33 underwent retransplantation, 26 died, and 39 stopped follow-up within one yr. One-year patient and graft survival were 89.3% and 81.1%, respectively. When looking at the Kaplan–Meier survival curves (Figs. 1a,b and 2a,b), it appears that the main decrease in both graft and patient survival occurs during the first months post-transplantation.

**RBC and FFP transfusion and survival**

One-yr patient survival after LT was significantly associated with the number of allogenic RBC and FFP units transfused during surgery. One-yr graft survival after LT was significantly associated with the number of allogenic RBC units transfused during surgery and the number of FFP units transfused in the first 48 h after LT (Figs 1 and 2).

**Uni- and multivariate analysis of patient and graft survival**

The results of univariate analysis of all potential risk factors for one-yr patient and graft survival are summarized in Table 2.

Of the 41 variables studied, 11 were associated with one-yr patient survival (p value < 0.10), namely recipient’s age and sex, indication for transplantation, serum creatinine before OLT, donor age, total ischemia time, RBC and FFP units transfused during surgery, FFP units transfused after transplantation, biliary complications, and post-transplant lymphoproliferative disorder. When these variables were entered into the multivariate Cox regression model, only five predicted one-yr patient survival, namely recipient’s age, total ischemia time, RBC and FFP units transfused during surgery, and biliary complications (Table 3).

Of the 41 variables studied, 14 were associated with one-yr graft survival (p value < 0.10), namely recipient’s age and weight, indication for transplantation, serum creatinine before LT, donor’s equivalent dose of norepinephrine, total

*Fig. 1.* (a,b) Kaplan–Meier curves representing cumulative patient survival in relation to blood product usage.
ischemia time, RBC and FFP units transfused during surgery, FFP units transfused in the first 48 h post-LT, PIM 2, length of PICU stay, vascular thrombosis complications, biliary complications, and post-transplant lymphoproliferative disorder, which were significantly associated with outcome in univariate analysis (Table 2). When these variables were entered into a multivariate Cox regression model, only four predicted one-yr graft survival, namely indication for transplantation, RBC units transfused during surgery, FFP units transfused in the first 48 h post-LT, and vascular thrombosis complications (Table 3).

Propensity score–adjusted analysis
Propensity score analysis was used to control for confounding factors that could potentially influence the use of blood product. As overall transfusion index, we adopted the total amount of blood product that patients received (total blood volume transfused = RBC units transfused during surgery + FFP units transfused during surgery + PTLs units transfused during surgery + RBC units transfused after transplantation + FFP units transfused after transplantation + PTLs units transfused after transplantation).

Variables that influenced the risk of receiving transfusion were summarized in a score (propensity score). Propensity score summed up recipient's sex, PTLs before LT, INR before LT, PELD, donor's sex, graft type, equivalent dose of norepinephrine, and total ischemia time.

For one-yr patient survival and one-yr graft survival, the adjustment for propensity score confirmed the results obtained from the multivariate analysis (Table 3).

**Discussion**
Mortality associated with transfusion has decreased over the last two decades (40), but it remains a great challenge in adult patients undergoing massive transfusion, such as during LT (9–12).

Advances in anesthetic and surgical management of patients undergoing LT and a better understanding of the factors associated with massive blood transfusion have greatly contributed to reduction in the blood product transfusion (15–23).

The negative effects of blood product administration on outcomes have received attention in recent years in the pediatric area (27, 29, 40), but has not been studied in detail in children undergone LT (4, 31).

In our previous study, the intraoperative and postoperative transfusion of RBC and FFP was significantly correlated with graft failure after pediatric LT (32). These findings prompted us to perform the present study analyzing in detail the impact of perioperative transfusion therapy on outcome in children undergone LT.

Postoperative transfusion variables in the acute phase post-LT (first 48 h post-LT) were considered as they represent a continuum with the intraoperative transfusion therapy. This range of time allowed including all children before discharge from the PICU (Table 2). To our knowledge, there are no data on the impact of postoperative transfusion on survival after pediatric LT.

Our study shows that intraoperative transfusion of three units of RBC is an independent risk factor for patient and graft survival after cadaveric LT. The restrictive strategy (28) used...
<table>
<thead>
<tr>
<th>Patient survival at one yr</th>
<th>Graft survival at one yr</th>
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<tbody>
<tr>
<td>N</td>
<td>Survival (%) p</td>
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</table>

### Recipient variables

**Age (m)**
- ≤16: 116, 94.7, 0.009* 85.9, 0.054*
- >16: 127, 83.4, 75.2

**Sex**
- F: 113, 92.7, 0.097* 82.7, 0.457
- M: 130, 85.5, 78.3

**Weight (kg)**
- ≤10: 152, 91.1, 0.159 83.8, 0.096*
- >10: 91, 84.8, 74.4

**Height (cm)**
- ≤70: 121, 92.4, 0.111 84.8, 0.109
- >70: 122, 85.2, 79.9

**BMI**
- ≤16.5: 120, 90.4, 0.378 80.8, 0.660
- >16.5: 123, 87.2, 79.9

**Indication for transplantation**
- Cholestasis cirrhosis: 176, 91.7, 0.010* 83.5, <0.001*
- Metabolic pathology: 15, 85.7, 86.2
- Cancer: 11, 66.3, 66.3
- Acute liver failure: 17, 82.4, 82.4
- Retransplantation: 8, 62.5, 12.5
- Miscellaneous: 16, 93.3, 79.8

**PELD**
- ≤14: 89, 92.1, 0.297 84.3, 0.792
- 15–22: 73, 84.9, 79.5
- ≥23: 79, 89.9, 83.5

**Serum creatinine before LT (mg/dL)**
- ≤0.3: 130, 90.9, 0.002* 81.2, 0.004*
- 0.4: 37, 100, 97.3
- ≥0.5: 68, 78.6, 69.4

**Serum total bilirubin before LT (mg/dL)**
- ≤7.0: 78, 86.5, 0.764 71.8, 0.119
- 7.1–20.0: 86, 90.4, 84.5
- ≥20.1: 79, 89.5, 84.5

**PTLs before LT (>1000/cc)**
- ≤90: 76, 90.2, 0.929 79.1, 0.506
- 91–180: 79, 88.5, 84.7
- ≥181: 79, 88.1, 77.7

**INR before LT**
- ≤1.3: 78, 89.6, 0.897 80.5, 0.799
- 1.4–1.9: 87, 89.0, 81.6
- ≥2.0: 78, 87.7, 78.6

**Fibrinogen before LT (mg/dL)**
- ≤140: 79, 93.4, 0.308 88.3, 0.145
- 141–220: 80, 88.4, 79.3
- ≥221: 82, 84.9, 74.8

**Hemoglobin before LT (g/dL)**
- ≤8: 64, 83.8, 0.157 81.0, 0.986
- 9–10: 85, 87.4, 78.6
- ≥11: 94, 93.4, 81.6

**Previous abdominal surgery**
- Yes: 139, 90.1, 0.430 79.2, 0.550
- No: 104, 87.0, 61.8

**Congenital cardiopathy**
- Yes: 8, 75.0, 0.165 75.0, 0.643
- No: 235, 89.3, 80.5

**PIM 2**
- ≤0.9: 75, 87.6, 0.144 78.1, 0.085
- 0.9–14.0: 84, 95.2, 89.0
- ≥14.1: 80, 86.1, 75.8

### Donors variables

**Age (yr)**
- ≤20: 115, 92.8, 0.077* 83.4, 0.247
- >20: 128, 85.3, 77.5

**Sex**
- M: 158, 90.1, 82.3
- F: 85, 86.5, 76.8

**Graft type**
- Full liver: 39, 94.3, 0.145 86.3, 0.315
- Split: 204, 88.7, 80.7

**Macrosteatosis (%)**
- ≤0: 208, 89.8, 0.194 80.8, 0.567
- >0: 35, 62.7, 76.9

**Arterial anomalies**
- Yes: 56, 94.3, 0.145 85.3, 0.315
- No: 187, 89.3, 80.5

**Sodium (mEq/L)**
- ≤145: 110, 92.7, 0.128 83.7, 0.235
- >145: 133, 86.5, 86.2

**Transplantation variables**

**Total ischemia time (min)**
- ≤420: 126, 92.9, 0.026* 86.0, 0.011*
- >420: 117, 84.3, 74.0

**Cold ischemia time (min)**
- ≤330: 16, 88.9, 0.229 88.9, 0.561
- >330: 15, 100, 86.2

**Warm ischemia time (min)**
- ≤45: 17, 100, 0.317 94.1, 0.526
- >45: 14, 90.9, 83.6

**RBC during surgery (units)**
- ≤1: 129, 94.3, 0.342 80.6, 0.372
- ≥1: 11, 81.8, 72.7

**FFP during surgery (units)**
- ≤1: 60, 91.3, 62.0
- ≥1: 51, 79.7, 65.7

**PTLs during surgery (units)**
- ≤1: 11, 81.8, 72.7
- ≥1: 60, 91.3, 62.0

**Complications in the first year post-LT**

**Surgery complications**
- Yes: 88, 88.1, 0.923 79.0, 0.729
- No: 155, 89.3, 81.1
in the PICU may explain the low requirement of RBC observed post-LT (Table 2). In addition, this study identified also intraoperative transfusion of three units of FFP and postoperative transfusion of one unit of FFP as a risk factor, respectively, for patient and graft survival after LT. There are no data on the negative effect of FFP transfusion on patient and graft survival after LT. Relationship between massive transfusion and vascular complications after pediatric LT could be interesting to explore because thrombosis is more than just a surgical complication and imbalanced hemostasis occurs after LT (44).

PTL transfusion is not associated, in our population, with one-yr patient and graft survival, in contrast with results as seen in the adults (11). However, only 11 patients during surgery and 15 patients in PICU received PTL transfusion, despite the fact that more than 70 patients received massive transfusion and had a low level of PTLs presurgery (<90 × 10^9/L). We cannot speculate whether this underuse of PTLs has a positive impact on survival, as suggested by an adult study (11), or has increased the use of RBC and FFP.

Table 2. (Continued)

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For variables, categorization was used as median (two categories) or tertiles (three categories).

\(^{\dagger}\)Log-rank test p-value

*Variables significantly associated with patient and graft survival (p-value < 0.10), entered into the multivariate Cox regression model.

The risk of viral transmission associated with blood products transfusion has significantly decreased over the last 20 yr (40), but non-infectious risk associated with blood product transfusion is well recognized and includes hemolytic and non-hemolytic transfusion reactions, allergic reactions, clerical errors, bacterial sepsis, TACO, TRALI, metabolic derangements, alloimmunization, and immunomodulation (13, 14, 40).

Residual amounts of donor leukocytes present in RBC, changes in erythrocytes preservation, and duration of storage seem to be involved in the adverse effect of RBC transfusion (13, 41, 42). All our children have received transfusion of RBCs stored for no longer than five days and subjected to leukoreduction.

Combined transfusion of three units of RBC and three units of FFP correspond to the infusion volume of about 1350 mL. Median weight of the analyzed population is equal to 9 kg with a corresponding intravascular volume of approximately 700 mL. Such transfusion practice shapes a massive transfusion of blood component with side effects related to circulatory overload, dilution coagulopathy, blood hyper-viscosity, and microaggregates infusion (43). All these suggest an alteration of vascular function, integrity, and patency. In our population, vascular thrombosis complication represents an independent risk factor for graft survival. Relationship between massive transfusion and vascular complications after pediatric LT could be interesting to explore because thrombosis is more than just a surgical complication and imbalanced hemostasis occurs after LT (44).

PTL transfusion is not associated, in our population, with one-yr patient and graft survival, in contrast with results as seen in the adults (11). However, only 11 patients during surgery and 15 patients in PICU received PTL transfusion, despite the fact that more than 70 patients received massive transfusion and had a low level of PTLs presurgery (<90 × 10^9/L). We cannot speculate whether this underuse of PTLs has a positive impact on survival, as suggested by an adult study (11), or has increased the use of RBC and FFP.

Although the observed stepwise relationship between the number of units transfused and the survival is suggestive of a potential causal role, these observations could also mean that blood product transfusion is simply a surrogate marker for sicker patients. For this reason, the multivariate regression analysis included possible confounding factors, such as severity of disease, comorbidity, previous abdominal surgery, and complications in the first year post-LT. The multivariate analysis confirmed the negative and independent impact of blood products transfusion on one-yr patient and graft survival.

The validity of these results is confirmed by the negative impact of blood products transfusion on survival in a propensity score–adjusted analysis, which is currently considered one of the most robust statistical methods to control for selection bias for the use of specific treatment (45).
Outcome for propensity score was defined as children with overall blood components transfusion above the median value of 700 mL vs. children below this value. This threshold was chosen as it represents the mean whole blood volume of our population with a median weight of 9 kg (Table 1), and we identified it as an index of massive transfusion.

It can be argued that it is really critical that we did not relate individual blood products transfusion to each child’s EBV, because of the wide range of ages and body weights in this series. We decided to study the blood products transfusion expressed as unit to focus the attention of the impact of different donors (1 unit = 1 donor) of blood products on survival.

The evaluation of blood products in terms of EBV percentage showed that transfusing more than 10% of EBV-related FFP after LT and more than 70% of EBV-related RBC during surgery increased about two times and four times, respectively, the hazard of death and graft loss (data not shown). This confirmed what is described in our analysis.

Biliary complication is associated with a better patient survival in our study. This result seems surprising and has to be commented. A preemptive diagnostic and therapeutic approach allows us to detect a number of asymptomatic biliary strictures eliminating any negative impact on patient and graft survival. Furthermore, the majority of patient and graft loss among children without biliary stenoses occurred early in the follow-up so that they cannot develop biliary complication (46).

This study has some limitations. First, it is a retrospective study. Second, we could not completely distinguish whether the survival of

Table 3. Multivariate analysis of one-yr patient and graft survival

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<tr>
<th></th>
<th>Standard analysis</th>
<th>Propensity score–adjusted analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Patient survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient’s age (m)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>3.377 (1.340–8.511)</td>
<td>0.010</td>
</tr>
<tr>
<td>&gt;16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total ischemia time (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤420</td>
<td>3.526 (1.490–8.347)</td>
<td>0.004</td>
</tr>
<tr>
<td>&gt;420</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBC during surgery (units)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>1.847 (0.647–5.267)</td>
<td>0.251</td>
</tr>
<tr>
<td>≥3</td>
<td>3.146 (1.097–9.022)</td>
<td>0.033</td>
</tr>
<tr>
<td>FFP during surgery (units)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>1.124 (0.341–3.705)</td>
<td>0.848</td>
</tr>
<tr>
<td>≥3</td>
<td>3.346 (1.196–9.364)</td>
<td>0.021</td>
</tr>
<tr>
<td>Biliary complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.232 (0.054–1.000)</td>
<td>0.050</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indication for transplantation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestatic cirrhosis</td>
<td>1.070 (0.248–4.620)</td>
<td>0.928</td>
</tr>
<tr>
<td>Metabolic pathology</td>
<td>1.853 (0.537–6.388)</td>
<td>0.329</td>
</tr>
<tr>
<td>Cancer</td>
<td>2.026 (0.590–6.956)</td>
<td>0.262</td>
</tr>
<tr>
<td>Acute liver failure</td>
<td>17.508 (6.908–44.376)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retransplantation</td>
<td>1.070 (0.323–3.546)</td>
<td>0.912</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBC during surgery (units)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>2.950 (1.425–6.109)</td>
<td>0.004</td>
</tr>
<tr>
<td>2</td>
<td>4.390 (1.944–9.914)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFP in the first 48 h post-LT (units)</td>
<td>2.205 (1.188–4.092)</td>
<td>0.012</td>
</tr>
<tr>
<td>Vascular thrombosis complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.330 (1.565–7.085)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Reference category.
the children was related to massive transfusion for low level of hemoglobin and coagulation factor or for over-transfusion of blood product. Definite proof should come from a prospective study comparing different triggers for transfusion.

A prospective randomized trial comparing two strategies for RBC transfusion has been performed in a pediatric critical care population (28), but we did not find similar studies in the LT population. The high variability of hemoglobin level and coagulation factors observed during LT procedure make it difficult to perform such a study.

Despite these limitations, this is the first pediatric study that shows the negative effect on patient and graft survival of the intraoperative RBC transfusion after LT. In addition, we have provided evidence that intraoperative and postoperative FFP transfusions are an independent risk factor for children and graft survival, respectively, after LT. The worse outcome related to blood product transfusion, extended to the early postoperative period, should induce pediatricians, anesthetists, surgeons, and intensivists to search for an integrated strategy (20, 47) to reduce blood product use during and after LT.

In conclusion, our findings have an important clinical implication when determining the risk–benefit ratio of the blood product transfusion in pediatric LT recipients. Most mortality and graft loss occur in the first months, and this confirms the findings of earlier studies (4, 7). Decreasing early surgical complications and perioperative transfusion will improve the overall long-term patient and graft survival after pediatric LT. Novel approaches and studies are likely to be required if we want to improve the care of this population.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose.

Author contributions

Nacoti M, Lorusso F, and Cazzaniga S were responsible for the concept, design, acquisition, analysis and interpretation of data and drafting. Naldi L and Lussana F analyzed and interpreted the data, drafted the manuscript, and critically revised the article. Brambillasca P, Benigni A, Sabrina B, and Vedovati S were involved in acquisition, analysis, and interpretation of data. Colledan M, Bonanomi E, and Barbui T were responsible for concept, design, and critical revision of the article. Corno V, Falanga A, and Sonzogni V were involved in concept, interpretation of the data, and critical revision of the article.

References


