The effects of intraoperative cryoprecipitate transfusion on acute renal failure following orthotopic liver transplantation

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Abstract

Purpose The definition of risk factors associated with acute renal failure (ARF) following orthotopic liver transplantation (OLT) is still controversial. Cryoprecipitate, which can supply fibrinogen and other coagulation factors, is widely used in OLT. However, the effects of intraoperative cryoprecipitate transfusion on ARF following OLT remain unclear.

Methods In a series of 389 adult patients who received grafts from deceased donors and underwent their first OLT, the clinical correlation between intraoperative cryoprecipitate transfusion and ARF following OLT was retrospectively studied after adjusting for potential confounders. The distribution of ARF and the causes of death within the first year after OLT were also compared separately in patients with and without cryoprecipitate transfusion.

Results The incidence of ARF in patients with cryoprecipitate transfusion was significantly higher than in patients without cryoprecipitate transfusion (15.9 vs. 7.8 %, \( p = 0.012 \)). A nonlinear relationship between intraoperative cryoprecipitate transfusion and ARF following OLT was observed. The risk of ARF increased with the cryoprecipitate transfusion level up to the turning point (16 U) (adjusted OR 1.1, 95 % CI 1.1–1.2; \( p < 0.001 \)). When the cryoprecipitate level exceeded 16 U, the level of cryoprecipitate transfusion was not associated with the risk of ARF (OR 0.95, 95 % CI 0.85–1.1; \( p = 0.319 \)). Deaths within the first year after the operation occurred more frequently in cases with cryoprecipitate transfusion (22.9 vs. 14.2 %, \( p = 0.029 \)).

Conclusions These findings suggested that intraoperative cryoprecipitate transfusion is associated with ARF following OLT. Cryoprecipitate transfusion during OLT should be performed carefully until more convincing evidence has been found.

Keywords Transfusion · Cryoprecipitate · Acute renal failure · Liver transplantation

Introduction

Acute renal failure (ARF) is a common complication following liver transplantation (OLT). In 1990, the incidence of ARF following OLT reached 94.2 % [1]. More recently, there was a decline in incidence to 30–60 % between 2003 and 2007 [2–4]. It has been estimated that between 8 and 17 % of patients with ARF following OLT require replacement therapy [5, 6]. Patients developing ARF are at increased risk of mortality [7–9], and their management results in a significant economic burden [10].
The etiology of ARF following OLT is usually multifactorial. Various factors may influence the occurrence of ARF to varying degrees [11]. Preoperative renal impairment, blood loss and sepsis may all contribute to ARF following OLT [3, 5, 12]. Although the many complications following OLT caused by blood product transfusion have increasingly been attracting attention recently [13–15], few researchers are concerned about the effects of intraoperative blood product transfusion on ARF following OLT.

Intraoperative cryoprecipitate transfusion, which supplies fibrinogen and other coagulation factors, can effectively stop bleeding and promote wound healing. Moreover, it does not require cross-matching and is convenient to obtain. Therefore, cryoprecipitation has been widely adopted in OLT, particularly in developing countries. However, no uniform criteria for the application of its complex components during OLT are available. As far as we know, no preceding work or report has considered the effects of intraoperative cryoprecipitate transfusion on ARF following OLT.

In this study, we applied a set of consensus criteria—risk, injury, failure, loss and end stage (RIFLE)—published by the Acute Dialysis Quality Initiative (ADQI) to define ARF following OLT [16]. Then we retrospectively collected perioperative variables of patients undergoing OLT in a single center to explore the clinical correlation between intraoperative cryoprecipitate transfusion and ARF following OLT. We also investigated the effect of cryoprecipitate transfusion on post-transplant survival. It was hoped that these data would provide experimental evidence to decrease the occurrence of ARF following OLT.

Materials and methods

Study population

A total of 459 consecutive patients underwent OLT at Shanghai First People’s Hospital between 1 January 2003 and 31 December 2010. All grafts were from deceased donors. We excluded data from children (n = 3), patients with renal dysfunction pre-transplantation (n = 40) and patients who had received re-transplantation (n = 27), and the remaining 389 cases formed the analysis population.

We defined pre-transplantation renal dysfunction as when the serum creatinine (Scr) level was greater than 133 mmol/l in two consecutive examinations performed within a 48-h period. Intraoperative blood product transfusion included whole blood, red blood cells, cryoprecipitate, fresh frozen plasma and cell saver. In our center, the indication for use of cryoprecipitate to compensate fibrinogen or coagulation factors in OLT was a plasma fibrinogen level of <1.0 g/l. As another procoagulant product, fresh frozen plasma was used in (1) cases of excessive microvascular bleeding in the presence of a PT greater than 1.5 times normal or INR greater than 2.0, or an APTT greater than two times normal; (2) patients transfused with more than one blood volume and when PT or INR and APTT could not be obtained in a timely fashion. We stopped transusing these procoagulant products when bleeding had been significantly improved as judged by the surgeon’s experience and the parameters of coagulation and fibrolysis had reached the cutoff value from the following blood test report. In our center, each unit of cryoprecipitate is made from 400 ml whole blood; the volume of each unit is 25 ± 5 ml and contains ≥80 IU factor VIII, ≥150 mg fibrinogen and other proteins in the concentrate including fibronecinit (20–25 %), albumin (5–8 %), IgG (5–8 %), IgM (1–2 %), von Willebrand factor and coagulation factor XIII.

After transplantation, hepatic and renal functions as well as the concentration of immunosuppressive drugs were monitored daily in the hospitalization period. If the patient’s SCR level became obviously abnormally elevated, we paused the procedure to give CNIs for 72 h. During this period, the patient was maintained on a regimen containing only steroids and mycophenolate mofetil. If the patient’s SCR level remained elevated despite good urine output, the patient was maintained on a low-dose CNI to allow for renal recovery. For patients who remained oliguric, sirolimus was sometimes substituted for a CNI in the regimen. This regimen has also been adopted in other transplant centers [12]. In addition, we defined postoperative infections as hemodynamic instability accompanied with positive blood cultures, and in this study we only analyzed infections occurring before ARF. All infections were treated with appropriate therapy.

According to the RIFLE classification, ARF following OLT was classified into three groups (risk, injury and failure) based on relative changes of Scr or urine output [16]. We defined ARF as renal function reaching the level of failure (an increase in Scr ≥3.0 × baseline or decrease in GFR ≥75 % or an absolute Scr ≥354 μmol/l with an acute increase of at least 44 μmol/l and/or urine output <0.3 ml/kg/h ≥24 h or anuria ≥12 h or anuria ≥12 h) within their hospital stay period. According to these criteria, a total of 43 patients experienced ARF following OLT.

Outpatient follow-up was performed once a week for the first 3 months and every 2 weeks within the first year after the operation. The causes of death for each patient were recorded. All follow-up data were collected until 31 December 2011.

Clinical and surgical data for the cases reviewed were obtained from the China Liver Transplant Registry (CLTR) and by the checking of original medical records. National legislation and the ethics committee of Shanghai First People’s Hospital approved this retrospective study.
Table 1 Demographic and clinical characteristics of the cases included in the study

| Characteristics                        | Without cryoprecipitate transfusion (n = 232) | With cryoprecipitate transfusion (n = 157) | p value |
|----------------------------------------|----------------------------------------------|------------------------------------------|---------|
| Age, mean (SD), years                  | 47.7 (9.2)                                   | 47.8 (9.4)                               | 0.924   |
| Gender, n (%)                          |                                              |                                          |         |
| Male                                   | 189 (81.5)                                   | 120 (76.4)                               | 0.228   |
| Female                                 | 43 (18.5)                                    | 37 (23.6)                                |         |
| Etiology, n (%)                        |                                              |                                          |         |
| Cirrhosis                              | 151 (65.1)                                   | 115 (73.2)                               | 0.002*  |
| Carcinoma                              | 62 (26.7)                                    | 19 (12.1)                                |         |
| Fulminant hepatic failure              | 12 (5.2)                                     | 18 (11.5)                                |         |
| Others                                 | 7 (3.0)                                      | 5 (3.2)                                  |         |
| ABO blood group, n (%)                 |                                              |                                          |         |
| Incompatibility                        | 31 (13.4)                                    | 24 (15.3)                                | 0.593   |
| Compatibility                          | 201 (86.6)                                   | 133 (84.7)                               |         |
| Child-Pugh grade, n (%)                |                                              |                                          |         |
| Grade A                                | 41 (17.7)                                    | 13 (8.3)                                 | <0.001* |
| Grade B                                | 28 (12.1)                                    | 5 (3.2)                                  |         |
| Grade C                                | 163 (70.2)                                   | 139 (88.5)                               |         |
| Preoperation Scr, mean (SD), µmol/l    | 83.7 (9.4)                                   | 82.5 (11.4)                              | 0.273   |
| Warm ischemia time, mean (SD), min     | 3.5 (1.2)                                    | 3.4 (1.0)                                | 0.237   |
| Cold ischemia time, mean (SD), h       | 9.2 (2.0)                                    | 9.3 (2.3)                                | 0.514   |
| Anhepatic phase, mean (SD), min        | 60.8 (12.7)                                  | 63.0 (32.8)                              | 0.362   |
| Operation time, mean (SD), h           | 7.3 (1.0)                                    | 7.4 (1.2)                                | 0.192   |
| Blood loss, mean (SD), ml              | 3418 (2,555)                                 | 3482 (2,107)                             | 0.796   |
| Transfusion of blood products          |                                              |                                          |         |
| Whole blood, mean (SD), U              | 1.4 (3.5)                                    | 1.9 (4.0)                                | 0.229   |
| Red blood cells, mean (SD), U          | 9.8 (7.5)                                    | 10.0 (6.4)                               | 0.295   |
| Fresh frozen plasma, mean (SD), U      | 1.5 (3.1)                                    | 2.1 (5.0)                                | 0.667   |
| Platelet, mean (SD), U                 | 0.6 (1.0)                                    | 0.6 (1.0)                                | 0.900   |
| Cell saver, mean (SD), ml              | 584 (1309)                                   | 508 (1246)                               | 0.385   |
| Immunosuppressive protocol, n (%)      |                                              |                                          |         |
| Including cyclosporine A               | 164 (70.7)                                   | 109 (69.4)                               | 0.846   |
| Including FK506                        | 62 (26.7)                                    | 45 (28.7)                                |         |
| Steroid, n (%)                         |                                              |                                          |         |
| Used after OLT                         | 203 (87.5)                                   | 134 (85.4)                               | 0.541   |
| Not used after OLT                     | 29 (12.5)                                    | 23 (14.6)                                |         |
| Infections, n (%)                      |                                              |                                          |         |
| Occurred before ARF                    | 34 (14.7)                                    | 21 (13.4)                                | 0.722   |
| Did not occur or occurred after ARF    | 198 (85.3)                                   | 136 (86.6)                               |         |

Cirrhotic patients and patients with Child-Pugh grade C were more frequently found in the cryoprecipitate transfusion group

*p <0.05 indicates a significant difference between the two groups

Statistical analysis

We first compared the data distribution of each covariate between the exposed and the non-exposed groups, using the t test (normal distribution) or Kruskal-Wallis rank sum test (non-normal distribution) for continuous variables and χ² tests for categorical data (Table 1). Next, univariate logistic regression (Table 2) and multivariate logistic regression models (Table 3) were used to examine whether intraoperative cryoprecipitate transfusion and other covariates had an independent effect on ARF following OLT separately. Then, Pearson’s test and two-way ANOVA analysis were performed to discover the correlation between blood loss, Child-Pugh grade and cryoprecipitate transfusion (Figs. 1, 2). The χ² test was used to analyze the distribution of ARF in patients with and without cryoprecipitate transfusion. Then we explored the relationship between intraoperative cryoprecipitate transfusion and ARF following OLT by the smoothing plot, with an adjustment for potential confounders (Fig. 3). We further applied a two-piecewise linear regression model to examine the threshold effect of the cryoprecipitate transfusion...
on ARF according to the smoothing plot (Table 4). The threshold level of cryoprecipitate transfusion at which the relationship between ARF and the cryoprecipitate transfusion level began to change and became notable was determined using a trial method. The trial inflection point was moved along a pre-defined interval and detected the inflection point that gave the maximum model likelihood.

We ruled out ARF patients and then compared the Scr level at days 1, 3, 5 and 7 after the operation between the groups with and without cryoprecipitate transfusion by Kruskal-Wallis rank sum test separately (Fig. 4). The causes of death within the first year after liver transplantation between the exposed and non-exposed patients were also compared separately by univariate logistic regression (Table 5). All data were double entered and then exported to tab-delimited text files. All analyses were performed with R (http://www.R-project.org) and EmpowerStats software (www.empowerstats.com, X&Y solutions, Inc. Boston MA).

### Table 2 Effects of risk factors on acute renal failure following OLT by univariate analysis

| Variables                               | Total | Odds ratio (95 % CI) | p value |
|-----------------------------------------|-------|---------------------|---------|
| Etiology, n (%)                         |       |                     |         |
| Others                                  | 12 (3.1 %) | 0.74 (0.093, 6.0) | 0.780   |
| Fulminant hepatic failure               | 30 (7.7) | 0.28 (0.037, 2.1) | 0.221   |
| Carcinoma                               | 81 (20.8) | 1.4 (0.69, 2.9)  | 0.341   |
| Cirrhosis                               | 266 (68.4) | 1                  |         |
| ABO blood group, n (%)                  |       |                     |         |
| Compatible                              | 334 (85.9) | 0.37 (0.18, 0.77) | 0.008*  |
| Incompatibility                         | 55 (14.1) | 1                  |         |
| Child-Pugh grade, n (%)                 |       |                     |         |
| Grade C                                 | 302 (77.6) | 0.94 (0.45, 2.0)  | 0.882   |
| Grade A/B                               | 87 (22.4) | 1                  |         |
| Blood loss, mean (SD), 500 ml           | 6.9 (4.8) | 1.1 (1.0, 1.1)    | 0.008*  |
| Intraoperative cryoprecipitate transfusion, ABO blood group compatibility, blood loss and infections occurring before ARF might be possible risk factors for ARF following OLT
* p <0.05 indicates a crude association between variables and ARF following OLT

### Results

Among the 389 patients included in the study, 157 (40.4 %) underwent cryoprecipitate transfusion during OLT, with a mean volume of 12.8 U per case. The demographic and clinical characteristics of the cases including etiology, surgical factors and intraoperative transfusion of blood products are summarized in Table 1. Cirrhotic patients were found more frequently in the cryoprecipitate transfusion group than in those who did not receive cryoprecipitate transfusion (73.2 vs. 65.1 %; p = 0.002). In addition, Child-Pugh grade C was also more common in the cryoprecipitate transfusion group (163/232 vs. 139/157; p < 0.001). Apart from these two factors, there was no noticeable difference in the basic characteristics between the two groups. Since we ruled out patients with pre-transplantation renal dysfunction, the Scr level of all transplant recipients was within the normal range before OLT in the analysis, and there was no significant difference.
between the two groups (83.7 vs. 82.5; \( p = 0.273 \)).

Moreover, as the coagulation status during surgery changed constantly and the criteria for using fresh frozen plasma or cryoprecipitate were not the same, many patients received fresh frozen plasma transfusion in addition to cryoprecipitate throughout the surgical procedure. The dose of fresh frozen plasma in the cryoprecipitate transfusion group was also not significantly different from that in the group without cryoprecipitate transfusion (1.5 vs. 2.1; \( p = 0.667 \)).

A total of 43 patients (11.1%) developed ARF following OLT in this study. The univariate regression analysis showed that intraoperative cryoprecipitate transfusion was significantly correlated with ARF (OR 1.1, 95% CI 1.0–1.1, \( p = 0.002 \)). In addition, ABO blood group compatibility (OR 0.33, 95% CI 0.15–0.73, \( p = 0.006 \)), intraoperative blood loss (OR 1.1, 95% CI 1.0–1.1, \( p = 0.008 \)), infections before ARF (OR 4.0, 95% CI 1.8–8.9, \( p < 0.001 \)) and postoperative infections (OR 3.1, 95% CI 1.5–6.5, \( p = 0.002 \)) might also be associated with ARF following OLT (Table 2). After multivariable risk adjustment for potential confounding factors (Table 3), cryoprecipitate transfusion (OR 1.1, 95% CI 1.0–1.1, \( p = 0.002 \)), infections before ARF (OR 4.0, 95% CI 1.8–8.9, \( p < 0.001 \)) and blood loss (OR 1.1, 95% CI 1.0–1.1, \( p = 0.018 \)) were still positively associated with ARF following OLT. Meanwhile, ABO blood group

### Table 3 Multivariate logistic regression model for risk factors associated with ARF following OLT

| Variables in model | Odds ratio (95% CI) | \( p \) value |
|--------------------|---------------------|--------------|
| Cryoprecipitate, U | 1.1 (1.0, 1.1)      | 0.002        |
| ABO blood group compatible | 0.33 (0.15, 0.73) | 0.006        |
| Infections before ARF | 4.0 (1.8, 8.9) | <0.001       |
| Blood loss, 500 ml | 1.1 (1.0, 1.1)      | 0.018        |

\( a \) Odds ratios were derived from multivariate logistic regression analysis. These factors were adjusted in the multivariate regression analysis: age, etiology, Child-Pugh grade, ABO blood group, blood loss, infections, cryoprecipitate and steroid

Cryoprecipitate transfusion, ABO blood group incompatible, infections before ARF and blood loss were the independent risk factors associated with ARF following OLT.
compatibility could significantly reduce the risk of ARF (OR 0.33, 95 % CI 0.15–0.73, p = 0.006). Furthermore, we found that cryoprecipitate transfusion was obviously correlated with the Child-Pugh grade (p < 0.001), but slightly positively correlated with blood loss (r = 0.00061) (Figs. 1, 2).

Twenty-five patients developed ARF in the cryoprecipitate transfusion group, and 18 patients developed ARF in the no-cryoprecipitate transfusion group. The distribution of ARF in patients with cryoprecipitate transfusion was significantly higher than in patients without cryoprecipitate transfusion (15.9 vs. 7.8 %, p = 0.012). After adjusting for these possible factors related to ARF, including age, etiology, ABO blood group, Child-Pugh grade, intraoperative blood loss and postoperative infections, a nonlinear relationship between cryoprecipitate transfusion and ARF was observed (Fig. 3). The risk of ARF increased with the cryoprecipitate transfusion level up to the turning point (16 U) (OR 1.1, 95 % CI 1.1–1.2; p < 0.001). When the cryoprecipitate level was ≥16 U, the level of cryoprecipitate transfusion was not associated with the risk of ARF (OR 0.95, 95 % CI 0.85–1.1; p = 0.319) (Table 4).

Although there was no significant difference in the Scr level between the two groups before OLT, this situation changed obviously after transplantation. After excluding all ARF patients from the analysis, in the cryoprecipitate transfusion group, the level of Scr at postoperative day 1, 3, 5 and 7 was significantly higher than in patients without cryoprecipitate transfusion group, respectively (p < 0.01) (Fig. 4).

### Table 4

| Inflection point of cryoprecipitate transfusion (U) | Odds ratioa | p value |
|---------------------------------------------------|-------------|---------|
| <16                                               | 1.1 (1.1, 1.2) | <0.001 |
| ≥16                                               | 0.95 (0.85, 1.1) | 0.319  |

A 16-U threshold for the cryoprecipitate transfusion volume existed for risk of ARF

a Adjusted: age, etiology, Child-Pugh grade, blood loss, ABO blood group and infections

### Table 5

| Causes of death, n (%) | Without cryoprecipitate transfusion (n = 232) | With cryoprecipitate transfusion (n = 157) | Odds ratio (95 % CI) | p value |
|------------------------|-----------------------------------------------|-------------------------------------------|----------------------|---------|
| Liver related          | 12 (5.0)                                      | 10 (6.4)                                  | 1.2 (0.53, 3.0)      | 0.617   |
| ARF related            | 4 (1.7)                                       | 10 (6.4)                                  | 3.9 (1.2, 12.6)      | 0.024*  |
| Myocardial infarction  | 2 (0.9)                                       | 2 (1.3)                                   | 1.5 (0.21, 10.6)     | 0.695   |
| Hypovolemic shock      | 2 (0.9)                                       | 4 (2.5)                                   | 3.0 (0.54, 16.6)     | 0.207   |
| Acute lung injury/ARDS | 3 (1.3)                                       | 1 (0.6)                                   | 0.49 (0.05, 4.7)     | 0.538   |
| Pulmonary embolism     | 2 (0.9)                                       | 2 (1.3)                                   | 1.5 (0.21, 10.6)     | 0.695   |
| Sepsis or MOF          | 7 (3.0)                                       | 5 (3.2)                                   | 1.1 (0.33, 3.4)      | 0.925   |
| Malignancy             | 0 (0.0)                                       | 1 (0.6)                                   | 3.0 (0.27, 33.2)     | 0.374   |
| Unknown                | 1 (0.4)                                       | 2 (1.3)                                   | 3.0 (1.1, 3.0)       | 0.029*  |
| Total                  | 33 (14.2)                                     | 37 (22.9)                                 | 1.8 (1.1, 3.0)       |         |

There was a significant difference in ARF-related deaths between the two groups. More deaths within the first year after OLT were observed in the patients with cryoprecipitate transfusion

ARDS acute respiratory distress syndrome

a p value <0.05 indicates a significant difference between the two groups

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**Fig. 4** Mean Scr levels over time. The Scr level reached a peak at postoperative day 3 and then began to decline gradually. After ruling out all of the ARF patients, the level of Scr in the group of patients with cryoprecipitate transfusion (n = 132) at day 1, 3, 5 and 7 was significantly higher than in patients without cryoprecipitate transfusion (n = 214) separately (p < 0.01)
More deaths within the first year after OLT were also observed in patients with cryoprecipitate transfusion than in those without cryoprecipitate transfusion (22.9 vs. 14.2 %, \( p = 0.029 \)). There was a significant difference in ARF-related deaths between the two groups (6.4 vs. 1.7 %, \( p = 0.024 \), but other significant differences in causes of death were not found (Table 5).

Discussion

To date, studies have investigated several risk factors for developing postoperative ARF. The impact of postoperative infection on patient’s renal function has been widely accepted [5, 17]. From the perspective of pathophysiology, serious infection can result in systemic arterial vasodilation and intra-renal vasoconstriction, and it is also conducive to other kidney injuries [18, 19]. In addition, blood loss during the surgical procedure can lead to hemodynamic instability and hypotension after graft reperfusion [20, 21], so blood loss was considered another risk factor related to ARF [5]. As the current analysis found, these two factors were also associated with the occurrence of postoperative ARF. Preoperative renal dysfunction has been evaluated as a potential strong predictor of postoperative ARF [22, 23]. To minimize the influence on the results, we excluded patients with preoperative Scr levels greater than 133 mmol/l from the analysis. Moreover, the total volume of cryoprecipitate transfusion was affected by the severity of end-stage liver disease and the etiology, so Child-Pugh grade and etiology were also adjusted in the analysis. After adjusting for these potential confounders, we still found a significant correlation between intraoperative cryoprecipitate transfusion and the occurrence of ARF following OLT. Because the definition of ARF in the current study was stringent, it might also have skewed the results because of the relatively small group of patients examined. We also compared the postoperative Scr level between the groups with and without cryoprecipitate transfusion after ruling out all patients with ARF. The results indicated that the Scr level in patients receiving cryoprecipitate transfusion was significantly higher than in those who did not receive it. This led to the same conclusion, linking cryoprecipitate to renal toxicity in this setting.

Cryoprecipitate was first reported by Pool et al. [24]. Its major components include fibrinogen, factor VIII/von Willebrand factor molecular complex (FVIII/vWF), factor XIII, fibronectin, platelet microparticles and immunoglobulins IgG and IgM [30, 32], platelet microparticles that are strongly immunogenic [33]. In our experience, transfusion of these immunogens might be involved in the occurrence of ARF following OLT. In addition, when large doses of cryoprecipitate transfusion are required, a patient might receive cryoprecipitate made from more than one blood donor’s plasma. This would increase the frequency of leukocyte system alloimmunity and might also be involved in the occurrence of ARF.

Immune factors might also play an important role in the increased risk of ARF with cryoprecipitate transfusion. Cryoprecipitate contains high concentrations of platelet microparticles together with low concentrations of immunoglobulins IgG and IgM [30, 32], platelet microparticles that are strongly immunogenic [33]. In our experience, transfusion of these immunogens might be involved in the occurrence of ARF following OLT. In addition, when large doses of cryoprecipitate transfusion are required, a patient might receive cryoprecipitate made from more than one blood donor’s plasma. This would increase the frequency of leukocyte system alloimmunity and might also be involved in the occurrence of ARF.

In the present study, compared with patients without cryoprecipitate transfusion, patients receiving cryoprecipitate transfusion showed significantly higher 1-year mortality after the operation. The main reason for this difference was ARF-related deaths. Renal replacement therapy (RRT) is always the only choice for the clinician if conservative treatment is ineffective. ARF patients died not only from renal failure but sometimes also from co-
convincing results from evidence-based medicine are associated with postoperative ARF and might increase shown that cryoprecipitate transfusion during OLT is in patients with end-stage liver disease, how to use it however, due to the specificity of the blood coagulation system embolism is also significantly higher in ABO blood group-incompatible cases than in ABO blood group-compatible cases. Interestingly, our analysis indicated that ABO blood group incompatibility may be associated with an increased risk of ARF following OLT. Because of the gradual reduction in the number of OLTs in ABO blood group-incompatible cases, multicenter and larger-scale analyses are required to support and validate this conclusion.

Although our analysis suggested that cryoprecipitate transfusion during OLT is associated with postoperative ARF, this research has several limitations that should be noted. First, the best definition of pre-transplantation renal dysfunction in the setting of liver cirrhosis is controversial; we choose Scr greater than 133 mmol/l as the cutoff value in the study because it has been selected in several consensus conferences. In addition, due to the limitations of a retrospective study, possible selection bias and the sample size from a single center might have been presented in this research.

In some countries, cryoprecipitate transfusion is replaced by a virus-inactivated fibrinogen concentrate, which is thought to reduce immune-related complications. However, cryoprecipitate is easy to obtain. Moreover, rational use of cryoprecipitate in OLT can effectively reduce blood loss and promote wound healing, so it is still being utilized in developing countries. However, due to the specificity of the blood coagulation system in patients with end-stage liver disease, how to use it properly in OLT remains controversial. Our study has shown that cryoprecipitate transfusion during OLT is associated with postoperative ARF and might increase mortality within the first year. Cryoprecipitate transfusion during OLT should be performed cautiously until more convincing results from evidence-based medicine are available.

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Conflict of interest Shuang Liu, Xiaoliang Wang, Yuanshan Lu, Tao Li, Zijun Gong, Tao Sheng, Bin Hu, Zhihai Peng and Xing Sun declare that they have no conflicts of interest.

Compliance with Ethics Requirements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Due to the retrospective nature of the study, this article did not involve any studies with human or animal subjects. National legislation and the ethics committee of Shanghai First People’s Hospital approved this retrospective study.

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