Relationship Between Intraoperative Bispectral Index and Consciousness Recovery in Patients With Hepatic Encephalopathy Undergoing Liver Transplant: A Retrospective Analysis

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ABSTRACT

Background. Although liver transplant (LT) improves liver function and restores symptoms of hepatic encephalopathy (HE), there is no index to predict the recovery of consciousness in patients with HE during LT. In this study, we evaluated the relationship between intraoperative bispectral index (BIS) values and the recovery of consciousness in patients with HE who were undergoing LT.

Methods. Patients with HE who underwent LT from June 2011 to December 2017 at our institution were enrolled. A total of 64 patients were enrolled, and, using the West Haven Criteria, they were divided into 2 groups: nonsevere HE group (n = 26), grades 1 to 2 HE; and severe HE group (n = 38), grades 3 to 4 HE. Grade of HE, intraoperative BIS, minimum alveolar concentration values, postoperative Glasgow Coma Scale (GCS) score, and the time to recover consciousness were compared.

Results. The severe HE group showed lower BIS after anesthetic induction compared with the nonsevere HE group (P = .005). In the severe HE group, intraoperative BIS gradient (the difference between values measured 4 hours after reperfusion and immediately after anesthesia induction) was significantly larger than in the nonsevere HE group (P = .001). Time to recovery of consciousness was prolonged in the severe HE group (P = .002). Model for End-Stage Liver Disease (MELD) score and the GCS score at 24 hours after LT were associated with delayed recovery of consciousness (MELD score: hazard ratio, 1.103; 95% CI, 1.002−1.214; P = .046; GCS score at 24 hours after LT: hazard ratio, 0.688; 95% CI, 0.566−0.835; P < .001).

Conclusions. Our study indicated that BIS values immediately after anesthesia induction were significantly lower in patients with severe HE. However, it did not show a significant relationship with the time to recovery of consciousness after LT. Multivariate analysis demonstrated that MELD score and GCS score at 24 hours after LT were associated with the time to recovery of consciousness.

HEPATIC encephalopathy (HE) is defined as changes in mental state in patients with severe liver dysfunction in the absence of organic brain disease [1]. It is a major complication of both liver failure and chronic liver disease, which invariably leads to brain abnormality and cognitive disturbance. Urgent liver transplant (LT) is required in a small group of these patients to reverse the worsening of their HE in the hopes that they will be able to achieve improved mental status after LT [2,3]. Currently available

diagnostic tools used to evaluate the brain function for HE include transcranial Doppler, jugular venous oximetry, and brain computed tomography [4–6]. According to the international working party on HE, psychometric standardized testing, the grading by West Haven Criteria, and neurophysiological measuring, such as electroencephalography (EEG), are recommended to diagnose HE [1]. However, it is impossible to apply psychometric tests or West Haven Criteria to unconscious patients who are intubated or to those undergoing surgery. Since Foley et al first reported that delta wave of the EEG correlated with HE [7], several studies have also suggested EEG analysis as an objective method to measure HE [7–9]. However, EEG is time consuming, and it is not applicable to candidates waiting to undergo emergency LT, despite the fact that it is the standard method for evaluating brain activity.

The bispectral index (BIS) has been proposed as a method for assessing the depth of anesthesia by analyzing frontal EEG derived from the forehead [10,11]. It is a noninvasive and simple method by which to evaluate consciousness, and it is widely used in various clinical situations. Previous research demonstrated that BIS is a valuable measurement tool for classifying the grade of HE [12,13]. Moreover, BIS has been shown to be useful as the indicator of consciousness levels even before and after LT surgery [14] and also effective in assessing consciousness of patients with fulminant hepatic failure undergoing LT [15].

In our previous study, we demonstrated that longer duration of preoperative HE and HE type C (encephalopathy associated with cirrhosis and portal hypertension or portal systemic shunts) were important contributing factors for consciousness recovery time after LT in patients with HE [16]. However, the relationship between intraoperative BIS value and the time until recovery of consciousness in patients has not been the subject of any clinical research. Therefore, the aim of this study was to assess whether intraoperative BIS values were different according to the severity of HE and to determine if BIS can be used to predict the timing of consciousness recovery in patients with HE undergoing LT.

METHODS
Study Population

This study was approved by our Institutional Review Board (IRB No. SMC 2017–08–139–001) who waived the requirement for written informed consent. We retrospectively reviewed the computerized medical records of patients who received LT from June 2011 to December 2017. Patients who had HE on the day of LT were included. The study excluded LT recipients who fell into the following categories: those who were younger than 18 years old, had mental status changes from a cause other than HE (eg, neurologic or major psychiatric disorder), had no BIS record during surgery, died during LT or after LT within 48 hours, received sedative agents during the post-transplant period in the intensive care unit (ICU), underwent reoperation without recovery of consciousness, and were diagnosed as having graft failure.

The following variables were recorded in assessing the relationship between pretransplant status and post-transplant cognitive function: demographic data of recipients, preoperative laboratory findings, Model for End-Stage Liver Disease (MELD) score, time to LT since the diagnosis of HE, severity and type of HE, medical history of recipients, etiology of liver disease, and type of graft. West Haven Criteria were used to grade the severity of HE in the following manner: grade 0, no HE; grade 1, trivial lack of awareness, euphoria, or anxiety, shortened attention span, impaired performance of addition or subtraction; grade 2, lethargy or apathy, minimal disorientation for time or place, subtle personality change, inappropriate behavior; grade 3, somnolence to semistupor but responsive to verbal stimuli, confusion, gross disorientation; grade 4, coma (unresponsive to verbal or noxious stimuli). Types A, B, and C were classified as follows: type A, encephalopathy associated with acute liver failure; type B, encephalopathy associated with portal-systemic bypass and no intrinsic hepatocellular disease; type C, encephalopathy associated with cirrhosis and portal hypertension or portal systemic shunts [1]. Based on our previous study, spontaneous eye opening and proper motor response to commands were considered as evidence that recipients had recovered consciousness. Delay in recovery of consciousness was noted if the time required to recover consciousness after LT was longer than 2 days [16].

To compare the gradient of intraoperative BIS and the time to recovery of consciousness, we divided recipients into 2 groups as follows; nonsevere HE group, grade 1 to 2 HE; severe HE group, grade 3 to 4 HE. We hypothesized that the BIS value after reperfusion would be elevated compared with the baseline BIS if the transplanted liver had normal function, and the duration of conscious recovery would not be significantly different between the 2 groups. The primary outcome was assessed by comparing the gradient of intraoperative BIS values and the time to recover consciousness after LT between the nonsevere HE group and the severe HE group.

Monitoring and Anesthesia

All operations were performed using standard techniques, and intraoperative anesthetic management was performed according to the standardized protocol for LT with continuous monitoring of peripheral capillary oxygen saturation, 5-lead electrocardiography, arterial blood pressure, central venous pressure, pulmonary arterial pressure, and cardiac output. Anesthesia was induced with sodium thiopental (5 mg/kg) and vecuronium. Following the manufacturer's procedures, a BIS (Aspect Medical System, Inc, Norwood, Mass, United States) sensor was applied to the patient's forehead after the induction of anesthesia. We defined the first BIS value after the induction of anesthesia as baseline BIS. The values of BIS monitored through the operation and recorded at intervals of 30 minutes throughout the LT procedure.

Anesthesia was maintained with isoflurane and vecuronium as a muscle relaxant. An anesthetic gas analyzer (Datex-Ohmeda, Helsinki, Finland) was used to measure end-tidal isoflurane concentration and minimum alveolar concentration (MAC). No opioids of any kind were administered intraoperatively. The depth of anesthesia was guided by the hemodynamic parameter, BIS, and MAC to prevent awareness during anesthesia. Change in the degree of BIS ($\triangle$ BIS) and MAC ($\triangle$ MAC) were calculated as the difference between values at postreperfusion phase and after the induction of anesthesia by the following formulas: Δ BIS 2 = the BIS value at 2 hours of postreperfusion period − BIS after anesthesia induction, Δ BIS 4 = the BIS value at 4 hours of postreperfusion period − BIS after anesthesia induction, Δ MAC

Table 1. Clinical and Biochemical Characteristics of Patients

	Nonsevere (n = 26)	Severe (n = 38)	P Value
Demographics			
Age, mean (SD), y	49.19 (12.56)	55.11 (10.136)	.042*
Male, No. (%)	17 (65.4)	23 (60.5)	.69
BMI, mean (SD)	22.81 (7.87)	24.37 (3.68)	.35
Type of graft, No. (%)			
Deceased donor OLT	13 (50)	14 (36.8)	.30
LDLT	13 (30)	24 (63.2)	
MELD score, mean (SD)	31.96 (10.64)	35.61 (7.96)	.15
Etiology, No. (%)			
HAV	3 (11.5)	3 (7.9)	.83
HBV	8 (30.8)	11 (28.9)	
HCV	3 (11.5)	2 (5.3)	
Alcoholic	3 (11.5)	5 (13.2)	
Others*	9 (34.6)	17 (44.7)	
HE type, No. (%)			
A	8 (30.8)	18 (47.4)	.04*
B	1 (3.8)	7 (18.4)	
C	17 (65.4)	13 (34.2)	
HE duration, mean (SD), d	8.81 (9.65)	10.11 (10.248)	.61
Intubated state (yes/no), No. (%)			
yes	1 (3.8)	9 (23.7)	.04*
ASA PS class, No. (%)			
III	18 (69.2)	27 (71.1)	.88
IV	8 (30.8)	11 (28.9)	
Laboratory parameters before LT, mean (SD)			
Hemoglobin, g/dL	10.27 (2.325)	9.58 (1.75)	.18
PT INR	2.76 (1.68)	2.92 (1.51)	.73
AST, U/L	142.38 (171.663)	220.63 (304.733)	.24
ALT, U/L	204.50 (490.867)	247.18 (528.464)	.75
Total bilirubin, mg/dL	25.88 (17.37)	23.79 (15.475)	.62
Sodium, mmol/L	135.73 (7.308)	139.03 (9.5)	.14
Albumin, g/dL	3.17 (0.602)	3.08 (0.647)	.41
Ammonia, μmol/L	87.27 (42.546)	88.29 (51.443)	.93

Others: Wilson disease, congenital portocaval shunt.

Abbreviations: ASA PS, American Society of Anesthesiologists physical status; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HE, hepatic encephalopathy; LDLT, Living donor liver transplant; MELD, Model for End-Stage Liver Disease; OLT, orthotopic liver transplant; PT (INR), international normalized ratio of prothrombin time.

*$P < .05$.

2 = the MAC value at 2 hours of postreperfusion period − MAC after anesthesia induction, Δ MAC 4 = the MAC value at 4 hours of postreperfusion period − MAC after anesthesia induction.

Monitoring of Consciousness

LT recipients were transferred to the ICU after the procedure for postoperative management. No sedative agents were administered, and Glasgow Coma Scale (GCS) scores were assessed in the ICU. We recorded these scores at admission to ICU, 6 hours, 12 hours, and 24 hours. Recipients were considered to have recovered consciousness if they opened their eyes spontaneously and showed motor response to commands. Length of ICU stay and in-hospital morbidity graded by Clavien-Dindo degree were also assessed.

Statistical Analysis

For descriptive data, continuous variables were presented as the mean (SD). Those variables were measured by the Wilcoxon rank sum test or the t test. Categorical variables were presented as numbers (%) and were analyzed by Fisher exact test. The changes

of intraoperative BIS and MAC according to the time of both groups were compared using repeated measures analysis of variance. Post hoc comparisons were adjusted by Bonferroni correction. Associated factors for recovery of consciousness were identified by univariate and multivariate logistic regression analyses. Relative risk was described by the estimated hazard ratio (HR) with a 95% CI. Two-sided P values were computed, and an effect was considered significant at the level of $P < .05$. SPSS version 20.0 (IBM Corp, Chicago, Ill, United States) was used to perform statistical calculations.

RESULTS
Clinical and Biochemical Characteristics

From June 2011 to December 2017, a total of 801 patients underwent LT. During this period, 72 patients (9%) were diagnosed as having HE before LT. Among them, 9 patients were excluded from this study when one of the following occurred: they died during LT (1 case), died within 48 hours after LT without regaining consciousness (3 cases), required
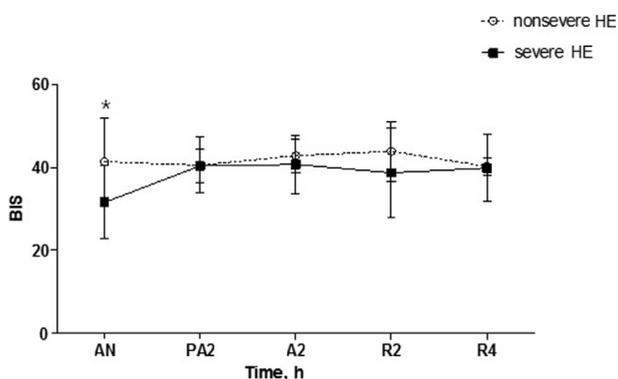
Fig 1. BIS trend during LT. Data are given as mean (SD). Repeated measures ANOVA was used to determine statistical difference. Post hoc comparisons were adjusted by Bonferroni correction. The BIS values were different between severe HE group and nonsevere HE group during LT. The difference in BIS values between the 2 groups appears at the time immediately after anesthesia induction. A2, 2 hours after anhepatic phase; AN, after anesthetic induction; ANOVA, analysis of variance; BIS, bispectral index; LT, liver transplant; PA, 2 hours after preanhepatic phase; R2, 2 hours after postreperfusion phase; R4, 4 hours after postreperfusion phase. *P < .05.

sedation for therapeutic purpose after LT (1 case), or underwent reoperation without recovery of consciousness (3 cases). The remaining 64 recipients were analyzed, and 40% (n = 26) had grade 1 to 2 HE and 60% (n = 38) had grade 3 to 4 HE. Patient demographic characteristics are shown in Table 1. There were no differences with baseline characteristics and laboratory findings before operation in both groups. However, HE type was different between the 2 groups (P = .04), and more patients in the severe HE group were already intubated when they entered the operating room (P = .04) (Table 1).
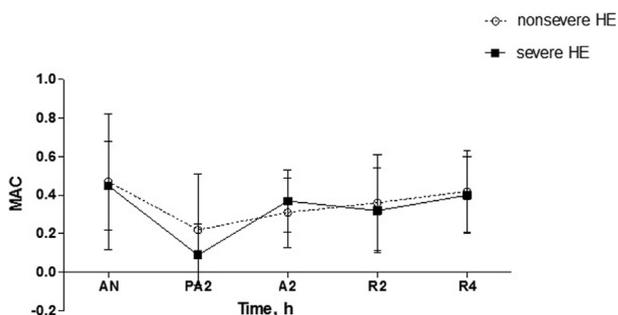

Fig 2. MAC trend during LT. Data are given as mean (SD). Repeated measures ANOVA was used to determine statistical difference. Post hoc comparisons were adjusted by Bonferroni correction. There were no significant differences over time in MAC between nonsevere and severe HE group. A2, 2 hours after anhepatic phase; AN, after anesthetic induction; PA, 2 hours after preanhepatic phase; LT, liver transplant; MAC, minimal alveolar concentration; R2, 2 hours after postreperfusion phase; R4, 4 hours after postreperfusion phase.

Intraoperative and Postoperative Data

Figure 1 and 2 show the trend of intraoperative BIS and MAC in the 2 groups. Although MAC of isoflurane demonstrated no significant difference over time between nonsevere HE and severe HE groups, BIS values were statistically different between the 2 groups during LT (P < .005 by repeated measures analysis of variance). After anesthesia induction, BIS values were significantly lower in the severe HE group than in the nonsevere HE group (nonsevere HE group, mean [SD], 41.27 [10.49]; severe HE group, mean [SD], 31.53 [8.79]; P = .005). In addition, △ BIS 4 was significantly larger in the severe HE group compared with the nonsevere group (postreperfusion 4 hours after induction: severe HE group, mean [SD], 8.95 [9.24]; nonsevere HE group, mean [SD], 3.08 [4.24]; P = .005) (Table 2).

As shown in Table 2, means (SD) GCS scores were significantly lower in the severe HE group than in the nonsevere group at 24 hours after LT (8.9 [4.5] vs 12.1 [4.2]; P = .02). The mean (SD) time to recover consciousness was significantly longer in the severe HE group than in the nonsevere HE group (2.8 [2.8] days vs 1.2 [1.3] days; P = .002).

Multivariate logistic regression analysis identified that MELD score (HR, 1.103; 95% CI, 1.002–1.214; P = .046) and GCS score at 24 hours after LT (HR, 0.688; 95% CI, 0.566–0.835; P < .001) were associated with consciousness recovery time (Table 3). Duration of anesthesia, ICU length of stay, and 30-day morbidity rates were comparable between the 2 groups. None of the study populations experienced graft failure.

DISCUSSION

BIS based on EEG analysis is a method used to assess an adequate depth of sedation and anesthesia. It provides a reliable index of consciousness, and, thus, its clinical application can be widened to assess the degree of HE. Previous research has shown that BIS values were significantly different among cirrhotic patients regarding the grade of HE [12,13]. In addition, numerous studies have shown variations in BIS values during the peritransplant period [14,15,17]. One case report presented that a patient with acute hepatitis who had altered mentality showed dramatic BIS changes according to the recovery of consciousness [17]. Okawa et al suggested that BIS may predict perioperative changes in the level of consciousness in recipients who underwent LT. Moreover, Kang et al [14] investigated the use of post-transplant BIS monitoring to measure consciousness in acute on chronic liver failure patients. Their data revealed that BIS is a simple method to measure consciousness in intubated patients and that it may replace GCS score. Notably, Hwang et al [15] assessed the usability of BIS during the peritransplant period in patients with fulminant hepatic failure and demonstrated that BIS values from the end of LT to the time of eye opening to voice were defined as the index of conscious recovery and showed

Table 2. Perioperative Data

	Nonsevere (n = 26)	Severe (n = 38)	P Value
Intraoperative			
BIS value, mean (SD)*			
After induction	41.27 (10.49)	31.53 (8.79)	.005[†]
ΔBIS 2	4.92 (4.48)	8.16 (7.27)	.06
ΔBIS 4	3.08 (4.24)	8.95 (9.24)	.005[†]
MAC, mean (SD)			
After induction	0.469 (0.35)	0.45 (0.233)	.81
ΔMAC 2	−0.07 (0.36)	−0.09 (0.28)	.75
ΔMAC 4	−0.06 (0.34)	−0.03 (0.28)	.73
Duration of anesthesia, mean (SD), h	9.684 (2.12)	9.6 (1.657)	.86
Postoperative			
GCS, mean (SD)*			
At ICU admission	3.42 (2.73)	3.03 (1.241)	>.99
6 h after LT	8.23 (4.33)	6.68 (3.933)	.14
12 h after LT	11.00 (4.138)	8.29 (4.439)	.06
24 h after LT	12.12 (4.16)	8.89 (4.525)	.02[†]
Time to recover consciousness, mean (SD), d	1.18 (1.334)	2.834 (2.761)	.002[†]
ICU length of stay, mean, d	15.46 (17.727)	14.32 (15.806)	.79
30-day morbidity, No. (%)			
Clavien–Dindo grade I-V	7 (26.9)	14 (36.8)	.41
Clavien–Dindo grade ≥ IIIb	5 (19.2)	11 (28.9)	.38

Abbreviations: BIS, bispectral index; ΔBIS 2, the gradient of BIS (after induction vs 2 h after postreperfusion period); ΔBIS 4, the gradient of BIS (after induction vs 4 h after postreperfusion period); GCS, Glasgow Coma Scale score; ICU, intensive care unit; LT, liver transplant; MAC, minimum alveolar concentration; ΔMAC 2, the gradient of MAC (after induction vs 2 h after postreperfusion period); ΔMAC 4, the gradient of MAC (after induction vs 4 h after postreperfusion period).
*Adjusted by Bonferroni correction.
[†]$P < .05$.

Table 3. Univariate and Multivariate Logistic Regression Analysis

	Univariable			Multivariable		
Variables	HR	95% CI	P Value	HR	95% CI	P Value
Age	1.023	0.975–1.072	.35			
Sex	0.379	0.132–1.094	.07[*,†]			
BMI	1.009	0.921–1.105	.85			
MELD score	1.090	1.014–1.172	.02[*,†]	1.103	1.002–1.214	.046[*,†]
HE duration	1.035	0.983–1.089	.19			
HE grade						
1	Reference					
2	0.556	0.041–7.457	.66			
3	4.375	0.455–42.080	.20			
4	15.000	1.031–218.300	.047[*,†]			
HE type						
A	Reference					
B	1.286	0.365–4.529	.70			
C	0.309	0.099–0.957	.04[*,†]			
Donor type	1.891	0.871–5.328	.23			
BIS[†]						
After induction	0.916	0.857–0.979	.01[*,†]			
ΔBIS 4	1.043	0.979–1.111	.19			
GCS[†]						
At ICU admission	0.642	0.730–1.258	.38			
6 h after LT	0.834	0.719–0.969	.02[*,†]			
12 h after LT	0.734	0.619–0.871	<.001[*,†]			
24 h after LT	0.692	0.578–0.829	<.001[*,†]	0.688	0.566–0.835	<.001*
ΔGCS	0.740	0.634–0.864	<.001[*,†]			

Abbreviations: BIS, bispectral index; ΔBIS, BIS value at postreperfusion 4 h − BIS value after induction; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HE, hepatic encephalopathy; HR, hazard ratio; GCS, Glasgow Coma Scale score; ΔGCS, GCS score at 24 h after LT − at ICU admission; ICU, intensive care unit; LT, liver transplant; MELD, Model for End-Stage Liver Disease.
*$P < .05$.
[†]Analyzed using multivariate analysis.

significant correlation with GCS score. In addition, they proposed that BIS may be valuable in predicting the timing of arousal in patients with fulminant hepatic failure and suggested that BIS monitoring may be useful during peri-transplant management for patients with HE. In line with these studies, our results also showed significantly different intraoperative BIS values between the 2 groups with notably lower BIS values immediately after anesthetic induction in the severe HE group, despite comparable anesthetic depths being maintained between the 2 groups.

Dahaba et al [18] assessed the use of BIS as an early indicator of graft function. They reported that recipients with normal graft function showed increased BIS under total intravenous anesthesia with propofol after reperfusion. They commented this means the return of cerebral activity with the restoration of hepatic function and suggested that the vitality of the transplanted graft might be assessed by BIS. In this regard, we surmised that when the graft function was normal, there would be no difference in the time to recover consciousness after LT, regardless of the severity of the HE. However, contrary to our expectations, our data revealed a prolonged time for recovery of consciousness in the severe HE group, despite the increase in BIS after reperfusion. Liver disease is often combined with both altered functions and structures in the brain [19]. Patients with liver failure frequently have brain edema, and this causes serious complications related to cerebral damage [20]. Moreover, patients with severe HE may have higher degrees of cerebral damage, which might contribute to delayed and/or incomplete reversal of HE, even after LT. Accordingly, a number of studies have suggested that patients with overt HE might be threatened with less than full recovery of brain function after LT [21,22]. In addition, patients with severe HE may be sensitive to various factors that contribute to the compromised mental status in the perioperative period, such as age, cerebrovascular accident, intraoperative brain damage due to ischemic events, hypoxia, hypotension, and toxicity of immunosuppressing agents [23]. For the aforementioned reasons, the patients in our study who had severe HE might have shown delayed recovery of consciousness compared with the patients in the nonsevere HE group after LT.

Previous studies reported that patients with HE had significantly lower MAC levels than patients with normal liver function during open abdominal surgery [24], and anesthetic requirements were significantly lower in patients with severe liver disease [13]. Severe hepatobiliary disease leads to increased plasma levels of endogenous opioid peptides [25,26]. In addition, bilirubin causes alterations in neurotransmission in the brain, contributing to a reduced anesthetic requirement in patients with end-stage liver disease [27]. Similarly, in our study, to maintain the BIS values below 60, the inhalational anesthetic requirement was generally low and it reflected by median MAC values below 0.5 throughout LT in patients with HE. Thus, we suggest that BIS is a useful method for assessing the anesthetic needs of HE patients.

In our study, high MELD score and low GCS score at 24 hours after LT were identified as independent factors affecting the consciousness recovery time after LT in recipients with pretransplant HE. First, MELD score is calculated using serum creatinine, bilirubin, and international normalized ratio of prothrombin time and is used to predict preoperative mortality in candidates for LT [28]. Research has explored the usability of MELD score as predictor of post-transplant outcome [29,30]. Although the relationship between MELD score and recovery of consciousness is unclear, a previous study reported that HE was an independent contributing factor for increasing mortality in end-stage liver disease [31], and, similarly, our results showed that higher MELD score was associated with delayed recovery of consciousness in HE patients. Second, GCS score is widely applied to patients with altered consciousness for the purpose of measuring cognitive function at various time points including postoperative period. In patients with severe HE, the recovery of cerebral activity was prolonged even after increasing the BIS level after reperfusion. Moreover, lower level of GCS score at 24 hours after LT was revealed as one of the associated factors for delayed recovery of consciousness in this study.

Our study has several limitations. First, there was no measurement of the preoperative BIS values. Because the first intraoperative BIS values were recorded after anesthetic induction, it could be affected by several variables, such as anesthetic agents and temperature. Nevertheless, the BIS value of the severe HE group was significantly lower in decreased MAC after the induction of anesthesia, which means that BIS is affected by HE severity, and the amount of anesthetic required is also reduced. Second, we were unable to adjust several confounding factors because this study was designed to be retrospective in nature. BIS values were only recorded during the operation, and, thus, we could not compare the consciousness and BIS values in the postoperative period. Third, our sample size is too small and contains a heterogeneous population. We faced limitations in recruiting sufficient subjects with homogeneous characteristics, considering the fact that the diagnosis of HE at the time of LT and its incidence was low. According to the diversity of the patients, it may be possible for our results to be used for the general LT recipient. Further study is warranted, which will evaluate the correlation with BIS and other numerous contributing factors or to clarify the relationship between the recovery of consciousness and the function of the graft after LT in HE patients.

In conclusion, this study demonstrated that BIS values immediately after anesthesia induction were significantly lower in patients with severe HE. However, it did not show a significant relationship with the time to recovery of consciousness after LT. Multivariate analysis demonstrated that MELD score and GCS score at 24 hours after LT were associated with the time to recovery of consciousness. Therefore, increased attention must be paid to severe HE patients to improve LT outcomes as delayed recovery of

consciousness may cause additional adverse effects in the post-transplant period.

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