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Preoperative BMI and Hb levels are important predictors of massive bleeding in liver transplant patients

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Abstract. – OBJECTIVE: This study aims to compare intraoperative bleeding during liver transplant procedures and analyze the predictive role of preoperative laboratory indicators in significant intraoperative bleeding.

PATIENTS AND METHODS: A retrospective analysis was conducted on 271 cases of allogeneic liver transplant patients from January 2018 to June 2023. Patients were categorized into the massive bleeding (MB) group and the non-massive bleeding (non-MB) group based on the occurrence of significant intraoperative bleeding. Preoperative laboratory parameters between the MB and non-MB groups were compared, and univariate and multivariate regression analyses were performed. ROC curves were performed to analyze the value of these parameters in distinguishing the MB and non-MB groups.

RESULTS: In the MB group, body mass index (BMI), hemoglobin (Hb), platelet count (PLT), fibrinogen (Fib), and total protein (TP) levels were significantly lower than those in the non-MB group ($p < 0.05$). Conversely, prothrombin time (PT), international normalized ratio (INR), total bilirubin (TBIL), creatinine (CRE), blood urea nitrogen (BUN), the model for end-stage liver disease (MELD) score, length of stay, and hospital stay were significantly higher in the MB group compared to the non-MB group ($p < 0.05$). Univariate and multivariate logistic regression analyses revealed that preoperative BMI and Hb were independent risk factors for massive bleeding during liver transplantation. ROC curve analysis for predicting massive intraoperative bleeding showed that the area under the curve (AUC) of Hb was considerable (AUC: 0.83).

CONCLUSIONS: Preoperative BMI and Hb levels are critical predictors of massive bleeding during liver transplantation, emphasizing the importance of proactive management based on these indicators for improved patient outcomes.

Key Words:
Liver transplant, Significant intraoperative bleeding, Laboratory indicators, Prognosis.

Introduction

Liver transplantation stands as a paramount intervention in managing end-stage liver disease, representing a vital therapeutic avenue that can potentially save lives for individuals grappling with terminal liver conditions[1]. Despite continual advancements in surgical and anesthesia techniques[2], a subset of patients faces the challenge of substantial intraoperative bleeding, posing severe complications and a potential threat to their lives[3,4]. When significant bleeding occurs after liver transplantation, it is urgent to adopt the strategy of massive transfusion. However, large transfusions often predict more negative clinical outcomes, such as higher rates of pulmonary infections, early rejection, and poorer survival[5]. Consequently, accurately evaluating preoperative bleeding risks and implementing targeted interventions are imperative to enhance the safety and success rates of liver transplant surgeries.

Aberrations in liver function and coagulation dynamics emerge as pivotal factors influencing intraoperative bleeding during liver transplantation[6,7]. Given the liver's crucial role in synthesizing clotting factors, liver failure can lead to impaired coagulation function. Furthermore, compromised liver function may result in vascular dilation and weakened vessel walls, amplifying the susceptibility to intraoperative bleeding[8,9]. Hence, preoperative assessment of liver function indicators, including aspartate transaminase (AST), alanine transaminase (ALT), and total bilirubin, is essential for predicting the risk of intraoperative bleeding.

Additionally, a diminished hemoglobin level is recognized as a risk factor for significant intraoperative bleeding[10,11]. Low hemoglobin levels may be linked to anemia, diminished oxygen transport

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capacity, and blood dilution, heightening the risk of intraoperative bleeding. Therefore, evaluating preoperative changes in hemoglobin levels contributes to predicting the likelihood of intraoperative bleeding.

While previous research[12,13] has predominantly focused on the correlation between laboratory indicators and massive blood transfusions in liver transplantation, there exists a gap in direct and pertinent studies exploring the relationship between laboratory indicators and intraoperative bleeding. Consequently, this study aims to unravel the correlation between preoperative laboratory indicators and substantial bleeding during liver transplantation. This investigation is pivotal for a more precise assessment of preoperative bleeding risk, providing a scientific foundation for preoperative assessment and targeted intervention.

Patients and Methods

Data

This is a single-center retrospective analysis conducted at Li Huili Hospital, Ningbo Medical Center, from January 2018 to June 2023. Inclusion criteria were: (1) age ≥ 18 years; (2) Patients undergoing allogeneic liver transplantation; (3) organ donation from brain-dead donors. Exclusion criteria were: (1) incomplete clinical data; (2) combined liver-kidney transplantation; (3) death within 24 hours postoperatively. A total of 271 liver transplant patients were included in this study. Liver transplant patient's basic clinical information, intraoperative blood usage, and laboratory test data were obtained through an electronic information system. Clinical information included gender, age, body mass index (BMI), the model for end-stage liver disease (MELD) score, and length of hospital stay. Intraoperative blood usage included the amount of packed red blood cells and frozen plasma. Laboratory test data encompass hemoglobin (Hb), platelet count (PLT), prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), fibrinogen (Fib), total protein (TP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), glutamyl transpeptidase (GGT), total bilirubin (TBIL), creatinine (CRE), blood urea nitrogen (BUN).

Grouping

Patients were categorized into the massive bleeding (MB) group and the non-massive bleeding (non-MB) group. All liver transplant surgeries were performed by the same surgical and anesthesia team. Major bleeding was defined as loss of systemic blood volume within 24 hours or 50% of systemic blood volume within 3 hours. Intraoperative blood loss was estimated using monitored hematocrit or hemoglobin levels, and the actual blood loss was calculated using the following formula: Actual blood loss = Blood volume [HCT (initial) - HCT (final)] / HCT (mean) + volume of allogeneic transfusion[11,12]. Human blood volume was calculated as 7% of the patient's body weight. Patients were categorized into the massive bleeding (MB) group and the non-massive bleeding (non-MB) group based on whether intraoperative bleeding exceeded 50% of the total effective circulating blood volume. According to the above principles, 56 patients were in the MB group, and 215 patients were in the non-MB group in this study. The study was approved by the hospital's Ethics Committee (approval No. KY2021PJ144).

Statistical Analysis

Statistical analysis was performed using SPSS 21.0 software (IBM Corp., Armonk, NY, USA). Frequency (percentage) was used for categorical data, and the Chi-square test was employed for inter-group comparisons. For normally distributed continuous data, mean ± standard deviation ($\bar{x} \pm s$) was used, and independent sample *t*-tests were performed for inter-group comparisons. For non-normally distributed data, the median (interquartile range) was used, and the Mann-Whitney U test was applied for inter-group comparisons. Additionally, major bleeding during surgery was taken as the dependent variable, and statistically significant laboratory indicators were analyzed using univariate and multivariate logistic regression. The Receiver Operating Characteristic (ROC) curve was used to assess the discriminatory ability of preoperative indicators in predicting major intraoperative bleeding. A significance level of $p < 0.05$ was considered statistically significant.

Results

Analysis of Preoperative Data and Length of Hospital Stay for Liver Transplant Patients with MB vs. Non-MB

While the majority of the study population comprises male patients, it is noteworthy that females exhibit a higher propensity for substantial

intraoperative bleeding (p = 0.013). In the MB group, BMI, Hb, PLT, TP, and Fib indicators were significantly lower compared to the non-MB group ($p < 0.05$, Table I). Conversely, the MELD score, PT, INR, TBIL, CRE, and BUN indicators were higher in the MB group than in the non-MB group ($p < 0.05$, Table I). Moreover, the length of hospitalization in the MB group was longer than that in the non-MB group, with a duration of 34.00 (23.25, 48.50) days in the MB group and 22.00 (16.00, 29.00) days in the non-MB group.

Predictive Analysis of Preoperative Laboratory Indicators for Massive Intraoperative Bleeding in Liver Transplant Patients

Taking intraoperative blood loss as the dependent variable, statistically significant indicators between the preoperative MB and non-MB groups were selected as independent variables. These specific indicators included BMI, Hb, PLT, PT, Fib, TP, TBIL, BUN, and MELD. Univariate regression analysis showed that BMI, Hb, PT, INR, Fib, TP, and TBIL were independent risk factors for massive blood transfusion during liver transplantation ($p < 0.05$, Table II), but only BMI and Hb were survival after multivariate regression analysis ($p < 0.05$, Table II).

ROC Curve Analysis of Preoperative Laboratory Indicators for Predicting Massive Blooding During Liver Transplantation

Taking massive intraoperative bleeding as the dependent variable and preoperative clinical indicators as independent variables, a ROC curve analysis was conducted. ROC curve analysis showed that BMI and Hb had moderate diagnostic values between MB and non-MB, with AUC of 0.67 and 0.83, respectively (Figure 1). The corresponding best cutoff values were 21.4 kg/m² (sensitivity: 55.4 %, specificity: 71.2 %) and 104 g/L (sensitivity: 78.6 %, specificity: 73.0 %), respectively (Table III).

Discussion

Liver transplantation surgery is an effective treatment for saving the lives of patients with end-stage liver disease[1]. Over the past few decades, with improvements in surgical techniques, anesthesia, organ preservation, and overall perioperative management, the success rate of liver transplantation has continued to rise. However, the possibility of massive bleeding during surgery still exists.

Table I. Comparison of preoperative indexes and length of hospital stay between the MB and non-MB groups.

Indicators	MB (n = 56)	non-MB (n = 215)	Statistical value	p
Age (y)	56.52 ± 9.25	54.35 ± 9.75	1.495	0.136*
Sex (male/female)	39/17	181/34	6.151	0.013#
BMI (kg/m²)	21.48 ± 2.71	23.59 ± 3.81	3.898	**< 0.001***
Hb (g/L)	89.46 ± 18.78	120.27 ± 25.43	10.10	**< 0.001***
PLT (×10⁹/L)	52.50 (37.00,93.50)	77.00 (49.00,118.00)	2.901	**0.004^**
PT (s)	17.75 (14.38,27.25)	15.00 (12.60,22.70)	3.006	**0.003^**
INR	1.55 (1.29,2.42)	1.32 (1.11,2.03)	3.101	**0.002^**
APTT (s)	37.75 (32.65,49.90)	36.10 (32.80,42.00)	1.481	0.139^
Fib (g/L)	1.76 ± 0.92	2.13 ± 0.88	2.816	**0.005***
TP (g/L)	60.57 ± 10.12	65.55 ± 9.05	3.584	**< 0.001***
ALT (U/L)	37.50 (20.25,78.50)	35.00 (25.00,81.00)	0.445	0.656^
AST (U/L)	63.50 (33.00,125.50)	47.00 (32.00,87.00)	1.320	0.187^
TBIL (μmol/L)	106.25 (32.30,236.85)	43.00 (19.50,229.40)	1.975	**0.048^**
CRE (μmol/L)	78.85 (53.35,132.35)	68.30 (55.80,86.80)	0.934	0.350^
BUN (μmol/L)	7.34 (4.52,14.01)	5.23 (3.89,7.39)	2.768	**0.006^**
UA (μmol/L)	279.50 (183.00,405.50)	283.00 (196.00,380.00)	0.021	0.983^
MELD (Score)	16.03 (10.37,27.82)	9.84 (5.55,23.49)	2.745	**0.007^**
Length of stay (Day)	34.00 (23.25, 48.50)	22.00 (16.00,29.00)	5.097	**< 0.001***

*p, tested by t-test (t-value was used as statistical value); #p, tested by Chi-square test (χ^2-value was used as statistical value); ^p, tested by Mann-Whitney U-test (Z-value was used as statistical value). body mass index (BMI), hemoglobin (Hb), platelet count (PLT), fibrinogen (Fib), total protein (TP), prothrombin time (PT), international normalized ratio (INR), total bilirubin (TBIL), creatinine (CRE), blood urea nitrogen (BUN), the model for end-stage liver disease (MELD), including aspartate transaminase (AST), alanine transaminase (ALT), activated partial thromboplastin time (APTT), uric acid (UA), massive bleeding (MB) group, the non-massive bleeding (non-MB).

Table II. Logistic regression analysis of preoperative laboratory indicators and intraoperative massive bleeding in liver transplantation.

	Univariate analysis			Multivariate analysis		
Indicators	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
BMI (kg/m²)	0.814	0.733-0.904	**< 0.001**	0.798	0.703-0.906	**0.001**
Hb (g/L)	0.946	0.930-0.961	**< 0.001**	0.949	0.931-0.967	**< 0.001**
PLT (×10⁹/L)	0.996	0.991-1.001	0.152	/	/	/
PT (s)	1.031	1.007-1.056	**0.010**	1.043	0.998-1.089	0.559
INR	1.434	1.088-1.889	**0.010**	4.316	0.078-239.40	0.475
Fib (g/L)	0.596	0.412-0.863	**0.006**	0.941	0.589-1.503	0.799
TP (g/L)	0.944	0.913-0.975	**0.001**	1.004	0.959-1.050	0.880
TBIL (μmol/L)	0.914	0.864-0.967	**0.002**	0.965	0.883-1.055	0.436
BUN (μmol/L)	1.019	0.994-1.044	0.134	/	/	/
MELD (Score)	1.020	0.999-1.040	0.058	/	/	/

Body mass index (BMI), hemoglobin (Hb), platelet count (PLT), fibrinogen (Fib), total protein (TP), prothrombin time (PT), international normalized ratio (INR), total bilirubin (TBIL), blood urea nitrogen (BUN), the model for end-stage liver disease (MELD).

The normal human blood volume ranges between 7% and 8%, and intraoperative blood loss exceeding 1,000 ml or 15% of a patient's blood volume can result in a significant drop in blood pressure, potentially leading to organ dysfunction and life-threatening situations[14-16]. Massive blood transfusion significantly improves the blood volume and systemic circulation of liver transplant patients, maintaining a stable blood volume during surgery[17,18]. In this study, the analysis of preoperative laboratory indicators of patients found that the red blood cell count, platelet count,

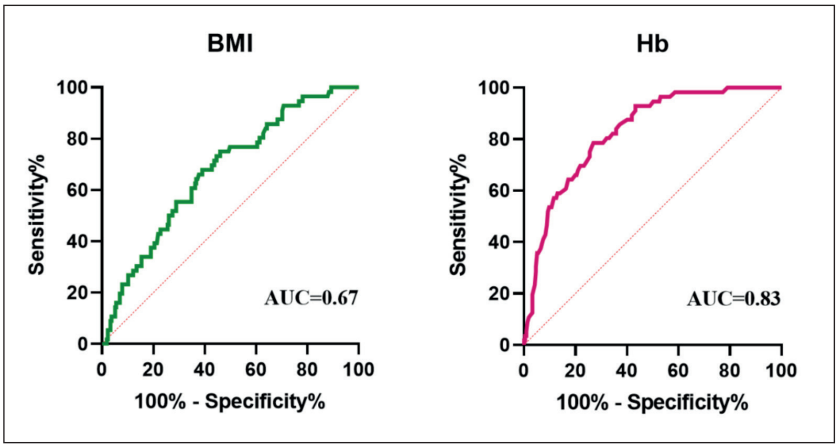

Figure 1. ROC curve analysis of BMI and Hb levels for distinguishing MB from non-MB group.

Table III. ROC curve analysis of BMI and Hb levels for predicting massive blood transfusion during liver transplantation.

Indicators	**AUC**	**Cut-off**	**Sensitivity**	**Specificity**	**95% CI**	***p***
BMI (kg/m²)	0.673	21.4	55.4	71.2	0.597-0.749	**< 0.001**
Hb (g/L)	0.829	104	78.6	73.0	0.775-0.884	**< 0.001**
PT (s)	0.630	14.3	45.1	78.6	0.553-0.708	**0.003**
INR	0.635	1.26	45.1	78.6	0.558-0.711	**0.002**
Fib (g/L)	0.631	1.56	72.6	57.1	0.543-0.719	**0.003**
TP (g/L)	0.634	62.5	63.7	57.1	0.551-0.718	**0.002**
TBIL (μmol/L)	0.586	24.5	36.3	85.7	0.508-0.664	**0.048**

Body mass index (BMI), hemoglobin (Hb), fibrinogen (Fib), total protein (TP), prothrombin time (PT), international normalized ratio (INR), total bilirubin (TBIL), Area under curve (AUC).

fibrinogen, and total protein in the MB group were lower than those in the non-massive bleeding group, and other coagulation functions and liver and kidney biochemical function indexes were higher than those in the non-MB transfusion group. Besides, patients with end-stage liver disease often exhibit splenomegaly, anemia, and coagulation disorders. Liver cancer patients may also experience tumor rupture, leading to bleeding. Additionally, the transfusion of stored red blood cells can cause hypothermia, further diluting the blood and exacerbating coagulation disorders, resulting in massive intraoperative bleeding[19,20].

Various factors contribute to bleeding during liver transplantation, including the severity of liver disease, inherent coagulation disorders, previous upper abdominal surgery, and the degree of preoperative anemia[21]. In a study by Steib et al[22], low preoperative Hb was considered to be one of the three risk factors for massive intraoperative bleeding. McCluskey et al[23] predicted the risk index of massive bleeding during liver transplantation and pointed out that the MELD score and international normalized ratio (INR) were considered independent predictors of bleeding. In a retrospective study, Cywinski et al[24] found that higher INR and lower PLT before transplantation were predictors of massive intraoperative bleeding. In this study, it was also confirmed that Hb, MELD score, PLT count, PT, INR, and other indicators were statistically significant between the two groups, which was consistent with the ideas of the above scholars[22-24].

In liver transplantation, patients lose the ability to synthesize coagulation factors during the period without a liver[6]. Even after the liver transplant, the new liver does not immediately synthesize an adequate amount of coagulation factors and fibrinogen to meet the body's needs. The massive bleeding during liver transplantation, along with the large blood loss from the liver wound, leads to continuous dilution of coagulation factors with extensive blood transfusion. This exacerbates coagulation dysfunction, making massive intraoperative bleeding highly likely and impacting postoperative recovery. Excessive use of blood products can also decrease the survival rate of transplant patients and increase the occurrence of transfusion reactions[25]. To predict massive intraoperative bleeding, our study identified low BMI and low Hb as independent risk factors for massive bleeding during liver transplantation. ROC curve analysis further affirmed the significance of BMI and Hb in predicting intraoperative bleeding. Therefore, preoperative transfusion of red blood cells and improvement of the nutritional status of patients can play a certain role in reducing intraoperative bleeding and promoting postoperative recovery[26].

While this study has limitations, including its retrospective, single-center nature and the lack of disease-specific investigations, we advocate for future multi-center studies to explore comprehensive risk factors for massive bleeding during liver transplantation.

Conclusions

Preoperative indicators, specifically BMI and Hb levels, emerge as pivotal predictors for massive bleeding during liver transplantation. The monitoring and optimization of these factors are essential for effective risk stratification and proactive management. These findings offer valuable insights for clinicians, contributing to enhanced patient outcomes.

Ethics Approval

The study received approval from the Li Huili Hospital Ethics Committee (approval No. KY2021PJ144).

Informed Consent

The study did not contain personal data and we applied for an informed consent waiver.

Authors' Contributions

Conception and design of the study: Ke-Da Chen, Wei Chen. Data acquisition: Ke-Da Chen, Bin Hu. Analysis and interpretation: Zhang-Sheng Zhao, Ke-Da Chen. The manuscript was drafted by Zhang-Sheng Zhao and Ke-Da Chen.

Conflict of Interest

The authors declared no conflicts of interest.

Data Availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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