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Intraoperative Hypertension and Thrombocytopenia Associated With Intracranial Hemorrhage After Liver Transplantation

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Background. Intracranial hemorrhage (ICH) is a devastating complication. Although hypertension and thrombocytopenia are well-known risk factors for ICH in the general population, their roles in ICH after liver transplantation (LT) have not been well established. **Methods.** We performed a retrospective study and hypothesized that intraoperative hypertension and thrombocytopenia were associated with posttransplant ICH. New onset of spontaneous hemorrhage in the central nervous system within 30 days after LT were identified by reviewing radiologic reports and medical records. Risk factors were identified by multivariate logistic regression. Receiver operating characteristic analysis and Youden index were used to find the cutoff value with optimal sensitivity and specificity. **Results.** Of 1836 adult patients undergoing LT at University of California, Los Angeles, 36 (2.0%) developed ICH within 30 days after LT. Multivariate logistic regression demonstrated that intraoperative mean arterial pressure ≥105 mm Hg (≥10 min) (odds ratio, 6.5; 95% confidence interval, 2.7-7.7; $P<0.001$) and platelet counts $\leq 30\times10^9$/L (odds ratio, 3.3; 95% confidence interval, 14-7.7; $P=0.006$) were associated with increased risk of postoperative ICH. Preoperative total bilirubin ≥7 mg/dL was also a risk factor. Thirty-day mortality in ICH patients was 48.3%, significantly higher compared with the non-ICH group (3.0%; $P<0.001$). Patients with all 3 risk factors had a 16% chance of developing ICH. **Conclusions.** In the current study, postoperative ICH was uncommon but associated with high mortality. Prolonged intraoperative hypertension and severe thrombocytopenia were associated with postoperative ICH. More studies are warranted to confirm our findings and develop a strategy to prevent this devastating posttransplant complication.

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INTRODUCTION

Intracranial hemorrhage (ICH), defined as spontaneous or nontraumatic bleeding in the skull, is one of the most devastating postoperative complications in liver transplantation (LT).[1,2] Posttransplant ICH is associated with high mortality with the reported rate as high as 80%.[2] Survivors are often left with various degrees of neurological deficits and disability.[3] Management of posttransplant ICH is complex and challenging since it has to balance with comorbidities including simultaneous multiorgan failure, graft dysfunction, severe coagulopathy, and thromboembolic events in LT patients.[3]

Thus, risk factor identification and management strategies for ICH prevention are of significant interest.[4] Elevated blood pressure and coagulopathy are 2 well-known risk factors for ICH in the general population,[4-6] but their roles in ICH after LT are less clear. Previous studies investigating risk factors of ICH in LT have been severely limited by small sample sizes and underpowered analyses.[1,5] This is primarily due to the low incidence of posttransplant ICH, necessitating a large number of patients for analysis. Furthermore, no study has attempted to delineate the role of intraoperative events and their relationship to ICH. This is unfortunate because dramatic changes in hemodynamics and coagulopathy frequently occur during LT surgery and can potentially play a role in the development of postoperative ICH.

In this retrospective study, we investigated if there was a relationship between intraoperative hemodynamic/coagulation parameters and development of ICH. Specifically,

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we tested the hypothesis that intraoperative hypertension or thrombocytopenia was associated with postoperative ICH in LT.

PATIENTS AND METHODS

We performed a retrospective study of all adult patients (≥16 y of age) who underwent LT over a 13-year period (between January 2004 and August 2016) at the University of California, Los Angeles. Patients who had retransplantation and combined LT with other solid organs were excluded. Our Institutional Review Board approved the study and waived informed consent.

Anesthesia management followed the standard institutional protocol that has been described in detail elsewhere.[7,8] All patients had general anesthesia with endotracheal intubation. Patients received, in general, combined intravenous and inhalational anesthetics, neuromuscular blockers, and opioids. In addition to the American Society of Anesthesiologists standard monitors, invasive monitors included an intraarterial catheter, central venous catheter, pulmonary artery catheter, and transesophageal echocardiogram. Blood products included packed red blood cells (RBCs), fresh frozen plasma, cryoprecipitate, and platelets. Vasopressors were administered either in a continuous infusion or in a bolus. After LT, patients were transferred to the intensive care units, where patients were cared for by a multidisciplinary team.

Preoperative and intraoperative variables were prospectively collected and stored in our transplant database and extracted for analysis. Preoperative variables included patient characteristics and comorbidities (hypertension, diabetes mellitus, the presence of encephalopathy, gastroesophageal bleeding, ascites, vasopressor requirement, endotracheal intubation, and dialysis). Preoperative baseline laboratory testing results were included. Intraoperative variables included transfusion requirement, the use of vasopressors, presence of postreperfusion syndrome, need for venovenous bypass and intraoperative dialysis.

Intraoperative hemodynamics were obtained by reviewing electronic anesthesia records. Systolic, diastolic, and mean arterial pressures (MAPs) in the intraoperative period were recorded. Other hemodynamics including intraoperative heart rate, central venous pressure, and pulmonary artery pressure were also documented. Intraoperative MAP was defined as the highest value of MAP lasting 10 minutes or longer recorded during LT surgery. Intraoperative platelet counts were the lowest values recorded during LT surgery. Other intraoperative coagulation tests including international normalized ratio (highest value) and fibrinogen levels (lowest values) were recorded.

The primary outcome was ICH, defined as new onset of spontaneous hemorrhage in the central nervous system confirmed within 30 days after LT. Patients with iatrogenic ICH such as related to the insertion of intracranial pressure monitor were excluded from the analysis. Neurology consult notes, intensive care unit notes, and radiologic reports were used to confirm the diagnosis of ICH. Secondary outcome included all-cause mortality.

Categorical or continuous variables are summarized as a percentage or mean ± SD. Continuous variables were analyzed using the Student *t* or Mann-Whitney *U* tests. Non-normally distributed continuous variables were converted to the logarithmic scale before analysis. Continuous variables were sometimes grouped in 4 quartiles, dichotomized at its median or a value based on a histogram or clinical judgment. Continuous variables found to be significantly different by univariate analysis were analyzed using receiver operating characteristic analysis. The cutoff value was determined by the maximum Youden index with optimal sensitivity and specificity. Categorical variables were compared using χ^2 or Fisher extract tests. Variables with significant differences ($P < 0.10$) in univariate analysis were included in multivariate analysis. Multivariate logistic regression was used to identify preoperative and intraoperative variables independently associated with postoperative ICH. Patient survival was analyzed using Kaplan-Meier survival analysis and compared using the log-rank test. Cox analysis was used to identify risk factors for mortality. Odds ratio or hazard ratio (HR) with 95% confidence intervals (CIs) were reported. A P value of <0.05 was considered significant. All statistical analyses were performed using IBM SPSS version 24 (IBM Corporation, Armonk, NY).

RESULTS

One-thousand eight-hundred thirty-six adult patients met the study criteria and were included in the analysis. Mean patient age was 54.0 years (±11.6 y) and Model for End-Stage Liver Disease (MELD) score 31.8 (±8.1). Sixty-three percent of patients were male, 39.6.0% had viral hepatitis B or C cirrhosis, and 26.3% had alcoholic liver disease. Preoperatively, patients requiring vasopressors, endotracheal intubation, and hemodialysis were 15.4%, 21.9%, and 32.9%, respectively.

Of the 1836 patients in the study, 36 (2.0%) developed ICH within 30 days of LT. As shown in Table 1, hemorrhage occurred most frequently in the frontal lobes (n = 6) and subarachnoid space (n = 6). Twelve patients had combined intraparenchymal and subarachnoid/subdural hemorrhage. As Figure 1 illustrates, the majority of ICH occurred in the early postoperative period; 24 of 36 (65%) occurred within the first week and 31 of 36 (86%) occurred within the first 2 weeks after LT.

Results comparing preoperative baseline characteristics between patients with and without ICH are shown in Table 2. Patients with ICH had higher MELD scores and were more likely to have preoperative encephalopathy, be on vasopressors, be ventilator dependent, and be on hemodialysis. In addition, patients with ICH had a significantly lower hematocrit, lower platelet counts, and higher

TABLE 1.

Types and locations of intracranial hemorrhage

Types and locations	Number of patients
Frontal lobes	6
Occipital lobes	3
Other intraparenchymal locations	4
Multiple intraparenchymal locations	6
Subarachnoid	6
Subdural	3
Combined intraparenchymal and subarachnoid hemorrhage	6
Combined subarachnoid and subdural hemorrhage	2
Total	36

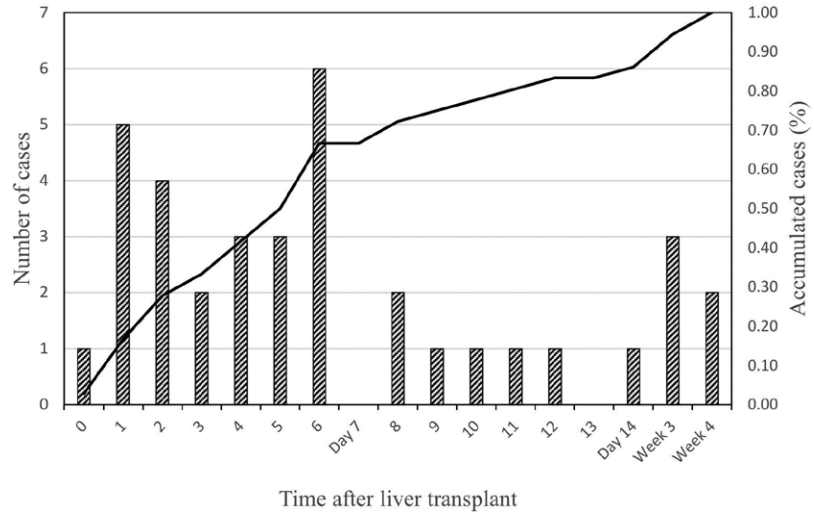

FIGURE 1. The number of intracranial cases (bars, values on the left axis) and percentage of accumulated cases (line, values on the right axis) in the postoperative period.

total bilirubin concentration. Etiologies of liver diseases in patients with and without postoperative ICH were not significantly different. Comparison of intraoperative variables between patients with and without ICH showed that patients with ICH required more frequent intraoperative dialysis, continuous infusions of vasopressors, and higher requirements for RBC, fresh frozen plasma, and platelet transfusions (Table 3). Mean intraoperative platelet counts in the ICH group were 29.3 (±14.4), significantly lower compared with platelet counts of 52.9 (±39.9; $P<0.001$) in the non-ICH group. Comparison of intraoperative hemodynamics showed that patients with ICH had a significantly higher MAP of 105.4 (±12.6 mm Hg) compared with MAP of 98.3 mm Hg (±11.4; $P=0.003$) in non-ICH patients.

TABLE 2.

Comparison of preoperative variables between patients with and without intracranial hemorrhage

Variables	No intracranial hemorrhage, n = 1800	Intracranial hemorrhage, n = 36	*P*
Age, y	54.0 ± 11.6	50.9 ± 13.3	0.164
Male sex	63.3	47.2	0.089
Weight, kg	80.8 ± 20.0	75.8 ± 22.3	0.202
Height, cm	169.4 ± 10.7	164.6 ± 11.1	0.029
MELD score	31.8 ± 8.1	35.8 ± 5.7	0.001
Encephalopathy	44.0	71.4	0.001
Intubation	21.7	34.3	0.074
Hypertension	29.6	15.2	0.072
Vasopressors	14.7	47.1	<0.001
Hemodialysis	32.6	50.0	0.032
Diabetes mellitus	25.7	26.5	0.920
Gastroesophageal hemorrhage	34.0	38.2	0.606
Ascites >1 L	43.4	58.8	0.073
Etiology of liver disease			
Acute hepatic failure	6.9	2.9	0.369
Chronic viral hepatitis (B or C)	39.9	23.5	0.053
Nonalcoholic steatohepatitis	7.5	2.9	0.311
Alcoholic cirrhosis	26.1	35.3	0.226
Baseline laboratory values			
Hematocrit, %	28.8 ± 6.3	26.6 ± 5.6	0.030
Platelet counts, $\times 10^9$/L	71.4 ± 55.5	55.9 ± 51.9	0.111
International normalized ratio	1.8 ± 0.7	2.0 ± 0.7	0.216
Creatinine, mg/dL	1.6 ± 1.3	1.9 ± 1.2	0.301
Potassium, mmol/L	3.9 ± 0.6	4.1 ± 0.6	0.089
Sodium, mmol/L	137.0 ± 5.0	136.6 ± 6.2	0.719
Fibrinogen, mg/dL	162.6 ± 80.6	136.9 ± 90.2	0.079
Total bilirubin, mg/dL	14.8 ± 15.9	26.4 ± 16.7	<0.001

MELD, Model for End-Stage Liver Disease.

TABLE 3.

Comparison of intraoperative variables between patients with and without intracranial hemorrhage

Variables	No intracranial hemorrhage, n = 1800	Intracranial hemorrhage, n = 36	*P*
Intraoperative dialysis	10.7	30.3	<0.001
Venovenous bypass	33.5	36.4	0.775
Pressor infusion	68.0	90.6	0.006
Pressor bolus	34.8	50.0	0.084
Red blood cells, unit	18.2 ± 16.7	33.9 ± 28.4	0.003
Fresh frozen plasma, unit	21.9 ± 18.0	35.6 ± 29.6	0.011
Platelet, unit	1.3 ± 1.2	1.9 ± 1.1	0.001
Cryoprecipitate, unit	1.2 ± 1.4	2.1 ± 1.8	<0.001
Donor age, y	40.5 ± 16.5	40.5 ± 16.8	0.983
Donor male sex	62.5	53.3	0.413
Cold ischemia time, min	416.8 ± 148.1	468.8 ± 147.7	0.046
Warm ischemia time, min	44.4 ± 11.7	48.0 ± 17.2	0.241
Surgical time, min	332.4 ± 104.3	294.9 ± 68.9	0.170
Postreperfusion syndrome	16.0	16.1	0.986
Platelet counts, $\times 10^9$/L	52.9 ± 39.9	29.3 ± 14.4	<0.001
International normalized ratio	2.0 ± 0.8	2.0 ± 0.5	0.891
Prothrombin time	20.3 ± 7.6	19.5 ± 4.9	0.413
Activated partial thromboplastin time	51.8 ± 30.8	49.7 ± 17.8	0.668
Intraoperative MAP	98.3 ± 11.4	105.4 ± 12.6	0.003

Platelet counts were the lowest values recorded during LT; prothrombin time was the highest value recorded during LT; activated partial thromboplastin time was the highest value recorded during LT; intraoperative MAP was the highest value of MAP lasting 10 min or longer recorded during LT.
LT, liver transplantation; MAP, mean arterial pressure.

Multivariate logistic regression analysis including all potentially positive preoperative and intraoperative variables confirmed that 3 variables, intraoperative MAP, intraoperative platelet counts, and preoperative total bilirubin concentration were risk factors for postoperative ICH (Table 4). Receiver operating characteristic analysis was used to identify potential cutoff points in these 3 variables. As shown in Table 5, intraoperative MAP of 105 mm Hg (intraoperative hypertension), intraoperative platelet count of 30×10^9/L, and preoperative total bilirubin of 7 mg/dL were associated with the maximum Youden indices with optimal sensitivity and specificity. As Figure 2A and B shows, when intraoperative MAP increases and intraoperative platelet counts decrease, the probability of postoperative ICH increases slightly. The probability increases significantly when intraoperative MAP is ≥105 mm Hg and intraoperative platelet counts are $\leq 30 \times 10^9$/L.

In a logistic regression model (Table 6), intraoperative MAP ≥105 mm Hg (≥10 min), intraoperative platelet counts $\leq 30 \times 10^9$/L, and preoperative total bilirubin ≥7 mg/dL were associated with 6.5, 3.3, and 21.0 times odds of developing ICH in the postoperative period, respectively. Using these cutoff values, we developed an ICH risk index by assigning one score to each risk factor. As shown in Figure 3, the incidence of postoperative ICH increases as the number of risk factors increases. Patients with 2 and 3 risk factors have a significantly higher risk of developing postoperative ICH compared with those with 0 or 1 risk factor. A total of 16% of patients with all 3 risk factors developed posttransplant ICH.

Further analysis showed that patients with higher MELD score, history of hypertension, no preoperative ascites, and lower preoperative creatinine level were more likely to have intraoperative hypertension. Patients with higher MELD scores, history of preoperative gastroesophageal bleed, lower preoperative platelet counts, and lower preoperative sodium levels tended to have intraoperative thrombocytopenia (Table 7).

TABLE 4.

Multivariate logistic regression for intracranial hemorrhage

Variable	Odds ratio (95% CI)	*P*
Preoperative bilirubin, mg/dL	1.03 (1.01-1.05)	0.002
Intraoperative MAP, mm Hg	1.07 (1.03-1.11)	<0.001
Intraoperative platelet counts, $\times 10^9$/L	0.96 (0.93-0.98)	0.002

Intraoperative MAP was the highest value of MAP lasting 10 min or longer recorded during LT; intraoperative platelet counts were the lowest values recorded during LT.
CI, confidence interval; LT, liver transplantation; MAP, mean arterial pressure.

TABLE 5.

Youden index with different cutoff values

Cutoff points	Sensitivity	Specificity	Youden Index
Preoperative bilirubin			
6 mg/dL	0.97	0.46	0.433
7 mg/dL	0.97	0.49	0.458
8 mg/dL	0.86	0.51	0.372
Intraoperative MAP			
95 mm Hg	0.79	0.44	0.228
105 mm Hg	0.75	0.72	0.474
115 mm Hg	0.21	0.92	0.124
Platelet counts			
20×10^9/L	0.91	0.28	0.188
30×10^9/L	0.76	0.58	0.344
40×10^9/L	0.56	0.72	0.284

Intraoperative MAP was the highest value of MAP lasting 10 min or longer recorded during LT; intraoperative platelet counts were the lowest values recorded during LT.
LT, liver transplantation; MAP, mean arterial pressure.

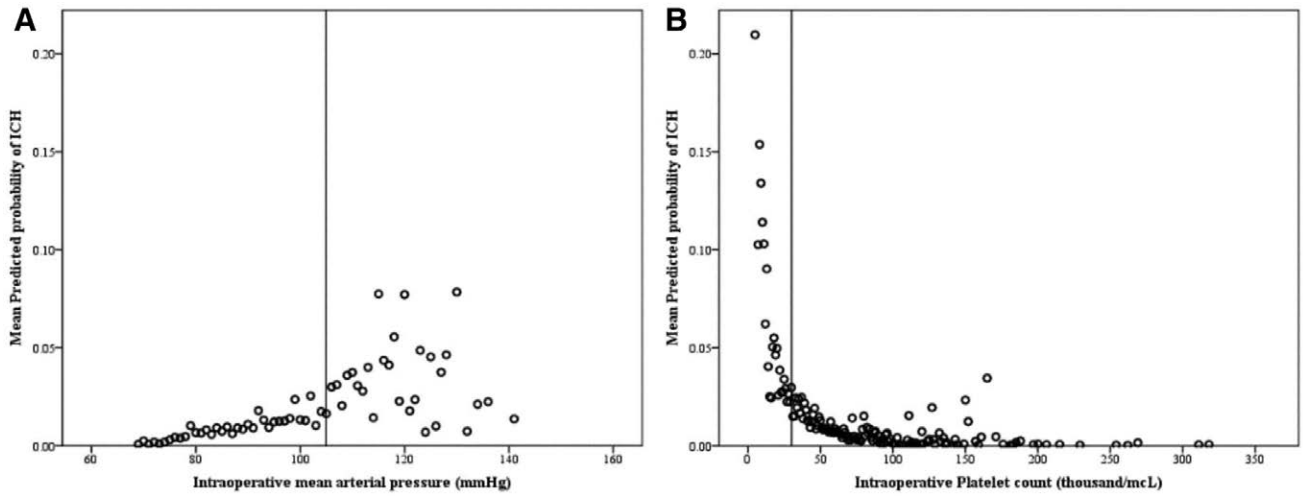

FIGURE 2. The relationship between postoperative intracranial hemorrhage (ICH) and 3 independent risk factors, preoperative total bilirubin concentration, intraoperative platelet counts, and intraoperative mean arterial pressure (MAP) was constructed using the following model: ICH = a + b1 × preoperative bilirubin + b2 × intraoperative MAP + b3 × intraoperative platelet count. A, The relationship between the predicted probability of ICH and intraoperative MAP. The reference line indicates intraoperative MAP at 105 mm Hg. B, The relationship between the predicted probability of ICH and intraoperative platelet counts. The reference line indicates platelet counts at 30×10^9/L.

TABLE 6.

Multivariate logistic regression for intracranial hemorrhage

Risk factors	Odds ratio (95% CI)	*P*
Preoperative bilirubin ≥7, mg/dL	21.0 (2.8-158.8)	0.003
Intraoperative MAP ≥105, mm Hg	6.5 (2.7-7.7)	<0.001
Intraoperative platelet counts ≤30, $\times 10^9$/L	3.3 (1.4-7.7)	0.006

CI, confidence interval; MAP, mean arterial pressure.

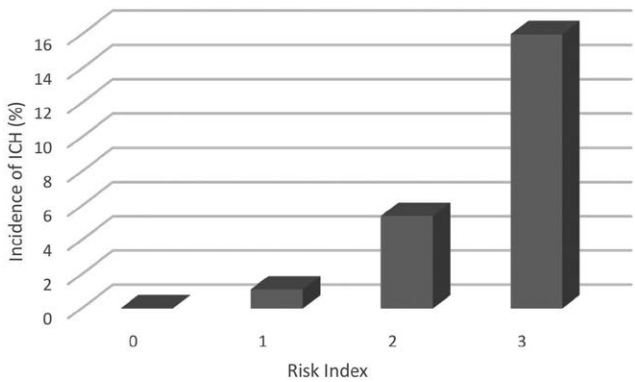

FIGURE 3. The incidences of intracranial hemorrhage (ICH) in patients with 0, 1, 2, and 3 risk factors were 0%, 1.1%, 5.4%, and 16.0%, respectively. Risk of developing postoperative ICH is significantly increased in patients with 2 or 3 risk factors.

Thirty-day mortality in the ICH group was 48.3%, significantly higher than in the non-ICH group (3.0%; $P < 0.001$ by log-rank test) (Figure 4). Patients with ICH had an 11-fold hazard of dying within 30 days after LT compared with those without ICH (HR, 11.1; 95% CI, 5.7–21.8; $P < 0.001$ by Cox analysis). Other risk factors for 30-day mortality included the requirement of preoperative vasopressors (HR, 2.56; 95% CI, 1.51–4.36; $P = 0.001$) and increased intraoperative RBC requirement (HR, 1.01; 95% CI, 1.01-1.03 per unit; $P < 0.001$).

TABLE 7.

Logistic models for intraoperative hypertension and thrombocytopenia

Risk factors	Odds ratio (95% CI)	*P*
Intraoperative MAP ≥105, mm Hg		
MELD score	1.03 (1.01-1.04)	0.012
History of essential hypertension	1.74 (1.33-2.29)	<0.001
No preoperative ascites	1.72 (1.28-2.33)	<0.001
Baseline serum creatinine, mg/dL	0.78 (0.68-0.91)	0.001
Intraoperative platelet counts ≤30, $\times 10^9$/L		
MELD score	1.06 (1.04-1.08)	<0.001
History of variceal bleeding	1.34 (1.01-1.79)	0.048
Baseline platelet counts, $\times 10^9$/L	0.97 (0.97-0.98)	<0.001
Baseline sodium, mmol/L	0.96 (0.94-0.99)	0.008

CI, confidence interval; MAP, mean arterial pressure; MELD, Model for End-Stage Liver Disease.

DISCUSSION

In this large retrospective study of 1836 patients, we found that ICH occurred at a rate of 2% within 30 days after LT. The majority (86%) of the cases occurred in the first 2 weeks following transplant. Postoperative ICH was associated with significantly high mortality. Preoperative bilirubin, intraoperative MAP ≥105 mm Hg for 10 minutes or longer, and intraoperative platelet counts ≤30 ($\times 10^9$/L) were associated with posttransplant ICH.

Elevation of the blood pressure, particularly an acute rise, places stress on the vascular walls, which can lead to rupture of the vessels.[5] Therefore, blood pressure control has been a key component of ICH prevention and treatment in the general population. Elevated blood pressure during LT surgery has been a longstanding suspect for the development of ICH. This is because, first, blood pressure fluctuations in the intraoperative period are more dramatic compared with the preoperative and postoperative periods of LT. Furthermore, cerebral autoregulation is blunted by general anesthesia during LT, leaving the brain at increased risk of pressure changes. Finally, the majority

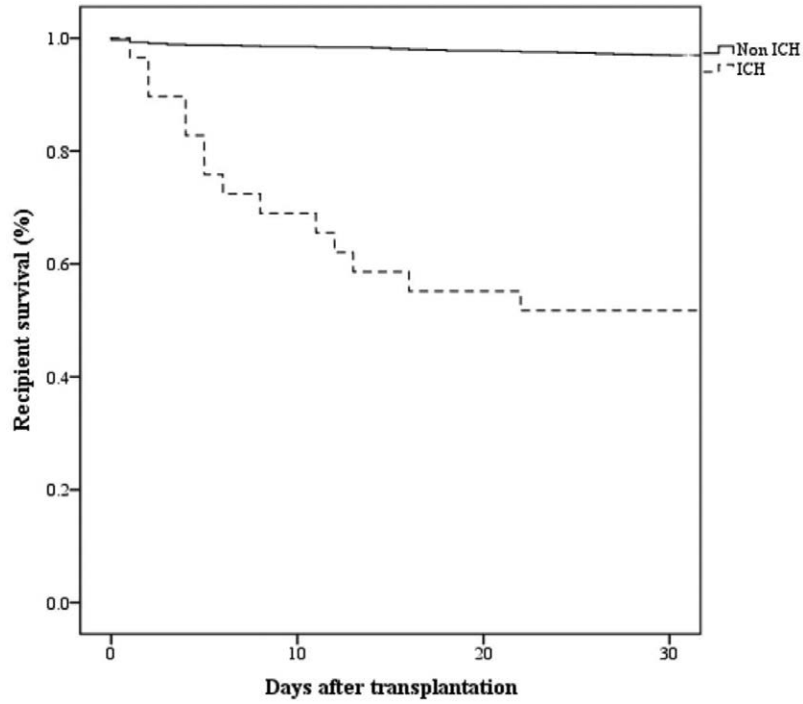

FIGURE 4. Thirty-day mortality in the intracranial hemorrhage (ICH) group was significantly increased compared with that in the non-ICH group.

of postoperative ICH occurs immediately after LT, which implies that intraoperative hypertension and postoperative ICH are closely related. Despite these, no previous study had shown that intraoperative hypertension was a risk factor for postoperative ICH. In our current study, we demonstrated that intraoperative hypertension was indeed a risk factor. Furthermore, we showed that a critical cutoff value for peak intraoperative blood pressure (MAP ≥105 mm Hg >10 min) was associated with a 6-fold increased odds of developing postoperative ICH.

Intraoperative hypertension can be caused by many factors. In this study, we showed that patients with higher MELD score were at increased risk of developing intraoperative hypertension. Patients with high MELD score may have diminished regulation of the sympathetic and parasympathetic systems, which may contribute to wider intraoperative blood pressure variability. We previously showed that patients with a large amount of preoperative ascites (>1 L) tend to develop intraoperative hypotension and require vasopressors.[9] Conversely, it may be presumed that patients with little to no ascites may have a tendency towards higher intraoperative blood pressures. There are factors such as overcorrection of blood loss, rapid blood transfusion, and need for larger than normal vasopressor boluses that can also lead to persistent hypertension or excessive swings in blood pressure.

Gallagher et al[1] report that an increase (≥28 mm Hg) in preoperative to postoperative systolic blood pressure is associated with ICH. Although this is interesting, the study's method of linking the increase in blood pressure seen within the first 96 hours after LT with the occurrence of ICH up to 12 months posttransplant raises many questions. In our analysis, intraoperative systolic pressure was an initial risk factor, the significance was lost when intraoperative MAP was introduced into the logistic model. The etiology of neurological complications after LT likely changes over time; ICH that occurs in the immediate postoperative period may be different from those occurring in a few months later.[10] This was why we defined ICH within 30 days after LT to limit interference by various ICH etiologies. Intraoperative hypotension has also been suggested as a risk for postoperative ICH.[2] We had examined a wide range of hemodynamics and could not confirm the relationship between intraoperative hypotension and postoperative ICH.

Platelets play critical roles in clot formation.[11] Adhesion, activation, and aggregation of platelets constitute the first wave of hemostasis. Activated platelets provide surfaces for coagulation factors and potentiate cell-based thrombin generation. Intraoperative thrombocytopenia is frequently observed during LT surgery and likely caused by multiple factors, including decreased production, increased destruction, consumption, dilution, and sequestration. Thrombocytopenia is a well-known factor contributing to intraoperative bleeding and blood transfusion. Similar to elevated blood pressure, thrombocytopenia is also considered as a risk factor for ICH in the general population.[12] We are the first to show that platelets play a key role in the development of postoperative ICH in LT. Patients with intraoperative platelet counts $\leq 30 \times 10^9$/L are at significant risk of developing postoperative ICH in our cohort.

To avoid severe intraoperative thrombocytopenia may have additional benefits since platelets involve in many physiological and pathological processes beyond bleeding. There is evidence suggesting that thrombocytopenia is associated with poor postoperative outcomes in LT.[13] It has been speculated that platelets contain many growth factors, which are required for organ development, tissue regeneration, and repair and participate in innate and adaptive immune responses, atherosclerosis, lymphatic vessel development, and angiogenesis.[12]

In contrast to reports showing that low platelet counts are associated with bleeding and poor outcome, there are studies reporting that high platelet counts and platelet transfusion are associated with poor outcomes in LT.[14-17] High platelet counts predispose patients to thrombotic complications, including hepatic artery thrombosis, portal vein thrombosis, and pulmonary embolization. Therefore, low platelet counts may be preferred in patients with anatomic derangements, history of thrombosis, and surgically complex hepatic artery anastomoses. A recent expert consensus recommends intraoperative platelet counts be kept at 50×10^9/L or higher.[18] It should be noted that this consensus is not without controversy and there is limited evidence supporting this recommendation.

Preoperative bilirubin level was another significant risk factor for postoperative ICH. Although our finding was consistent with the study by Gallagher et al[1], the underlying mechanism has not been well explained. Despite being a component of the MELD score formula, bilirubin is rarely studied as an independent risk factor for postoperative outcome. In a separate study, we found that high preoperative bilirubin level was significantly associated with posttransplant acute respiratory distress syndrome.[8] We suspect that high bilirubin is not only a component of the index for severity of liver disease but also a potential toxin to tissues in the brain and lungs.

Despite being the largest study thus far, our study has several limitations. First, this is a retrospective study with its inherent limitations. Although most of our data come from a prospectively designed database, some data points required retrospective collection, which subjected to selection bias. Secondly, our study was based on the data from a single center. Because of different patient populations and preference in clinical management, cautions should be used to interpret our findings. Thirdly, hemodynamic change and platelet counts fluctuate significantly and rapidly during LT surgery. Although we attempted our best efforts to capture and define those changes, it is impossible to catch all significant changes. Fourthly, ICH is a rare event, which can sometimes lead to unreliable statistical models and even inaccurate results. Finally, in this study, we focused on identifying preoperative and intraoperative risk factors, which may give us more time for potential interventions. Postoperative factors, although relevant and important, have not been analyzed in this study.

In summary, in this large retrospective study of 1836 adult patients, we found 2% of patients developed postoperative ICH within 30 days after LT. Posttransplant ICH is associated with a grave prognosis. Preoperative total bilirubin, intraoperative MAP ≥105 mm Hg, and platelet counts $\leq 30 \times 10^9$/L were associated with the increased risk of development of ICH after LT. Our findings may have significant clinical implications and suggest prolonged hypertension and severe thrombocytopenia should be avoided during LT. More studies are warranted to confirm our findings and develop a strategy to prevent this devastating posttransplant complication.

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