Low-Dose, Early Fresh Frozen Plasma Transfusion Therapy After Severe Trauma Brain Injury: A Clinical, Prospective, Randomized, Controlled Study

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BACKGROUND: **To investigate role of Low-dose, Early Fresh frozen plasma Transfusion (LEFT) therapy in preventing perioperative coagulopathy and improving long-term outcome after severe traumatic brain injury (TBI).**

METHODS: **A prospective, single-center, parallel-group, randomized trial was designed. Patients with severe TBI were eligible. We used a computer-generated randomization list and closed opaque envelops to randomly allocate patients to treatment with fresh frozen plasma (5 mL/kg body weight; LEFT group) or normal saline (5 mL/kg body weight; NO LEFT group) after admission in the operating room.**

RESULTS: **Between January 1, 2018, and November 31, 2018, 63 patients were included and randomly allocated to LEFT (n = 28) and NO LEFT (n = 35) groups. The final interim analysis included 20 patients in the LEFT group and 32 patients in the NO LEFT group. The study was terminated early for futility and safety reasons because a high proportion of patients (7 of 20; 35.0%) in the LEFT group developed new delayed traumatic intracranial hematoma after surgery compared with the NO LEFT group (3 of 32; 9.4%) (relative risk, 5.205; 95% confidence interval, 1.159–23.384; P = 0.023). Demographic characteristics and indexes of severity of brain injury were similar at baseline.**

CONCLUSIONS: **LEFT therapy was associated with a higher incidence of delayed traumatic intracranial hematoma than normal fresh frozen plasma transfusion in patients with severe TBI. A restricted fresh frozen plasma transfusion protocol, in the right clinical setting, may be more appropriate in patients with TBIs.**

INTRODUCTION

Severe traumatic brain injury (TBI) is one of the most common causes of morbidity and mortality.[1] Among patients with TBI, 15%–30% have been reported to experience blood coagulation disorders, mainly in the form of uncontrolled hemorrhage.[2] Talving et al.[3] reported that the development of TBI coagulopathy is associated with longer intensive care unit length of stay and an almost 10-fold increased risk of death.

In the case of excessive bleeding, fresh frozen plasma (FFP) is frequently transfused to provide coagulation factors either preventively or after hemorrhagic complications.[4] It has been proposed that correction of coagulopathy by FFP transfusion can have beneficial effects on the outcome of the disease.[5] In addition, May et al.[6] suggested that patients with a Glasgow Coma Scale (GCS) score of ≤6 would benefit from empiric infusion of FFP. The most common reason for FFP transfusion is the correction of an elevated international normalized ratio (INR), although evidence is lacking to support such a practice (INR >1.6).[7] FFP does not reliably correct mild to moderate elevations in INR or induce a more procoagulant state.[8,9] Restrictive strategies have been recommended because of the poor evidence of FFP efficacy, the risk of adverse effects, and the cost and difficulties in providing an appropriate supply of FFP.[10] The decision to administer plasma to a critically ill patient in

Key words
- Delayed traumatic intracranial hematoma
- Fresh frozen plasma
- Glasgow Outcome Scale
- Traumatic brain injury

Abbreviations and Acronyms
CI: Confidence interval
DTICH: Delayed traumatic intracranial hematoma
FFP: Fresh frozen plasma
GCS: Glasgow Coma Scale
INR: International normalized ratio
LEFT: Low-dose, Early Fresh frozen plasma Transfusion
RBC: Red blood cell
TBI: Traumatic brain injury
TCDB: Traumatic Coma Data Bank

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the absence of active bleeding remains controversial.[11] Early and low-dose resuscitation with FFP might improve neurologic outcomes as well as decrease incidences of transfusion overload.[12] Generally, FFP transfusion in cardiac surgery is recommended only in cases of excessive bleeding associated with a documented coagulation defect.[13] Until now, no previous randomized controlled trials have demonstrated the effect of Low-dose, Early Fresh frozen plasma Transfusion (LEFT) therapy on perioperative complications and outcomes of patients with severe TBI. A post hoc follow-up study of patients with severe TBI was conducted.

MATERIALS AND METHODS

Study Design

This study was approved by the Ethics Committee of Cangzhou Central Hospital (Current Controlled Trials number, ChiCTR-INR-17013901). The double-blind randomized clinical trial was conducted in Cangzhou Central Hospital, which is a tertiary referral center in Cangzhou (Hebei Province, China) between January 1, 2018, and November 31, 2018. Written informed consent was obtained from all competent patients. Eligible adult patients who underwent emergency craniotomy evacuation of hematomas and decompressive hemicraniectomy for subdural hematoma were randomly assigned to receive either 5 mL/kg of FFP or normal saline (5 mL/kg) upon admission to the operating room.

Based on computed tomography, the Traumatic Coma Data Bank (TCDB) score was used to evaluate the anatomic severity of TBI by 2 of the investigators (J.B. and W.Z.) who were unaware of the treatment assignments.[10] This score is divided into 6 classifications as follows: 1) diffuse injury I (no intracranial pathology); 2) diffuse injury II (cisterns present with midline shift 0–5 mm and no high or mixed-density lesions >22 cm^3); 3) diffuse injury III (cisterns compressed or absent with midline shift 0–5 mm and no high or mixed-density lesions >25 cm^3); 4) diffuse injury IV (midline shift >5 mm and no high or mixed-density lesions >25 cm^3); 5) evacuated mass lesion (any lesion surgically evacuated); 6) nonevacuated mass lesion (high or mixed-density lesion >25 cm^3 and not surgically evacuated). The inclusion criteria for patients who underwent surgery were as follows: 1) preoperative GCS score of 3–8; 2) subdural hematoma with TCDB ≥4; 3) <3 hours after admission. The exclusion criteria included 1) severe cardiac, pulmonary, hepatic, or renal dysfunction; 2) history of dementia or prior central nervous system disease; and 3) history of coagulating disorders or anticoagulant drug usage (e.g., aspirin, clopidogrel, warfarin).

Patients were randomly and equally allocated into a LEFT group and a NO LEFT group as control by card shuffling of sealed opaque envelopes. FFP (5 mL/kg body weight) was infused (over 20–30 minutes) to patients in the LEFT group upon admission in the operating room. In the NO LEFT group, normal saline (5 mL/kg of body weight) was infused (over 20–30 minutes). The administration of FFP or normal saline was carried out by anesthesiologists or nurses who were not involved in the patient assessment.

Baseline Assessment and Follow-Up Data Collection

We obtained baseline information on age, sex, weight, body mass index, and severity of the illness and the injury. The Abbreviated Injury Scale was calculated, and then initial Injury Severity Score was assessed by trained assessors. The indexes specific to brain injuries that we used were the last recorded GCS score before randomization (while the patient was not sedated), pupillary light reflex score, and TCDB score from the last computed tomography scan performed before randomization. After randomization, heart rate, systolic and diastolic arterial blood pressure, duration of surgery (total time in the operating room), urine volume, estimated blood loss, red blood cell (RBC) transfusion, FFP transfusion, hydroxyethyl starch transfusion, second surgery, and postoperative complications (delayed traumatic intracranial hematoma [DTICH], acute respiratory distress syndrome, pneumonia, and acute renal failure) as well as the measurements of hemoglobin, platelet count, INR, glucose, serum sodium, potassium, use of mechanical ventilation, and length of antibiotic administration were recorded daily until discharge from the intensive care unit, death, or until postoperative day 28.

At 6 months after discharge, outcomes in patients with TBI were determined according to the Glasgow Outcome Scale. According to the Glasgow Outcome Scale, death, vegetative state, and severe disability were defined as poor outcomes, and moderate disability and good recovery were defined as good outcomes.

Statistical Analysis

The study was designed to have 90% power (at a 2-sided α error of 5%) to detect a difference in the incidence of mortality based on our previous retrospective study.[5] This generated a sample size of at least 20 patients for each group. Finally, we decided on a sample of approximately 1.5 times the required size calculation.

The data were exported from the study database and analyzed using SPSS Version 18 software (SPSS, Inc., Chicago, Illinois, USA). The patients with missing data were excluded from the current study. Univariate analyses of proportions were compared using χ^2 test or Fisher exact test, and continuous variables were compared using unpaired t tests or analysis of variance. The results of comparisons of event rates in the 2 groups are presented as relative risk with 95% confidence interval (CI). Bivariate logistic regression analysis was used to assess DTICH and LEFT treatment for the dependent variable. The results are presented as odds ratio with 95% CI. Survival times were compared in the 2 groups with the use of the log-rank test and are presented as a Kaplan-Meier curve unadjusted for baseline covariates.

RESULTS

During the study period, 63 patients were admitted to the hospital who had undergone craniotomy evacuation of hematomas resulting from acute TBIs. Patients were excluded if they had no FFP transfusion ($n = 1$; 1.6%), withdrew consent for follow-up ($n = 4$; 6.3%), or had incomplete or misclassified data ($n = 6$; 9.5%). Of the remaining 52 patients, 20 (38.5%) were assigned to receive 5 mL/kg of FFP and 32 (61.5%) were assigned to receive saline at the beginning of surgery after admission to the operating room (**Figure 1**).

Patient and Traumatic Characteristics

The patients included in this final cohort were all Han Chinese with the following characteristics: mean age, 64.7 ± 8.8 years;

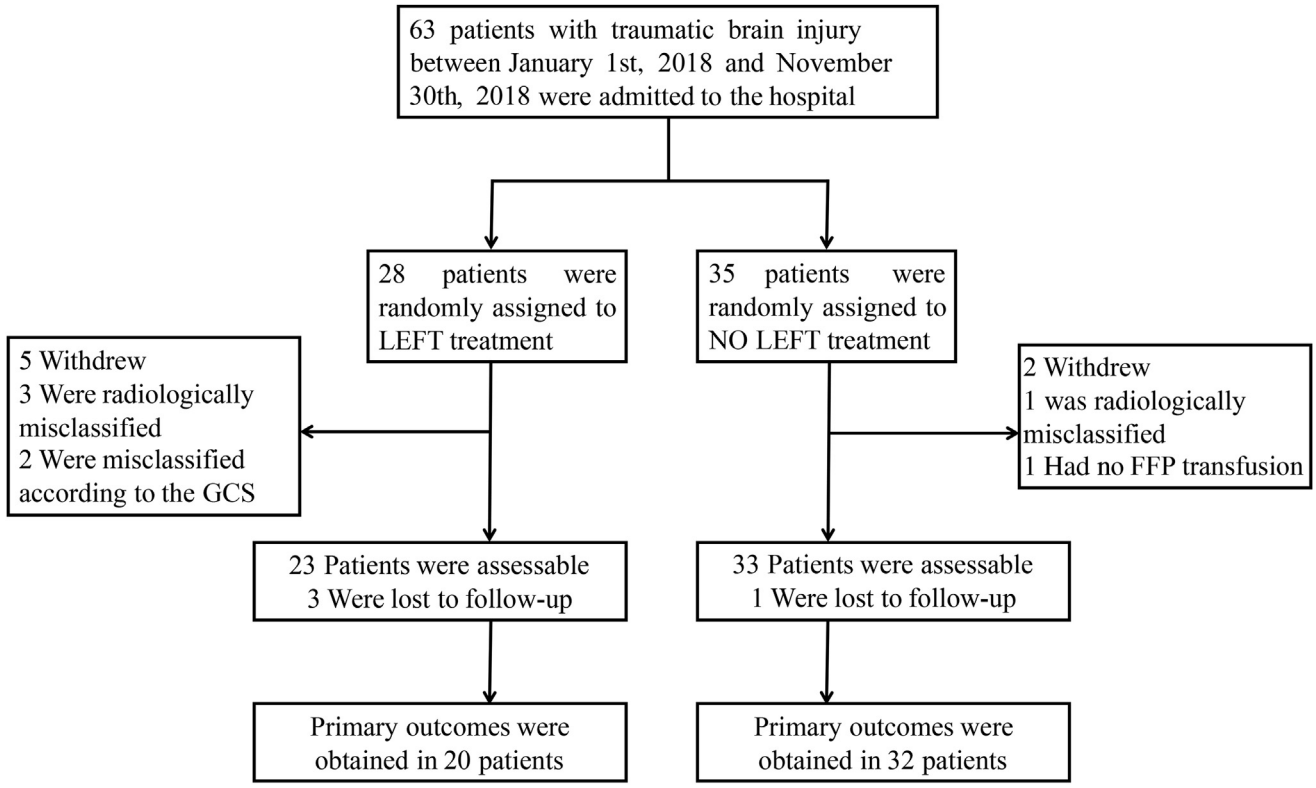

Figure 1. Enrollment of patients and assessment of primary outcomes. LEFT, Low-dose, Early Fresh frozen plasma Transfusion; GCS, Glasgow Coma Scale; FFP, fresh frozen plasma.

female, 25.0%; body mass index, 24.6 ± 3.3 kg/m^2; heart rate before anesthesia induction, 103.5 ± 24.1 beats/minute; systolic blood pressure, 154.5 ± 32.11 mm Hg; diastolic blood pressure, 90.6 ± 15.8 mm Hg; GCS score, 5.1 ± 2.6; Injury Severity Score, 21.1 ± 8.7; TCDB, 2.7 ± 1.5; and pupillary light reflex, 0.8 ± 0.9 (Table 1). These 2 groups were well balanced for patient characteristics.

Intraoperative Variables

For the whole group, the average operative time was 264.8 ± 131.1 minutes, and there were no differences between the LEFT group (267.9 ± 166.7 minutes) and NO LEFT group (262.9 ± 106.0 minutes). During surgery, the predominant solution of intravenous fluid transfusion was crystalloid. Patients lost 18.5 ± 12.2 mL/kg of blood and 13.9 ± 9.5 mL/kg of urine and received 7.1 ± 3.6 mL/kg of FFP, 40.8 ± 51.3 mL/kg of crystalloid, and 12.1 ± 5.2 mL/kg of colloid. Also, 47 patients (90.4%) received 9.1 ± 5.7 mL/kg of RBCs during the perioperative period (Table 2). There was no significant difference in the volumes of crystalloid and colloid administered during surgery. However, patients in the LEFT group received significantly more FFP than patients in the NO LEFT group ($P = 0.018$) (Table 2). Moreover, RBC transfusion was markedly higher in the LEFT group than in the NO LEFT group during surgery ($P = 0.023$) (Table 2).

Outcome Data

The mortality rate was 48.1%, and the most common cause of death was postoperative cerebral hernia. At 6 months, 10 of 20 patients in the LEFT group (50.0%) had died compared with 15 of 32 patients in the saline group (46.9%) (relative risk, 1.133; 95% CI, 0.370–3.467; $P = 1.000$) (Table 3). In addition, the probability of survival was not significantly different in the LEFT and NO LEFT groups ($P = 0.883$) (Figure 2).

Among patients with LEFT treatment, 7 of 20 patients (35.0%) developed new DTICH after surgery compared with 3 of 32 patients in the NO LEFT group (9.4%) (relative risk, 5.205; 95% CI, 1.159–23.384; $P = 0.023$). Adjustment for baseline covariates, including RBC transfusion and GCS score on admission, did not change the study findings. Comparing the LEFT group with the NO LEFT group, the adjusted odds ratio of DTICH was 5.493 (95% CI, 1.053–28.652; $P = 0.043$). Moreover, hospital stay in patients in the LEFT group (45.2 ± 39.4 days) was prolonged compared with patients in the NO LEFT group (25.9 ± 23.6 days) ($P = 0.032$) (Table 3).

In the LEFT group, we also observed significantly decreased platelets (86.2 ± 36.3 × 10^9/L) on postoperative day 1 compared with the NO LEFT group (122.5 ± 40.7 × 10^9/L) ($P = 0.008$). Additionally, 6 of 20 patients (30.0%) in the LEFT group underwent a second surgery after the first surgery compared with 3 of 32

Table 1. Baseline Characteristics of Patients

Characteristics and Variables	All Patients (n = 52)	LEFT Group (n = 20)	NO LEFT Group (n = 32)	P Value
Age, years, mean (SD)	64.71 (8.8)	65.7 (10.4)	64.1 (7.7)	0.548
Sex, female, number (%)	13 (25.0)	7 (21.9)	6 (30.0)	0.510
Weight, kg, mean (SD)	70.4 (12.9)	69.5 (11.7)	71.0 (13.7)	0.677
Height, cm, mean (SD)	168.6 (8.3)	168.1 (8.6)	168.9 (8.1)	0.720
BMI, kg/m^2, mean (SD)	24.6 (3.3)	24.4 (2.4)	24.8 (3.8)	0.703
ASA, score, mean (SD)	3.9 (0.5)	4.0 (0.32)	3.8 (0.5)	0.231
Initial GCS, score, mean (SD)	5.1 (2.6)	4.7 (1.9)	5.3 (2.9)	0.434
PLR, score, mean (SD)	0.8 (0.9)	0.6 (0.8)	1.0 (0.9)	0.132
Initial ISS, score, mean (SD)	21.1 (8.7)	19.8 (7.4)	23.2 (10.2)	0.171
TCDB, score, mean (SD)	2.8 (1.5)	2.8 (1.5)	2.6 (1.5)	0.776
Systolic blood pressure, mm Hg, mean (SD)	154.5 (32.1)	156.4 (35.4)	153.3 (30.4)	0.746
Diastolic blood pressure, mm Hg, mean (SD)	90.6 (15.8)	88.4 (16.5)	91.9 (15.5)	0.442
Heart rate, beats/minute, mean (SD)	103.5 (24.1)	106.5 (26.8)	101.7 (22.5)	0.491
Hemoglobin, g/L, mean (SD)	126.0 (20.7)	120.3 (24.7)	129.5 (17.3)	0.116
PLT, $\times$ 10^9/L, mean (SD)	181.5 (70.2)	161.5 (60.2)	194.4 (74.1)	0.103
APTT, seconds, mean (SD)	31.8 (6.9)	31.9 (6.8)	31.8 (7.1)	0.914
FIB, g/L, mean (SD)	2.5 (1.1)	2.6 (1.2)	2.5 (1.1)	0.824
INR, score, mean (SD)	1.2 (0.4)	1.2 (0.4)	1.1 (0.3)	0.431
PT, seconds, mean (SD)	12.8 (4.1)	13.3 (4.5)	12.5 (3.8)	0.505
TT, seconds, mean (SD)	15.3 (3.8)	15.48 (3.4)	15.18 (4.1)	0.785
Serum glucose, mg/dL, mean (SD)	10.8 (4.5)	11.14 (4.1)	10.6 (4.8)	0.672
Serum sodium, mmol/L, mean (SD)	138.5 (4.9)	138.75 (5.2)	138.3 (4.8)	0.774
Serum potassium, mmol/L, mean (SD)	3.8 (0.61)	3.9 (0.6)	3.7 (0.6)	0.213

Categorical value is displayed as count (percentage). Continuous variables are displayed as mean (SD).

LEFT, Low-dose, Early Fresh frozen plasma Transfusion; NO LEFT, no Low-dose, Early Fresh frozen plasma Transfusion; BMI, body mass index; ASA, American Society of Anesthesiologists; GCS, Glasgow Coma Scale; PLR, pupillary light reflex; ISS, Injury Severity Score; TCDB, Traumatic Coma Data Bank; PLT, platelets; APTT, activated partial thromboplastin time; FIB, fibrinogen; INR, international normalized ratio; PT, prothrombin time; TT, thrombin time.

patients (9.4%) in the NO LEFT group (relative risk, 4.143; 95% CI, 0.901–19.049; P = 0.071) (Table 3).

DISCUSSION

We conducted a post hoc follow-up study of patients with severe TBI recruited into the LEFT study. The demographic characteristics and severity of brain injury at baseline were similar in the patients assigned to LEFT treatment and patients assigned to NO LEFT for blood transfusion. We determined the incidence of DTICH was significantly higher among patients in the LEFT group compared with patients assigned to the NO LEFT group. Additionally, length of antibiotic administration prolonged in the LEFT group compared with NO LEFT group.

Since the Ministry of Public Safety issued the alcohol penalty law in 2011, which declared that all drivers found to be over the legal alcohol limit (≥80 mg alcohol in 100 mL blood) were liable to prison sentences, TBIs caused by road traffic accidents now more frequently involve mopeds (called electric bicycles in China) than automobiles.[14] In contrast to automobile drivers who are generally in their 20s to 50s, moped riders are of all ages. In addition, with the significant prolongation of life span in China, falls are becoming the leading cause of TBI in individuals ≥55 years of age.[15,16] Thus, in contrast to some previous studies, the current study reported mean age for both groups in the 60s.

For patients with severe TBI, dehydration administration before surgery and vasodilation by anesthetics might directly induce hypovolemia after dural opening when Cushing response disappeared. The quick improvement of hypovolemia by colloid effectively avoids hypotension that might lead to more cerebral ischemia.[10] Moreover, perioperative rotational thromboelastometry clot formation and structure, plasma fibrinogen, and factor XIII levels were generally within the normal range after appropriate amount of colloid transfusion (<1 L).[17] In our previous study, the safety of hydroxyethyl starch administration was discussed and verified.[10] In the current

Table 2. Perioperative Characteristics of Patients

Characteristics and Variables	All Patients (n = 52)	LEFT Group (n = 20)	NO LEFT Group (n = 32)	P Value
Surgical duration, minutes, mean (SD)	264.8 (131.1)	267.9 (166.7)	262.9 (106.0)	0.895
Isotonic crystalloid transfusion, mL/kg, mean (SD)	37.2 (19.5)	38.5 (21.3)	36.9 (19.2)	0.491
Hydroxyethyl starch 130/0.4, mL/kg, mean (SD)	12.1 (5.2)	11.9 (5.3)	12.3 (5.3)	0.758
Estimated blood loss, mL/kg, mean (SD)	18.5 (12.2)	17.9 (9.6)	18.9 (13.8)	0.776
Urine volume, mL/kg, mean (SD)	13.9 (9.5)	14.2 (9.8)	13.7 (9.5)	0.877
RBC transfusion, mL/kg, mean (SD)	9.1 (5.7)	11.3 (6.8)	7.6 (4.5)	0.023
FFP transfusion, mL/kg, mean (SD)	7.1 (3.6)	8.6 (4.4)	6.2 (2.8)	0.018
Interval from onset of operating room admission to FFP transfusion, minutes, mean (SD)	72.3 (51.0)	18.9 (13.0)	99.0 (40.7)	0.000
Autologous blood, mL/kg, mean (SD)	5.5 (7.2)	4.0 (4.8)	6.5 (8.3)	0.223
Dexamethasone administration, mg/kg, mean (SD)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.067

Continuous variables are displayed as mean (SD).
LEFT, Low-dose, Early Fresh frozen plasma Transfusion; NO LEFT, no Low-dose, Early Fresh frozen plasma Transfusion; RBC, red blood cell; FFP, fresh frozen plasma.

study, an average amount of 12.1 ± 5.2 mL hydroxyethyl starch (500–1000 mL for 1 patient) was administered.

A previous study revealed the beneficial effects of FFP treatment in a long-term survival model of combined TBI and hemorrhagic shock.[12] It was shown that early treatment with FFP substantially attenuates degree of neurologic impairment, improves rate of recovery, and preserves cognitive functions. This might be associated with neuroprotection by improving cerebral perfusion, diminishing glutamate-mediated excitotoxic secondary brain injury, and reducing mitochondrial dysfunction induced by early FFP transfusion. A previous study reported that a significant improvement in INR was observed in patients with higher pretransfusion FFP. In addition, FFP resuscitation caused an immediate increase in adenosine diphosphate–induced and arachidonic acid–induced platelet aggregation.[18,19] Bianchi et al.[13] also reported that FFP in the priming solution appears slightly superior to late administration in terms of postoperative bleeding in infants undergoing cardiac surgery. However, before

Table 3. Postoperative Characteristics of Patients

Characteristics and Variables	All Group (n = 52)	LEFT Group (n = 20)	NO LEFT Group (n = 32)	P Value
Hemoglobin, g/L, mean (SD)	101.4 (24.1)	102.3 (22.1)	100.9 (25.5)	0.859
PLT, $\times 10^9$/L, mean (SD)	108.2 (42.5)	86.2 (36.3)	122.5 (40.7)	0.008
DTICH, number (%)	10 (19.2)	7 (35.0)	3 (9.4)	0.033
Second surgery, number (%)	9 (17.3)	6 (30.0)	3 (9.4)	0.071
Intracranial infection, number (%)	9 (17.3)	5 (25.0)	4 (12.5)	0.280
ARDS, number (%)	8 (15.4)	3 (15.0)	5 (15.6)	1.000
Pneumonia, number (%)	23 (44.2)	11 (55.0)	12 (37.5)	0.216
ARF, number (%)	5 (9.6)	2 (10.0)	3 (9.4)	1.000
Length of hospital stay, days, mean (SD)	33.3 (31.7)	45.15 (39.4)	25.91 (23.6)	0.032
Length of antibiotics administration, days, mean (SD)	21.3 (18.3)	28.3 (21.4)	16.91 (14.8)	0.027
Length of mechanical ventilation, days, mean (SD)	2.13 (3.8)	2.4 (3.8)	1.97 (3.9)	0.697
GOS, score, mean (SD)	2.2 (1.1)	1.9 (0.8)	2.41 (1.2)	0.082
Mortality, number (%)	25 (48.1)	10 (50.0)	15 (46.9)	1.000

Categorical values are displayed as count (percentage). Continuous variables are displayed as mean (SD).
LEFT, Low-dose, Early Fresh frozen plasma Transfusion; NO LEFT, no Low-dose, Early Fresh frozen plasma Transfusion; PLT, platelet; DTICH, delayed traumatic intracranial hematoma; ARDS, acute respiratory distress syndrome; ARF, acute renal failure; GOS, Glasgow Outcome Scale.

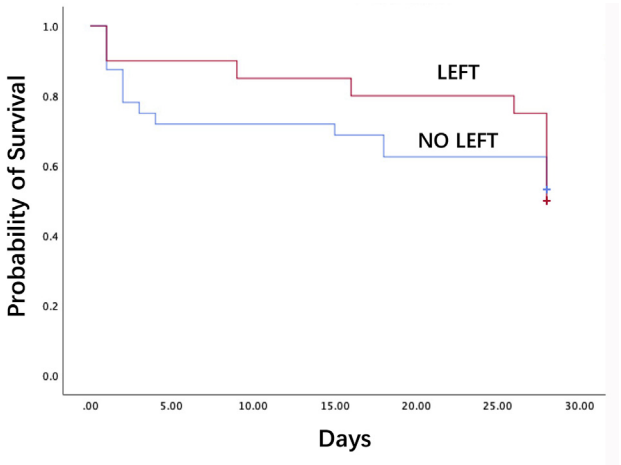

Figure 2. The 30-day survival rates for patients with severe traumatic brain injuries with or without Low-dose, Early Fresh frozen plasma Transfusion (LEFT). Kaplan-Meier analysis was performed to assess the outcomes of patients with traumatic brain injury who received LEFT treatment compared with patients who did not receive LEFT treatment.

our current study, a randomized, controlled trial examined the effect of FFP in severe closed head injury.[20] It was suggested that early empiric infusion of FFP (10–15 mL/kg) in patients with severe head injury may lead to adverse effects, such as an increase in the frequency of DTICH and an increase in mortality. In our previous study, a robust positive association was demonstrated between FFP transfusion and mortality or worse outcomes (Glasgow Outcome Scale score ≤3) for patients with severe TBIs.[10] Besides plasma transfusion–related acute lung injury and overload, inordinate coagulation might be exacerbated.[21] Moreover, FFP may accelerate the coagulation process and consumptive coagulopathy, inducing bleeding tendency in brain. In addition, FFP may increase the cerebral blood flow and blood pressure, thus inducing bleeding from previously injured vessels.[20] Our data show poor efficacy of early, low-dose FFP therapy in limiting RBC transfusion or preventing coagulopathy (i.e., DTICH), a finding that is in agreement with results of several studies using FFP.[5,22,23]

Our study was a double-blind comparison of FFP transfusion in patients with severe TBI. First, the patients in the LEFT group received more FFP transfusion compared with the NO LEFT group. It was revealed that early FFP administration not only decreased total volume of FFP, but also increased additional FFP transfusion. Although there was no significant difference between the LEFT and NO LEFT groups in mortality and functional outcomes, the incidence of DTICH was significantly higher among patients assigned to LEFT treatment than among patients assigned to NO LEFT treatment. Moreover, platelets on postoperative day 1 in patients with LEFT treatment significantly decreased compared with patients in the NO LEFT group. This might be a vital reason why the incidence of DTICH was significantly higher in the LEFT group than in the NO LEFT group. As blood volume increased, relative concentration of platelets induced by FFP transfusion decreased, and blood would easily flow out from previously injured vessels. The incidence of second surgery between these 2 groups was not different, but the P value of 0.056 also emphasized the risk of further surgeries after early and low-dose (5 mL/kg) FFP transfusion. Also, Sezik et al.[24] reported that pretransfusion INR was strongly correlated with change in INR with 1 unit FFP. A weaker improvement in INR was observed in patients with lower pretransfusion INR. Transfusion for patients not meeting current FFP guidelines does not reliably reduce the INR and exposes patients to unnecessary risk.[25] Additionally, prolonged antibiotic administration in the LEFT group was also found in the current study. It might be correlated with wet lung induced by volume overload and left heart failure.

Our study provides post hoc data to guide the choice of resuscitation fluid in patients with TBI, and we maintained blinding of treatment assignment throughout the study period and achieved 6-month follow-up completion rates >90%. Persistent intracranial pressure monitoring was missing due to high incidences of intracranial infection. Moreover, the biologic mechanisms for the observed differences in DTICH are unclear. Further detailed analyses of biologic mechanisms associated with intracranial hypertension are required.

CONCLUSIONS

In our study comparing LEFT with NO LEFT treatment for coagulation during surgery, DTICH and prolonged length of antibiotic administration were observed in patients with severe TBI. These findings suggest that a restricted FFP transfusion protocol in the right clinical setting may be more appropriate in patients with severe TBIs.

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