ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

Weekly Volume 31 Number 47 December 21, 2025

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

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Weekly Volume 31 Number 47 December 21, 2025

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NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

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PUBLICATION DATE
December 21, 2025

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Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

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World Journal of Gastroenterology

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World J Gastroenterol 2025 December 21; 31(47): 114370

DOI: 10.3748/wjg.v31.i47.114370

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Study

Interpretable machine learning model for early complication prediction after split liver transplantation

Di Wang, Jun-Yan Zhang, Yan Xie, Kun-Ning Zhang, Wen-Tao Jiang

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade A, Grade B

Novelty: Grade A, Grade B

Creativity or Innovation: Grade A, Grade B

Scientific Significance: Grade A, Grade A

P-Reviewer: Al-Hussaniy HA, PhD, Professor, Iraq; Tian L, Assistant Professor, China

Received: September 22, 2025

Revised: October 7, 2025

Accepted: November 4, 2025

Published online: December 21, 2025

Processing time: 89 Days and 21 Hours

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Abstract

BACKGROUND

Split liver transplantation (SLT) effectively expands the donor pool but carries a higher risk of early postoperative complications (EPC) due to the extensive transection surface and altered hemodynamics of partial grafts.

AIM

To establish an interpretable machine learning framework to identify risk factors for EPC in adult recipients undergoing right tri-segment SLT.

METHODS

We retrospectively analyzed 109 adult SLT recipients, including 37 who developed EPC. A comprehensive set of perioperative donor and recipient variables was evaluated using four machine learning algorithms (random forest, support vector machine, extreme gradient boosting, and logistic regression). SHapley Additive exPlanations were employed to rank variable importance. Independent predictors were further validated through multivariate logistic regression, and a diagnostic nomogram was constructed. Restricted cubic spline, receiver operating characteristic, and survival analyses were conducted to evaluate model performance and clinical outcomes.

RESULTS

EPC occurred in 33.9% of recipients. Among the machine learning models, random forest demonstrated the best predictive performance. SHapley Additive exPlanations analysis identified the log-transformed systemic immune-inflammation index (LnSII), albumin-to-fibrinogen ratio, model for end-stage liver

disease (MELD) score, partial lobectomy of segment IV (IV PL), intraoperative blood loss, and operation time as major contributors to the model. Multivariate logistic regression confirmed LnSII, MELD scores, IV PL, and blood loss as independent predictors of EPC. The nomogram constructed from these factors showed good discrimination and calibration (area under the curve = 0.788, 95% confidence interval: 0.734-0.906). Kaplan-Meier analysis revealed that both LnSII and MELD scores were associated with five-year overall survival ($P < 0.05$), while MELD score and IV PL were significantly correlated with early postoperative liver function recovery.

CONCLUSION

IV PL during right tri-segment SLT appears to reduce the risk of EPC and enhance postoperative liver function recovery. Together with LnSII, blood loss, and MELD score, these factors offer a reliable foundation for individualized perioperative risk stratification and management.

Key Words: Early postoperative complications; Machine learning; Partial lobectomy of segment IV; Split liver transplantation; Systemic immune-inflammation index

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Core Tip: This study employed an interpretable machine learning framework to assess risk factors for early postoperative complications in adult recipients of right tri-segment split liver transplantation. We identified systemic immune-inflammation index, model for end-stage liver disease score, intraoperative blood loss, and partial lobectomy of segment IV as independent predictors. A nomogram incorporating these variables demonstrated robust predictive accuracy. These findings highlight the clinical utility of integrating inflammatory status, surgical factors, and intraoperative variables for individualized perioperative management in split liver transplantation.

Citation: Wang D, Zhang JY, Xie Y, Zhang KN, Jiang WT. Interpretable machine learning model for early complication prediction after split liver transplantation. *World J Gastroenterol* 2025; 31(47): 114370
URL: https://www.wjgnet.com/1007-9327/full/v31/i47/114370.htm
DOI: https://dx.doi.org/10.3748/wjg.v31.i47.114370

INTRODUCTION

Liver transplantation (LT) remains the only curative treatment for patients with end-stage liver disease[1]. Despite its well-established efficacy, the broader application of LT continues to be constrained by the persistent shortage of suitable donor organs. Split LT (SLT) has emerged as a promising strategy to address this limitation by increasing graft availability, thereby shortening waiting times and potentially reducing pre-transplant mortality[2]. However, SLT poses considerable technical challenges and has been associated with increased perioperative risks and, in some studies, less favorable long-term outcomes compared with whole LT (WLT)[3]. These challenges underscore the urgent need for continued research to optimize SLT techniques and improve both safety and clinical efficacy.

Previous studies have demonstrated that overall post-transplant survival among SLT recipients is comparable to that observed in WLT patients[4]. Similarly, in case of hepatocellular carcinoma, SLT does not appear to increase recurrence or adversely affect outcomes relative to WLT[5]. Intraoperatively, ischemic regions are frequently observed within segment IV of extended right grafts. These areas not only reduce the functional liver mass but also promote the generation of reactive oxygen species in hepatocytes, leading to apoptosis and necrosis[6]. Despite these observations, the clinical impact of excising such ischemic foci on early postoperative complication (EPC) remains poorly understood. These complications can negatively affect graft survival and long-term prognosis, emphasizing the importance of identifying and elucidating their underlying risk factors[7].

SLT is inherently associated with an elevated risk of EPC, which present substantial clinical challenges. The procedure involves increased technical complexity and introduces unique surgical and physiological stresses. The extensive transection surface of partial grafts, combined with resultant hemodynamic alterations, predisposes recipients to complications such as bile leakage, hemorrhage, and impaired graft function[8,9]. These events can markedly worsen patient outcomes by increasing morbidity and mortality. Among them, bile leakage, is one of the most frequent complications; it is influenced by both surgical technique and graft quality and is associated with prolonged hospitalization, increased infection risk, and potential graft loss[10,11]. Hemorrhage represents another critical adverse event, directly contributing to heightened morbidity and mortality. Impaired graft function, ranging from transient dysfunction to primary nonfunction, further complicates postoperative recovery, with incidence varying according to donor and recipient characteristics[12,13]. Collectively, these complications impose a substantial clinical and economic clinical burden, resulting in extended intensive care unit stays, higher healthcare costs, and reduced patient quality of life. The unpredictable nature of EPC highlights a significant unmet need: The absence of reliable predictive tools capable of identifying high-risk patients and guiding preventive interventions. Developing such predictive models is crucial for optimizing perioperative management, improving resource allocation, and enhancing the long-term success of SLT. The present study aims to fill

this gap by identifying key predictors of EPC, ultimately facilitating more precise risk assessment and informed clinical decision-making.

EPC play a pivotal role in shaping both recovery and long-term outcomes after LT. Traditional statistical approaches have been used to identify risk factors for post-transplant complications, yet they often struggle to capture the complex, nonlinear interactions among clinical variables[14,15]. Recent advances in interpretable machine learning offer a powerful alternative for more accurate and transparent risk stratification in transplantation medicine[16]. By integrating donor characteristics, recipient profiles, and intraoperative parameters, machine learning models, augmented with explainability frameworks such as SHapley Additive exPlanations (SHAP)[17] can provide both accurate predictions and mechanistic insights, thereby supporting evidence-based and individualized clinical decision-making in SLT.

MATERIALS AND METHODS

Study population

Between July 2018 and March 2025, all recipients who underwent SLT at First Central Hospital of Tianjin Medical University were screened for eligibility. Pediatric patients and those with a history of multiorgan transplantation prior to SLT were excluded. During this period, 128 adult recipients underwent right tri-segment SLT. Of these, 109 met the inclusion criteria and were included in the final analysis. Patients were excluded if they underwent re-transplantation (n = 7, different surgical background and prognosis), combined multi-organ transplantation (n = 10, additional confounding factors), or were lost to follow-up (n = 2, outcomes not available). All organ donation and transplantation procedures strictly adhered to the regulations of the China Organ Donation Committee, the Organ Transplant Committee, as well as to the principles of the Declaration of Helsinki (2013 revision). All donor livers were obtained from deceased citizen donors, with no involvement of organs from executed prisoners. The requirement for informed consent was waived, as the study utilized previously collected data that contained no personally identifiable information.

SLT procedures and follow-up

During the study period, all adult recipients who underwent right tri-segment SLT were evaluated for inclusion. Patients were excluded if they had received multiple transplantations (≥ 2 procedures), underwent multi-organ transplantation, or were lost to follow-up. In accordance with standard splitting protocols, donor livers were divided into a left lateral graft (segments II and III) for pediatric recipients and an extended right lobe graft for adult recipients[18]. *In situ* liver splitting was performed in most cases. Following separation, grafts were immediately immersed in cold preservation solution and maintained on ice until implantation. Vascular and biliary reconstructions were performed following established surgical techniques[19]. After transplantation, all recipients underwent routine postoperative monitoring and follow-up assessments according to institutional protocols.

Data sources

The dataset included comprehensive information on donors, recipients, perioperative parameters, and clinical outcomes. Donor characteristics comprised age, graft-to-recipient weight ratio (GRWR), and ABO compatibility. Recipient variables encompassed age, sex, body mass index, comorbidities such as hypertension, diabetes mellitus, and coronary artery disease, as well as Child-Pugh score, model for end-stage liver disease (MELD) score, and indication for transplantation. Perioperative data encompassed cold ischemia time, warm ischemia time, operative duration, partial lobectomy of segment IV (IV PL), duration of the anhepatic phase, and estimated blood loss. Preoperative laboratory parameters included complete blood count, liver and renal function tests, and coagulation profiles. Systemic immune-inflammation (SII) was calculated as previously described using the formula: SII = platelet count × neutrophil count/Lymphocyte count [20]. To reduce skewness and improve interpretability, SII values were natural log-transformed (LnSII)[21]. Albumin-to-fibrinogen ratio (AFR) was calculated as albumin level divided by fibrinogen level[22]. Graft survival was defined as the time from LT to recipient death. EPC were defined as adverse events occurring within the first month after SLT, including intra-abdominal bleeding, vascular thrombosis, biliary complications, ascites, and infections[23]. EPC were defined as adverse events occurring within 30 days after surgery, including intra-abdominal hemorrhage, vascular complications, biliary complications, ascites, and infections. The primary study endpoint was the occurrence of EPC, while overall survival (OS) served as the secondary endpoint.

Machine learning

Comprehensive perioperative donor and recipient variables were evaluated using four machine learning algorithms [random forest (RF), support vector machine (SVM), extreme gradient boosting (XGBoost), and logistic regression (LR)]. RF is an ensemble learning method that constructs multiple decision trees, each functioning as a flowchart that predicts outcomes based on patient characteristics (*e.g.*, age, or biomarker levels). RF combines the predictions of all trees through voting to produce a robust result. Its ability to capture complex, non-linear relationships in data makes it well-suited for identifying ECP risk factors in our diverse dataset. SVM identifies an optimal boundary (or hyperplane) that separates patients into groups, such as those likely to develop ECP *vs* those who are not, based on clinical features. It maximizes the separation between groups to ensure reliable classification. SVM's strength in handling high-dimensional data makes it effective for pinpointing key ECP predictors. XGBoost is an advanced ensemble method that builds decision trees sequentially, with each tree correcting errors from the previous ones. This iterative approach enhances prediction accuracy, particularly for complex datasets. XGBoost excels at capturing subtle, non-linear patterns in the data that might be missed

by traditional models. LR, a classical statistical model, estimates the probability of an outcome (*e.g.*, ECP occurrence) by analyzing relationships between patient features and the outcome. It is straightforward and interpretable, making it valuable for identifying linear relationships between clinical variables and ECP risk.

Statistical analysis

The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Variables with a normal distribution are presented as mean ± SD, whereas non-normally distributed variables are expressed as median with interquartile range (IQR). Comparisons between groups were conducted using the Student's *t*-test for normally distributed data or the Mann-Whitney *U* test for non-normal data. Categorical variables are reported as counts and percentages, and differences between groups were evaluated using the χ^2 test or Fisher's exact test, as appropriate. Changes in laboratory parameters before and after surgery were analyzed with paired *t*-tests, Wilcoxon signed-rank tests, or McNemar's test. Potential predictors of ECP were first examined by univariate LR, followed by multivariate analysis. Variables with a P value < 0.05 in univariate analysis were entered into the multivariate model using a forward likelihood ratio selection method. Survival outcomes were estimated using the Kaplan-Meier method and compared with the log-rank test. A two-sided P value < 0.05 was considered statistically significant. All analyses were performed using GraphPad Prism version 9.0, Python version 3.9, R version 4.5.1, and SPSS version 26.0.

RESULTS

Baseline characteristics

Among the 128 adult recipients who underwent right trilobe SLT, 109 patients fulfilled the inclusion criteria. Exclusions included patients who underwent re-transplantation (n = 7), combined multi-organ transplantation (n = 10), or lost to follow-up (n = 2) (Figure 1). Baseline clinical characteristics of the study cohort are summarized in Table 1. The median follow-up duration was 34.5 months. The main indications for transplantation were hepatitis B virus infection (37.6%), alcoholic liver disease (8.2%), autoimmune liver disease (16.5%), and malignancy (35.8%). Among the 39 recipients with malignant disease, 32 had hepatocellular carcinoma, three had cholangiocarcinoma, and four had neuroendocrine tumors. The median GRWR was 1.5% (IQR: 1.2%-1.8%), and no cases of small-for-size syndrome (SFSS) were observed[24]. EPC occurred in 37 patients and included intra-abdominal hemorrhage (n = 3), vascular complications (n = 4), biliary complications (n = 9), ascites (n = 12), and infections (n = 9). Comparative analysis between the EPC and non-EPC groups revealed that patients with EPCs had significantly higher MELD score and longer operative times (P < 0.05), indicating more advanced liver disease and greater surgical complexity. Moreover, omission of IV PL was associated with an increased risk of EPC. Cold ischemia time and warm ischemia time did not differ significantly between the groups. In contrast, intraoperative blood loss was markedly greater in the EPC group, with a median volume of 2000 mL (IQR: 1000-2800 mL). Laboratory data showed patients who developed EPCs had higher elevated neutrophil counts, fibrinogen levels, and international normalized ratio values, consistent with a heightened systemic inflammatory response. The distribution of underlying liver diseases was similar between the two groups, with viral hepatitis remaining the predominant etiology (46.0% in the EPC group *vs* 33.3% in the non-EPC group).

Risk biomarkers for EPC predicted by machine learning models

We evaluated the predictive performance of four machine learning algorithms, XGBoost, SVM, RF and LR, using multiple metrics, including area under the curve (AUC), sensitivity, specificity, F1 scores, Brier scores, and overall accuracy. Among these models, the RF algorithm achieved the highest predictive accuracy (Figure 2). A summary of discriminative metrics for all four models is presented in Supplementary Table 1, and the top ten features identified by SHAP analysis for each model are shown in Supplementary Figure 1. Given its superior performance, the RF model was selected for further analysis to identify the most influential biomarkers associated with EPC. To improve interpretability, SHAP analysis, was employed to quantify the contribution of each variable to model predictions. This approach revealed not only which factors was most important overall but also how they influenced the predicted risk for individual patients. The six strongest predictors of EPCs were higher LnSII, AFR, and MELD score, greater intraoperative blood loss, longer operative time, omission of segment IV WPL (Figure 2). SHAP dependence plots further illustrated how variations in these predictors affected the predicted probability of EPC. Positive SHAP values were associated with an increased predicted risk, as shown in Figure 2.

Univariate and multivariate analyses of risk factors for EPC

We next performed regression analyses, with the results summarized in Table 2. In the univariate LR, several factors were significantly associated with the occurrence of EPC, including MELD scores [odds ratio (OR) = 1.074; 95% confidence interval (CI): 1.020-1.137; P = 0.012], intraoperative blood loss (OR = 1.001; 95%CI: 1.000-1.001; P = 0.002), operative time (OR = 1.003; 95%CI: 1.000-1.007; P = 0.039), IV PL (OR = 0.242; 95%CI: 0.080-0.617; P = 0.005), LnSII (OR = 1.971; 95%CI: 1.290-3.165; P = 0.003), AFR (OR = 0.942; 95%CI: 0.890-0.986; P = 0.024), Child-Pugh class B (OR = 5.600; 95%CI: 1.491-21.036; P = 0.011), and Child-Pugh class C (OR = 5.778; 95%CI: 1.140-23.342; P = 0.014). Given the substantial overlap between the MELD score and Child-Pugh classification in reflecting hepatic functional reserve, only MELD score was retained in the multivariate model to minimize collinearity and maintain model simplicity. In the multivariate LR, MELD score (OR = 1.104; 95%CI: 1.027-1.186; P = 0.008), intraoperative blood loss (OR = 1.001; 95%CI: 1.000-1.001; P = 0.043), IV PL (OR = 0.226; 95%CI: 0.070-0.727; P = 0.013), and LnSII (OR = 1.729; 95%CI: 1.028-2.907; P = 0.039) emerged as

Table 1 Comparison of demographic and clinical characteristics and outcomes between non-early postoperative complications and early postoperative complications, *n* (%)/median (interquartile range)

Characteristics	All (*n* = 109)	Non-EPC (*n* = 72, 66.1%)	EPC (*n* = 37, 33.9%)	*P* value
Recipient age (years)	53.0 (44.0, 60.0)	53.0 (43.7, 59.0)	53.0 (45.0, 61.0)	0.557
Gender				0.999
Male	69 (63.3)	46 (63.9)	23 (62.2)	
Female	40 (36.7)	26 (36.1)	14 (37.8)	
BMI (kg/m^2)	22.9 (20.7, 25.3)	22.5 (20.7, 25.3)	23.1 (20.7, 25.9)	0.485
Blood pressure				0.769
No	95 (87.2)	62 (86.1)	33 (89.2)	
Yes	14 (12.8)	10 (13.9)	4 (10.8)	
CHD				0.335
No	92 (84.4)	63 (87.5)	29 (78.4)	
Yes	17 (15.6)	9 (12.5)	8 (21.6)	
Diabetes				0.999
No	86 (78.9)	57 (79.2)	29 (78.4)	
Yes	23 (21.1)	15 (20.8)	8 (21.6)	
MELD scores	18.0 (12.0, 23.0)	16.0 (11.0, 21.0)	20.0 (15.0, 26.0)	0.009
Child-Pugh scores	9.0 (7.0, 11.0)	9.0 (6.0, 11.0)	10.0 (8.0, 11.0)	0.131
Transplant indication				0.124
Hepatitis (B and C)	41 (37.6)	24 (33.3)	17 (46.0)	
Tumor	39 (35.8)	24 (33.3)	15 (40.5)	
Alcohol liver disease	9 (8.2)	7 (9.8)	2 (5.4)	
Autoimmune disease	18 (16.5)	16 (22.2)	2 (5.4)	
Polycystic liver	2 (1.9)	1 (1.4)	1 (2.7)	
GRWR (%)	1.5 (1.2, 1.8)	1.5 (1.2, 1.8)	1.6 (1.2, 2.0)	0.648
Donor age (years)	40.0 (31.0, 45.0)	39.0 (29.7, 44.0)	43.0 (33.0, 46.0)	0.189
ABO incompatibility				0.999
No	104 (95.4)	69 (95.8)	35 (94.6)	
Yes	5 (4.6)	3 (4.2)	2 (5.4)	
Anhepatic phase	45.0 (40.0, 50.0)	43.50 (37.5, 50.0)	45.0 (40.0, 57.0)	0.153
Blood loss (mL)	1500.0 (1000.0, 2400.0)	1200.0 (800.0, 2000.0)	2000.0 (1000.0, 2800.0)	0.003
Operation time (minutes)	500.0 (440.0, 590.0)	480.0 (408.7, 578.2)	540.0 (468.0, 625.0)	0.040
CIT (minutes)	130.0 (80.0, 210.0)	120.0 (80.0, 190.0)	170.0 (90.0, 230.0)	0.100
WIT (seconds)	83.0 (43.0, 110.0)	85.5 (41.5, 108.2)	82.0 (58.0, 133.0)	0.420
IV PL				0.006
No	71 (65.1)	40 (55.6)	31 (83. 8)	
Yes	38 (34.9)	32 (44.4)	6 (16.2)	
WBC (10^9/L)	4.03 (2.66, 5.60)	3.49 (2.30, 5.13)	4.84 (3.90, 5.93)	< 0.001
Neutrophile counts (10^9/L)	2.64 (1.71, 4.10)	2.16 (1.49, 3.27)	3.51 (2.44, 5.14)	< 0.001
Lymphocyte counts (10^9/L)	0.70 (0.45, 0.96)	0.71 (0.43, 0.97)	0.60 (0.46, 0.90)	0.650
HB (g/L)	96.0 (83.0, 110.0)	96.8 (85.7, 111.7)	94.0 (77.0, 108.0)	0.146
PLT (10^9/L)	69.0 (41.0, 101.0)	64.5 (40.7, 96.2)	77.0 (45.0, 111.0)	0.279

ALB (g/L)	32.6 (29.7, 37.6)	32.5 (29.5, 36.6)	32.9 (31.4, 38.4)	0.396
TBIL (μmol/L)	62.3 (27.7, 191.0)	58.7 (23.8, 150.1)	69.4 (34.4, 310.0)	0.117
ALT (U/L)	56.4 (24.9, 117.7)	54.1 (24.9, 98.6)	56.4 (26.4, 129.6)	0.554
AST (U/L)	79.4 (46.1, 194.6)	69.8 (43.4, 187.3)	106.4 (56.3, 226.8)	0.347
ALP (U/L)	144.0 (97.0, 198.0)	142.0 (96.7, 186.0)	144.0 (99.0, 268.0)	0.541
GGT (U/L)	62.0 (32.0, 124.0)	58.0 (31.0, 114.2)	83.0 (37.0, 152.0)	0.301
Cr (μmol/L)	58.0 (49.0, 76.0)	57.5 (49.4, 74.5)	63.0 (48.0, 77.0)	0.663
FIB (g/L)	1.71 (1.26, 2.24)	1.52 (1.12, 2.06)	1.84 (1.54, 2.49)	0.014
APTT (seconds)	40.3 (34.3, 47.3)	40.3 (34.5, 46.1)	40.7 (34.1, 52.4)	0.582
INR	1.63 (1.31, 1.99)	1.54 (1.17, 1.95)	1.70 (1.46, 2.13)	0.014

EPC: Early postoperative complications; BMI: Body mass index; CHD: Coronary heart disease; MELD: Model for end-stage liver disease; GRWR: Graft-to-recipient weight ratio; CIT: Cold ischemia time; WIT: Warm ischemia time; IV PL: Partial lobectomy of segment IV; WBC: White blood counts; HB: Hemoglobin; PLT: Platelets; ALB: Albumin; TBIL: Total bilirubin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; Cr: Creatinine; FIB: Fibrinogen; APTT: Activated partial thromboplastin time; INR: International normalized ratio.

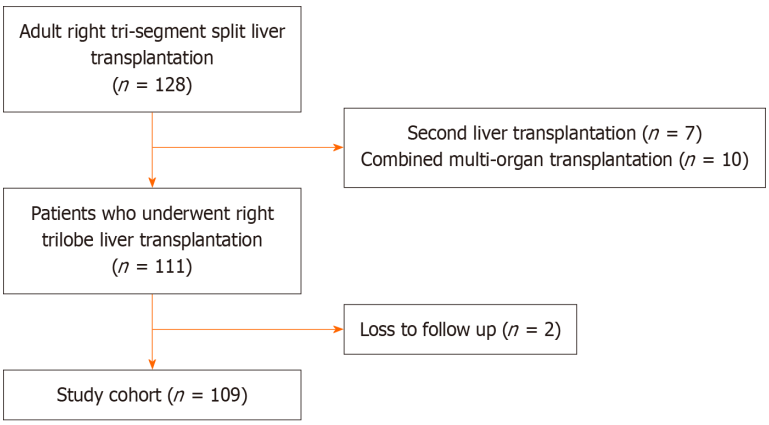

Figure 1 Flow chart for patient enrollment.

independent predictors of EPC. To further explore potential dose-response relationships, restricted cubic spline analyses were conducted for these predictors (Supplementary Figure 2). After adjusting for all covariates, MELD score, intraoperative blood loss, and LnSII demonstrated linear associations with EPC risk, with no evidence of significant nonlinearity (P for nonlinearity > 0.05).

To develop a diagnostic nomogram for predicting EPC

Based on the multivariate analysis, four independent risk factors: MELD score, intraoperative blood loss, IV PL, and LnSII were incorporated into a diagnostic nomogram to predict individual EPC risk (Figure 3A). Model calibration showed close agreement between the predicted and observed probabilities, aligning well with the ideal reference line (Figure 3B), thus indicating excellent calibration and reliability for clinical use. The discriminative performance of each variable was evaluated using receiver operating characteristic analysis. The AUC values were 0.654 for MELD score, 0.673 for intraoperative blood loss, 0.641 for IV PL, and 0.639 for LnSII (Figure 3C). When combined in the nomogram, the AUC increased to 0.788 (Figure 3D), representing a marked improvement in predictive accuracy. Furthermore, decision curve analysis demonstrated that the nomogram provided greater net clinical benefit across a wide range of threshold probabilities compared with any single predictor, underscoring its superior applicability in clinical decision-making (Figure 3E). To illustrate its clinical application, a representative case was analyzed: A patient with an SII value of 5.87, intraoperative blood loss of 2500 mL, no resection of segment IV, and a MELD score of 11 yielded a total nomogram score of 159, corresponding to a 44.6% predicted probability of developing EPC. This example demonstrates how the nomogram translates individual patient characteristics into a quantitative risk estimate, facilitating personalized perioperative risk assessment and management.

Impact of four factors on patient prognosis and perioperative liver function recovery

Kaplan-Meier survival analysis demonstrated patients with high SII values had significantly poorer OS compared with those with low SII (P = 0.007, Figure 4). Similarly, individuals with elevated MELD score showed worse survival

Table 2 Logistic regression evaluation of factors associated with early postoperative complications following split liver transplantation

Characteristics[1]	Univariable		Multivariable	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Recipient age (years)	1.012 (0.970-1.052)	0.544		
Gender (female)	1.077 (0.470-2.436)	0.859		
BMI (kg/m^2)	1.048 (0.950-1.159)	0.349		
Blood pressure (yes)	0.752 (0.190-2.440)	0.650		
CHD (yes)	1.931 (0.660-5.559)	0.219		
Diabetes (yes)	1.048 (0.380-2.711)	0.924		
MELD scores[2]	1.074 (1.020-1.137)	0.012	1.104 (1.027-1.186)	0.008
Child-Pugh class[2]				
A[2]	Reference			
B[2]	5.600 (1.491-21.036)	0.011		
C[2]	5.778 (1.140-23.342)	0.014		
Transplant indication				
Hepatitis (B and C)	Reference			
Tumor	0.882 (0.360-2.161)	0.784		
Alcohol liver disease	0.403 (0.074-2.186)	0.292		
Autoimmune disease	0.176 (0.036-0.870)	0.033		
polycystic liver	1.412 (0.082-24.178)	0.812		
GRWR (%)	1.345 (0.540-3.384)	0.526		
Donor age (years)	1.019 (0.980-1.061)	0.331		
ABO incompatibility (yes)	1.314 (0.210-8.233)	0.770		
Anhepatic phase	1.023 (0.990-1.059)	0.179		
Blood loss[2] (mL)	1.001 (1.000-1.001)	0.002	1.001 (1.000-1.001)	0.043
Operation time[2] (minutes)	1.003 (1.000-1.007)	0.039	1.002 (0.998-1.006)	0.271
CIT (minutes)	1.003 (1.000-1.008)	0.140		
WIT (seconds)	1.005 (1.000-1.014)	0.261		
IV PL[2] (yes)	0.242 (0.080-0.617)	0.005	0.226 (0.070-0.727)	0.013
LnSII[2]	1.971 (1.290-3.165)	0.003	1.729 (1.028-2.907)	0.039
AFR[2]	0.942 (0.890-0.986)	0.024	0.942 (0.879-1.010)	0.093
HB (g/L)	0.985 (0.970-1.003)	0.111		
ALT (U/L)	1.000 (1.000-1.004)	0.914		
AST (U/L)	1.000 (1.000-1.003)	0.706		
ALP (U/L)	1.002 (1.000-1.006)	0.240		
GGT (U/L)	1.003 (1.000-1.007)	0.200		
APTT (seconds)	1.020 (0.990-1.051)	0.171		

[1]The associations of early postoperative complications with clinical characteristics were assessed by univariate and multivariable logistic regression.
[2]*P* values statistical significance.
OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; CHD: Coronary heart disease; MELD: Model for end-stage liver disease; GRWR: Graft-to-recipient weight ratio; CIT: Cold ischemia time; WIT: Warm ischemia time; IV PL: Partial lobectomy of segment IV; LnSII: Log-transformed systemic immune inflammatory index; AFR: Albumin-to-fibrinogen ratio; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; APTT: Activated partial thromboplastin time.

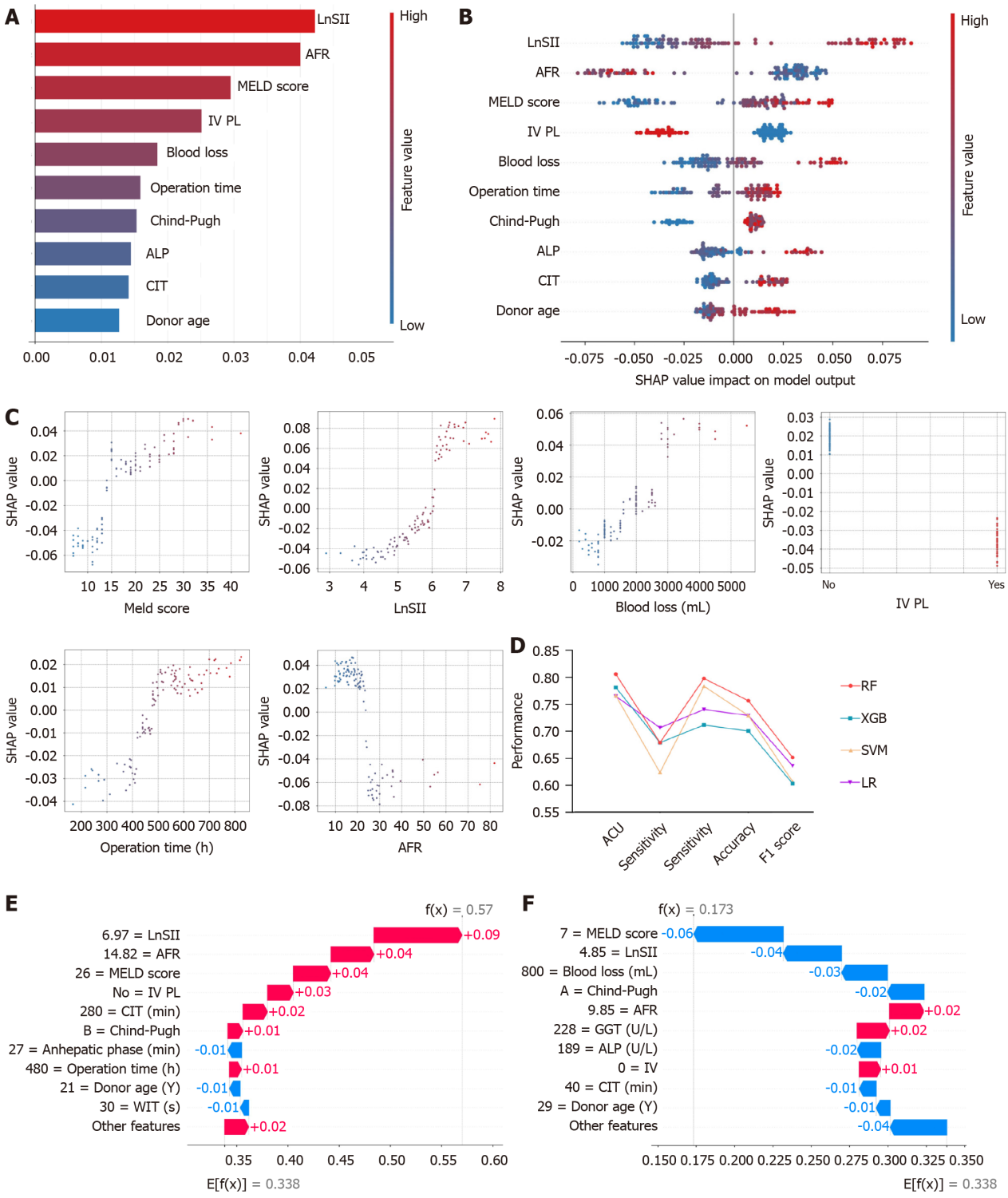

Figure 2 Global model explanation by the SHapley Additive exPlanations method. A: SHapley Additive exPlanations (SHAP) summary bar plot; B: SHAP summary dot plot. The probability of acute kidney injury development increases with the SHAP value of a feature. A dot is made for SHAP value in the model for each single patient, so each patient has one dot on the line for each feature. The colors of the dots demonstrate the actual values of the features for each patient, as red means a higher feature value and blue means a lower feature value. The dots are stacked vertically to show density; C: SHAP dependence plot. Each dependence plot shows how a single feature affects the output of the prediction model, and each dot represents a single patient; D: Performance metrics of the four machine learning models in the cohort; E and F: Waterfall plots demonstrating individual patient feature contributions towards risk classification: Panel E indicates a patient classified as "early postoperative complications", panel F a patient classified as "non-early postoperative complications". LnSII: Log-transformed systemic immune inflammatory index; IV PL: Partial lobectomy of segment IV; AFR: Albumin-to-fibrinogen ratio; MELD: Model for end-stage liver disease; RF: Random forest; SVM: Support vector machine; XGB: Extreme gradient boosting; LR: Logistic regression; ALP: Alkaline phosphatase; CIT: Cold ischemia time; SHAP: SHapley Additive exPlanations; WIT: Warm ischemia time; GGT: Gamma-glutamyl transferase.

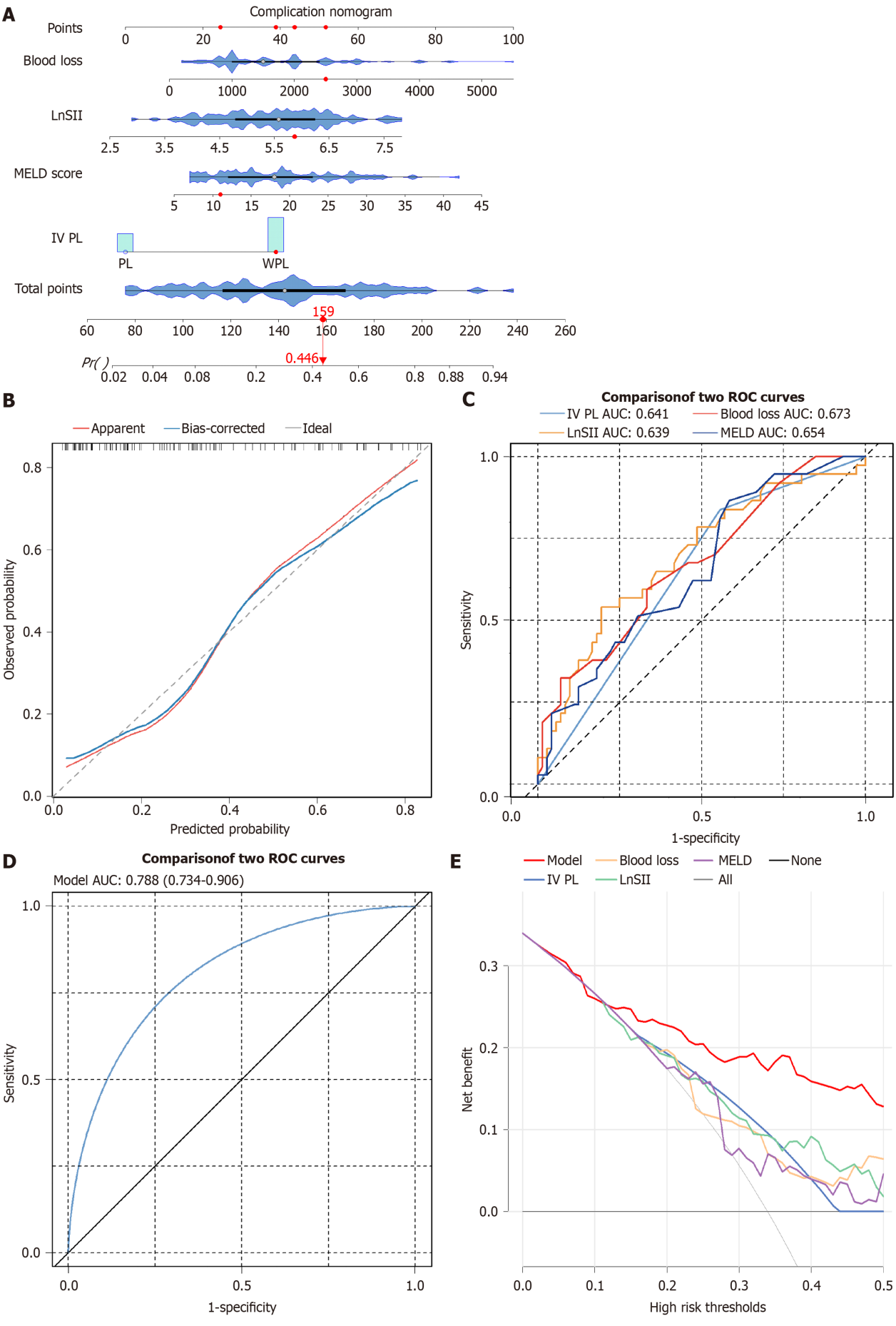

Figure 3 Establishing a diagnostic nomogram for early postoperative complications. A: Nomogram for the diagnosis of early postoperative

complications; B: Calibration curve for prediction accuracy; C: Receiver operating characteristic curves of four indexes in the cohort; D: The receiver operating characteristic curve of the combination of four indexes; E: Decision curve analysis for the nomogram. LnSII: Log-transformed systemic immune inflammatory index; IV PL: Partial lobectomy of segment IV; AUC: Area under the curve; MELD: Model for end-stage liver disease.

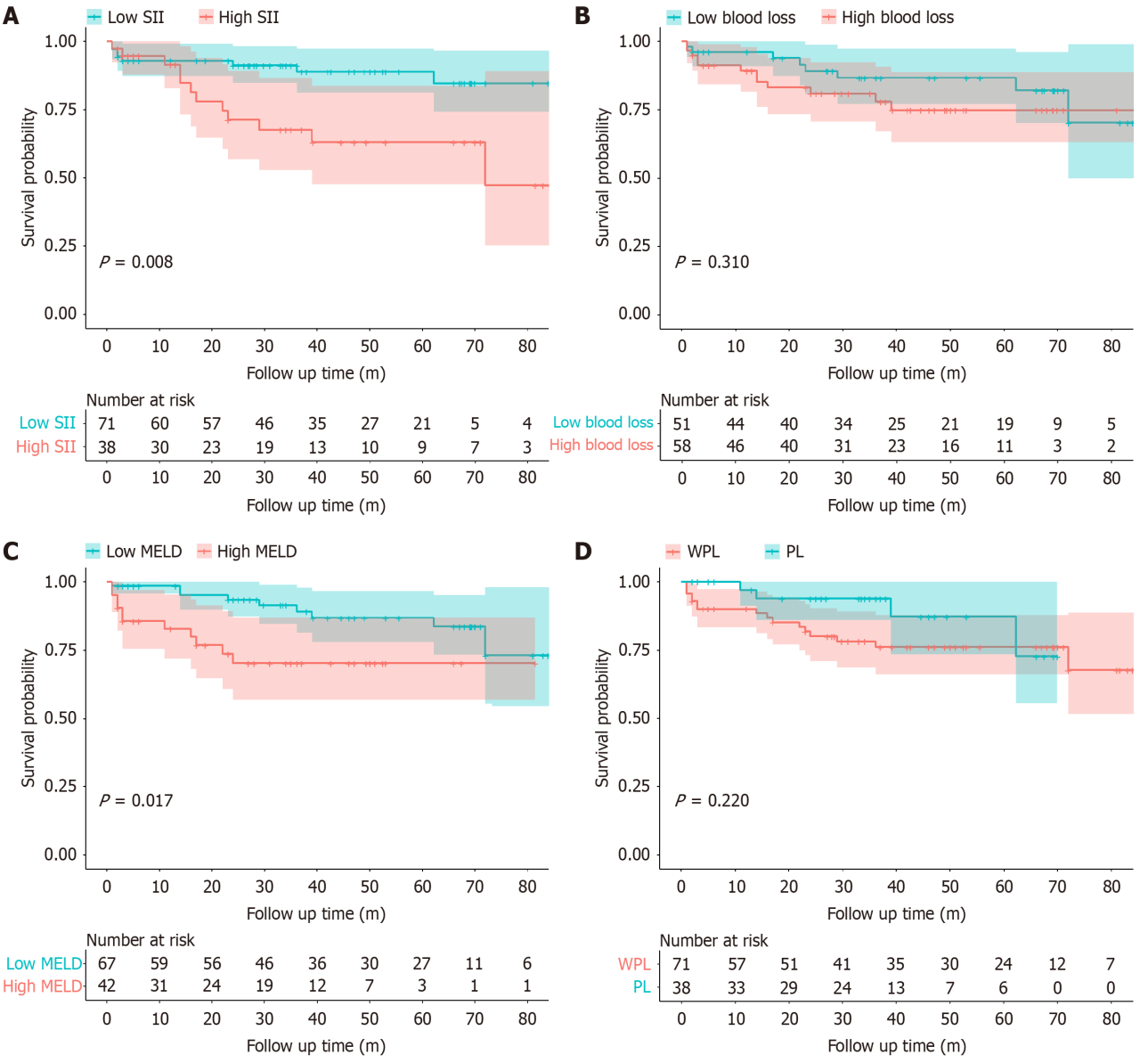

Figure 4 Survival of split liver transplantation recipients with four indexes. Kaplan-Meier survival curves were compared using the log-rank test. A: Systemic immune inflammatory; B: Blood loss; C: Meld scores; D: Partial lobectomy of segment IV. SLT: Split liver transplantation; SII: Systemic immune inflammatory; PL: Partial lobectomy; WPL: Without partial lobectomy; MELD: Model for end-stage liver disease.

outcomes than those the low MELD group (P = 0.011, Figure 4). In contrast, neither intraoperative blood loss (P = 0.180, Figure 4) nor IV PL (P = 0.097, Figure 4) were significantly associated with OS. These finding suggest that SII and MELD score serve as reliable prognostic indicators, whereas intraoperative blood loss and IV PL alone have limited predictive value. Analysis of postoperative liver function further revealed that the effect of IV PL on alanine aminotransferase (ALT) levels was transient. On postoperative day 1, patients who underwent IV PL had significantly lower ALT levels than those without resection (P < 0.05); however, this difference disappeared by day 7 (Figure 5A). No significant difference in aspartate aminotransferase (AST) levels was observed between the two groups (Figure 5B). In contrast, subgroup analysis based on MELD score showed patients with higher score exhibited markedly elevated ALT and AST levels on postoperative day 1 (both P < 0.05), with ALT levels remaining significantly higher through day 7 (P < 0.01, Figure 5C and D). No significant differences in ALT (Supplementary Figure 3A) or AST (Supplementary Figure 3B) were found between patients with high and low SII values. Similarly, postoperative liver enzyme levels did not differ significantly between patients with high *vs* low intraoperative blood loss (Supplementary Figure 3C and D). Taken together, these results indicate that a high MELD score is closely associated with delayed early postoperative liver function recovery,

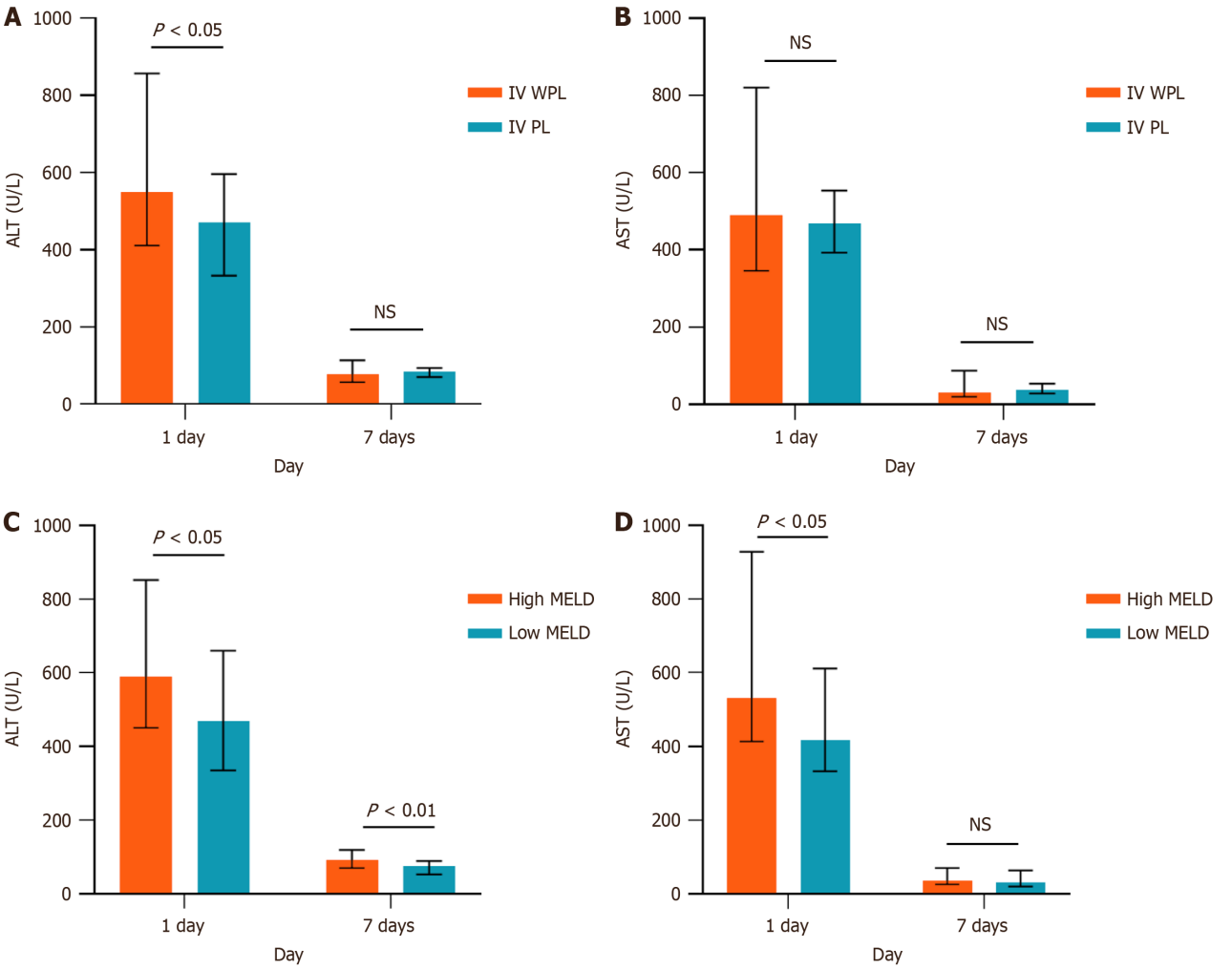

Figure 5 Comparison of alanine aminotransferase and aspartate aminotransferase levels (U/L) in recipients at 1 day and 7 days post-transplant. A: Significantly higher alanine aminotransferase levels without partial lobectomy of segment IV *vs* partial lobectomy of segment IV at 1 day ($P < 0.05$); B: No significant difference in aspartate aminotransferase levels between without partial lobectomy of segment IV and partial lobectomy of segment IV; C: Significantly higher alanine aminotransferase levels in the high model for end-stage liver disease group compared to the low model for end-stage liver disease group at 1 day ($P < 0.05$); D: Significantly higher aspartate aminotransferase levels in the high model for end-stage liver disease group at 1 day ($P < 0.05$), with no significant differences observed at 7 days. IV WPL: Without partial lobectomy of segment IV; IV PL: Partial lobectomy of segment IV; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; NS: Not significant; MELD: Model for end-stage liver disease.

whereas the effect of segment IV resection appears transient and limited.

DISCUSSION

In this study, we employed an interpretable machine learning framework to systematically identify risk factors for EPC following right tri-segment SLT. Feature importance analysis revealed that inflammatory status (LnSII), preoperative disease severity (MELD score), surgical approach (IV PL), and intraoperative blood loss were the most influential predictors. Notably, the IV PL approach was associated not only with a reduced incidence of EPC but also with a faster recovery of postoperative liver function. Furthermore, survival analysis demonstrated that both LnSII and MELD scores were significant determinants of long-term outcomes. Collectively, these findings highlight the value of integrating patient characteristics, operative factors, and interpretable machine learning techniques to improve perioperative risk stratification in SLT recipients.

A recent meta-analysis reported that both graft and patient survival following SLT are most vulnerable during the early postoperative period, primarily due to a higher incidence of complications[25]. Consistent with previous studies, our cohort also exhibited a relatively high yet comparable, rate of postoperative complications[26-28]. These findings underscore the critical importance of careful recipient selection to maximize the safety and efficacy of SLT. Developing a comprehensive prognostic framework that integrates preoperative disease severity, surgical approach, and intraoperative parameters may enhance risk prediction and optimize recipient stratification. Moreover, our predictive nomogram aligns with a growing body of literature advocating for individualized prediction models to support clinical decision-making [29]. Importantly, by combining interpretable machine learning (*via* SHAP) with traditional regression analyses, our

approach ensures both predictive robustness and interpretability addressing a long-standing challenge in clinical risk modeling[30].

Our results are consistent with previous evidence showing that the preoperative MELD score remains one of the most reliable and reproducible predictors of postoperative complications and survival after LT[31,32]. Originally developed to estimate short-term mortality in patients with end-stage liver disease, the MELD score incorporates serum bilirubin, creatinine, and international normalized ratio, reflecting both hepatic functional reserve and systemic physiological status. Higher MELD score have consistently been linked to greater hepatic dysfunction, reduced metabolic capacity, and heightened vulnerability to perioperative stress, all of which contribute to adverse surgical outcomes[33,34]. In parallel, systemic inflammatory indices have emerged as important prognostic biomarkers in both oncology and transplantation research. Parameters such as the SII and neutrophil-to-lymphocyte ratio capture the balance between pro-inflammatory activation and immune regulation[35,36]. Elevated levels typically indicate increased neutrophil-driven inflammation and impaired lymphocyte-mediated immune surveillance, fostering an immune environment that impairs recovery and worsens outcomes[37]. Extending this evidence, our study identified LnSII as one of the most influential predictors across multiple machine learning models. Importantly, LnSII retained its predictive power in multivariable analyses and demonstrated an independent association with patient survival, underscoring its potential as a clinically meaningful biomarker. These findings suggest that systemic inflammation is not merely a secondary manifestation but an active driver of postoperative trajectories after LT[38]. Another key factor identified was intraoperative blood loss, long recognized as a surrogate marker of surgical complexity and intraoperative instability[39]. Consistent with prior reports, our study confirmed its strong association with EPC. Excessive blood loss during transplantation may result from anatomical variations, technical difficulties, or fragile hepatic parenchyma, all of which prolong operative time and increase transfusion requirements[40]. Beyond hemodynamic instability, major bleeding can trigger profound metabolic and immunological disturbances, including dilutional coagulopathy, transfusion-related immunomodulation, and ischemia-reperfusion injury[41,42]. Taken together, the predictive contributions of MELD scores, systemic inflammation, and intraoperative hemodynamic challenges highlight the multifactorial nature of post-transplant outcomes. These findings emphasize the need for an integrated prognostic framework to guide risk stratification and optimize perioperative management in this complex surgical population.

Whereas earlier studies have suggested that additional parenchymal transection may increase operative trauma and postoperative morbidity, our data indicate that, when graft volume is adequately preserved, IV PL exerts a protective effect by reducing complications and promoting recovery of liver function[43]. A plausible explanation is the ischemia that commonly develops along the split surface of the graft during transplantation, predisposing patients to perioperative complications[44]. In particular, ischemic necrosis within segment IV may serve as a trigger for EPC. Necrotic tissue not only elevates the risk of intra-abdominal infection, bile leakage, and hemorrhage, but under the influence of postoperative Immunosuppression, renders infections more difficult to control and potentially fatal[45]. To mitigate these risks, we resected the ischemic portion of segment IV and observed a significant reduction in EPC, accompanied by improved functional recovery. Nevertheless, such resection inevitably reduces graft volume, underscoring the importance of careful assessment of the GRWR to prevent postoperative SFSS[46]. In our cohort, after meticulous intraoperative evaluation, no cases of SFSS were occurred following segment IV resection.

Our findings hold several practical implications for transplant surgeons and perioperative teams. First, the observation that IV PL can reduce complications and facilitate recovery supports its consideration as a preferred surgical strategy in right tri-segment SLT, particularly in cases where graft regenerative capacity is crucial. Second, identification of high LnSII or elevated MELD scores as risk factors underscores the need for preoperative optimization and enhanced postoperative monitoring in these patients. Third, intraoperative blood loss should not be viewed merely as a byproduct of surgical complexity but rather as a modifiable risk factor. Techniques such as maintaining low central venous pressure anesthesia, employing refined hemostatic procedures, and using real-time hemodynamic monitoring may directly contribute to reducing complication rates. Finally, the predictive nomogram developed in this study offers a practical bedside tool for risk stratification, enabling clinicians to identify high-risk recipients, allocate resources efficiently, and conduct informed discussions with patients and families regarding prognosis. More broadly, the evidence that SLT outcomes can be improved through technical refinements and individualized risk assessment may encourage policy makers to promote wider adoption of SLT, thereby alleviating the organ shortage crisis while maintaining procedural safety.

This study adopted a multi-step analytical strategy to strengthen the robustness of our conclusions. Initially, potential confounders were screened using several machine learning models (RF, SVM, XGBoost, and LR), and an interpretable framework was established through SHAP analysis. Subsequent univariate and multivariate LR analyses identified four variables significantly associated with EPC. To further investigate potential nonlinear relationships, restricted cubic spline models were applied, and the most relevant predictors were incorporated into a diagnostic nomogram. Finally, survival analyses were performed based on these four key predictors to assess their influence on early postoperative liver function recovery. Despite these strengths, several limitations should be acknowledged. First, this was a retrospective, single center study with a relatively small sample size, which may limit the generalizability of our findings. Second, although multiple machine learning algorithms and SHAP-based interpretation were applied, external validation was not performed, and the stability of the nomogram requires confirmation in independent cohorts. Third, the dataset lacked detailed immunological and genetic parameters that might have improved the precision of risk prediction. Fourth, the limited sample size may constrain the statistical power of our analyses. Future studies with larger cohorts are warranted to further validate the performance of the model. Additionally, we plan to incorporate multiple, multi-center statistical approaches to reduce the risk of overfitting associated with smaller datasets. Lastly, given the rapid increase in SLT procedures in China in recent years, our analysis was constrained by both sample size and follow-up duration. Because most deaths and complications occurred during the early postoperative phase, this study primarily focused on short-term

outcomes.

CONCLUSION

In conclusion, our study demonstrates that integrating inflammatory markers, preoperative disease severity, surgical characteristics, and intraoperative variables creates a robust framework for predicting EPCs in right tri-segment SLT. The combined use of interpretable machine learning and conventional regression methods not only strengthens methodological rigor but also generates clinically meaningful insights. Beyond refining current risk assessment, our findings provide practical strategies to optimize patient outcomes and lay the groundwork for future research in transplant surgery.

ACKNOWLEDGEMENTS

The authors thank the staff and colleagues from the First Central Hospital of Tianjin Medical University for their valuable support and contributions to the development of this manuscript.

FOOTNOTES

Author contributions: Wang D and Zhang JY made equal contributions as co-first authors; Wang D, Zhang JY, and Xie Y contributed to conceptualization and investigation; Jiang WT did project administration; Wang D and Zhang KN contributed to methodology and supervision; Jiang WT and Xie Y acquired the funding and contributed equally as co-corresponding authors; Wang D and Xie Y performed validation and visualization; all authors contributed to manuscript writing and approved the final version to publish.

Supported by Tianjin Key Medical Discipline Construction Project, No. TJYXZDXK-3-006A; Tianjin Municipal Health Commission General Fund Project, No. TJWJ2024MS017; Key Project of Tianjin Science and Technology Bureau Applied Basic Research, No. 23JCZDJC01200; The Independent Research Fund of the Institute of Transplant Medicine at Nankai University, No. NKTM2023004; The General Project of the China Medicine Education Association, No. ZJWYH-2023-YIZHI-028; and General Project of Scientific Research Plan of Tianjin Municipal Education Commission, No. 2024ZX013.

Institutional review board statement: The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the First Central Hospital of Tianjin Medical University, No. 2019N168KY.

Informed consent statement: Due to the retrospective study design, this study waived the need for written informed consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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S-Editor: Wu S
L-Editor: A
P-Editor: Xu J

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