



Nomogram to Predict Postoperative Acute Kidney Injury after Liver Transplantation

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Abstract

Background: Liver transplantation serves as an essential therapeutic intervention for patients with end-stage liver disease. However, the occurrence of postoperative acute kidney injury (AKI) can markedly affect the clinical prognosis of these patients. Existing models to predict AKI after liver transplantation have limitations in specificity and accuracy, necessitating an updated model.

Methods: We conducted a study adhering to the TRIPOD guidelines, including patients who underwent liver transplantation at West China Hospital from 2016 to 2020. Clinical data encompassing demographics, comorbidities, and intraoperative variables were collected. The LASSO regression was used to identify optimal predictors of AKI, leading to the development of a predictive nomogram. The model's discrimination and calibration were assessed using AUC and calibration curves, respectively.

Results: The nomogram, developed from 296 patients in the development cohort and validated on 142 patients, identified surgery duration, intraoperative blood loss, and preoperative serum creatinine as predictors of AKI. It demonstrated good discrimination with AUCs of 0.720 and 0.725 for the development and validation cohorts, respectively. The calibration curve confirmed the model's accuracy in predicting AKI probabilities.

Conclusion: The developed nomogram offers a novel model for predicting AKI risk after liver transplantation, with robust discrimination and calibration. Further multicenter validation and potential integration of genetic and molecular biomarkers for improved accuracy are needed.

Keywords

Liver Transplantation, Acute Kidney Injury, Predictive Model

Introduction

Liver transplantation is a critical treatment for end-stage liver disease, but postoperative complications seriously affect the prognosis and quality of life of patients [1-3]. Acute Kidney Injury (AKI) is a common and serious complication after liver transplantation, which is related to various factors such as surgery duration, ischemia-reperfusion injury, and drug

toxicity [4,5]. Early recognition of AKI risk and timely intervention are very important to improving patient outcomes.

Currently, there are several models used to predict AKI after liver transplantation, but most models have limitations such as lack of specificity, insufficient accuracy, or lack of extensive validation [6-10].

Additionally, with the advancement of medical technology and changes in patient characteristics, existing models may need updating to adapt to current clinical practice.

This study aims to develop and validate a new nomogram to improve the accuracy of predicting AKI risk after liver transplantation. By comprehensively analyzing patients' clinical data, we aim to construct a nomogram to provide a more accurate risk assessment tool.

Methods

This study followed the TRIPOD (Transparent

Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) statement for reporting multivariable prediction model development and validation [11].

Patients undergoing liver transplantation at West China Hospital between January 2016 and December 2020 were identified from the Chinese Liver Transplant Registry and the hospital information system. Patients aged 18 years or older who underwent donor-after-brain-death liver transplantation were included. Exclusion criteria were as follows: history of liver transplantation, combined liver and other organ transplantation, and unavailable relevant data.

Table-1: Baseline Characteristics in Development Cohort and Validation Cohort

Baseline characteristics	Development cohort (N=296)	Validation cohort (N=142)	P value
Gender (Female)	20(20.3%)	33 (23.2%)	0.558
Age, y	50.0 (44.0, 54.0)	50.0 (45.0, 56.0)	0.226
BMI	23.2 (21.3, 25.3)	23.1 (20.7, 25.3)	0.789
Hepatocellular carcinoma			0.234
Yes	141 (47.6%)	77 (54.2%)	
No	155 (52.4%)	65 (45.8%)	
MELD score	16.0 (9.0, 25.0)	13.0 (9.0, 23.0)	0.072
Child-Pugh grade			0.36
A	11 (3.7%)	4 (2.8%)	
B	133 (44.9%)	74 (52.1%)	
C	152 (51.4%)	64 (45.1%)	
Comorbidities			
Hypertension	27 (9.1%)	10 (7.0%)	0.583
Diabetes	42 (14.2%)	19 (13.4%)	0.935
CKD	23 (7.8%)	6 (4.2%)	0.234
COPD	10 (3.4%)	4 (2.8%)	0.982
GRWR			0.062
GRWR≤0.8%	17 (5.7%)	8 (5.6%)	
0.8%<GRWR<2.5%	242 (81.8%)	104 (73.2%)	
GRWR≥2.5%	37 (12.5%)	30 (21.1%)	
Cold Ischemia Time			0.652
≤6h	132 (44.6%)	61 (43.0%)	
<6h≤12h	146 (49.3%)	69 (48.6%)	
>12h	18 (6.1%)	12 (8.5%)	
Surgery duration(min)	453.0 (390.0, 530.0)	455.0 (395.0, 519.0)	0.963
Blood loss(ml)	1200.0 (800.0, 2000.0)	1150.0 (800.0, 2000.0)	0.483
preoperative creatinine(umol/L)	53.5 (44.0, 67.0)	49.5 (43.0, 63.0)	0.116
AKI	121 (40.9%)	53 (37.3%)	0.544

BMI: Body Mass Index, MELD: Model for End-Stage Liver Disease, CKD: Chronic Kidney Disease, COPD: Chronic Obstructive Pulmonary Disease, GRWR: Graft Recipient Weight Ratio, AKI: Acute Kidney Injury

Demographic and clinical data were collected, including age, gender, body mass index (BMI), Model for End-stage Liver Disease (MELD) score, Child-Pugh grade, diagnosis, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney disease), Graft-to-Recipient Weight Ratio (GRWR), cold ischemic time, surgery duration, intraoperative blood loss, and preoperative serum creatinine.

The outcome of our study was postoperative AKI, defined according to the KDIGO criteria [12]. The highest serum creatinine level was measured within the first 7 days following surgery and compared to the baseline level. The most recent preoperative results were used as the baseline.

The results are presented as mean $\pm$ SD or median with interquartile range for continuous variables, and number (percentage) for categorical variables. The normality of the distribution was tested using the Kolmogorov-Smirnov test. Continuous variables were tested by Student's t-test or Mann-Whitney U test. Categorical variables were tested by Pearson's chi-squared test or Fisher's exact test. The least absolute shrinkage and selection operator (LASSO) regression was used to select predictive variables. A nomogram was developed based on the results of LASSO regression analysis. Subsequently, we assessed the model's predictive efficacy by evaluating its discrimination and calibration performance across both the development and validation cohorts. The model's discrimination was measured by the area under the receiver operating characteristic (ROC) curve (AUC). Meanwhile, the model's calibration accuracy was determined through the analysis of the calibration curve. $P < 0.05$ was considered statistically significant. We used R software version 4.2.2 for analyses.

Results

A total of 438 patients were included in the analyses, with 296 patients in the development cohort and 142 patients in the validation cohort. There was no significant difference in baseline characteristics between the two cohorts, as shown in **Table-1**.

LASSO Regression for Predictor Selection:

Fifteen variables were included in the LASSO regression analysis based on the 296 patients in the development cohort. The model variables were reduced to three when $\log(\lambda)$ reached a standard error of the minimum distance, as determined by the LASSO internal cross-validation. Ultimately, LASSO regression selected three optimal variables: surgery duration, intraoperative blood loss, and preoperative serum creatinine (**Fig-1**).

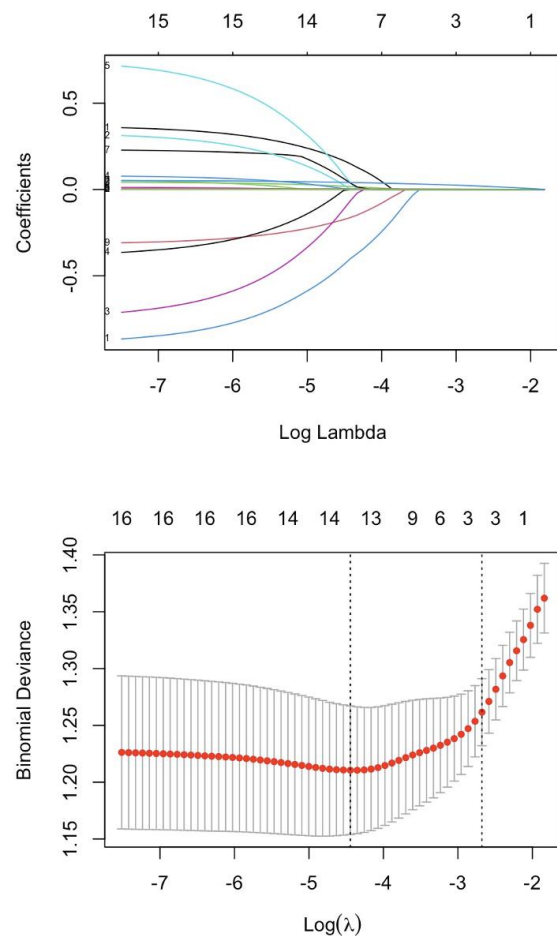


Fig-1: LASSO Regression for Predictors Selection

Development and Validation of a Predictive Nomogram:

We constructed a predictive nomogram illustrated in **Fig-2**, allocating scores to the three significant predictors in accordance with their respective regression coefficients. The estimated probability of AKI after liver transplantation can be calculated by summing up the points attributed to each factor. The nomogram was validated in both the development and validation cohorts. The discrimination was measured

with AUC, which was 0.720 in the development cohort and 0.725 in the validation cohort (**Fig-3**). The calibration curve for the nomogram confirmed a concordance between the estimated probabilities of AKI and the actual observed rates, as depicted by the nomogram (**Fig-4**). These results confirmed the accuracy of the nomogram model in predicting the risk of AKI after liver transplantation.

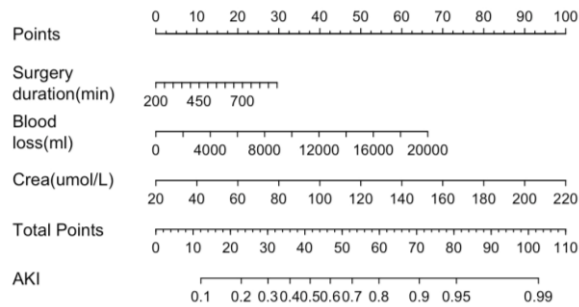


Fig-2: Nomogram of AKI after Liver Transplantation

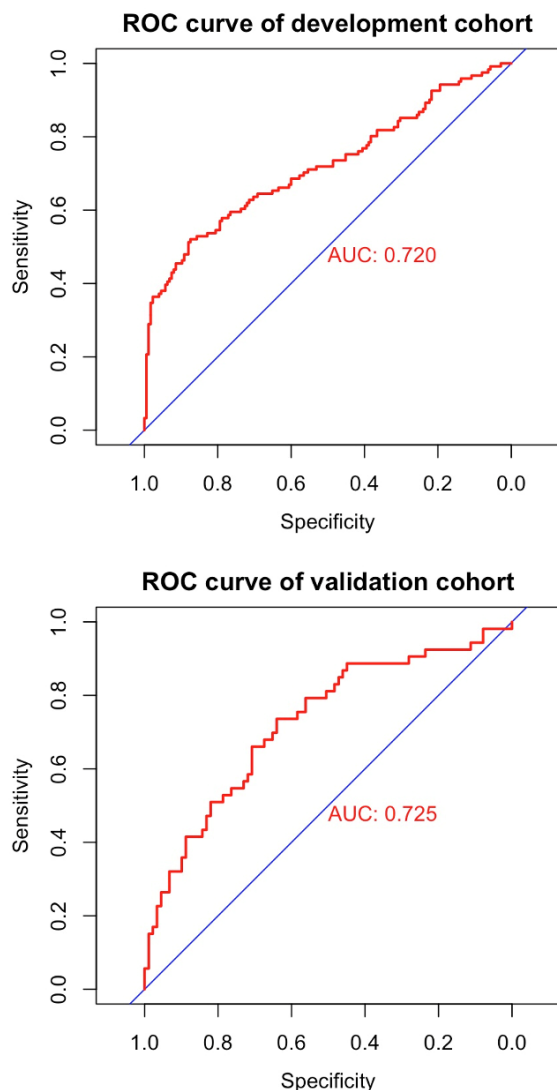


Fig-3: ROC Curve

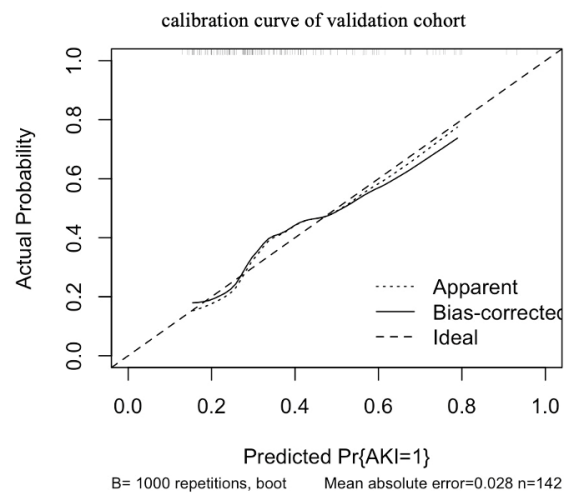
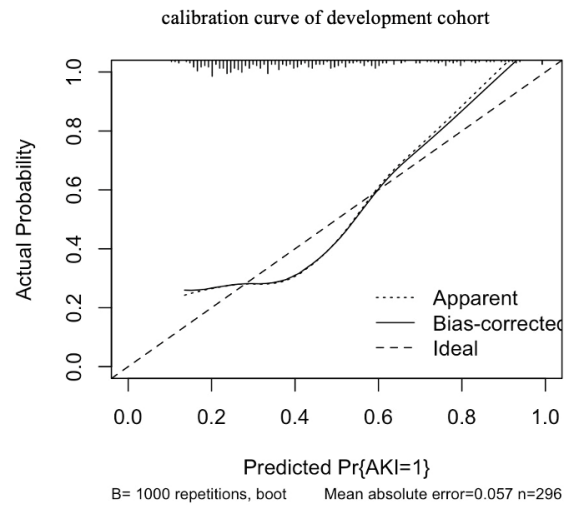


Fig-4: Calibration Curve

Discussion

The present study successfully developed and validated a novel nomogram for predicting the risk of postoperative AKI in recipients of liver transplantation. Our model, based on a comprehensive analysis of clinical data, identified surgery duration, intraoperative blood loss, and preoperative serum creatinine as predictors of AKI. The predictive accuracy of the nomogram was substantiated by AUC, indicating a robust discrimination capability.

Our nomogram demonstrates a competitive edge over existing scoring systems, which often suffer from a lack of specificity and accuracy. The updated nomogram is particularly beneficial in the context of liver transplantation, where early recognition of AKI risk is pivotal for timely intervention and improved patient outcomes.

One of the strengths of our study is the rigorous methodology employed, adhering to the TRIPOD guidelines for transparent reporting of prediction model development and validation. The use of LASSO regression for variable selection ensured a parsimonious model that balances complexity and predictive power. Furthermore, the calibration curve confirmed the model's accuracy, aligning predicted probabilities with observed outcomes. Our study's novelty is underscored by the creation of a new nomogram, incorporating clear scoring for pivotal clinical indicators, which simplifies the prediction process for clinicians. This visual tool can be readily applied in clinical settings, aiding healthcare providers in making informed decisions regarding the risk of AKI after liver transplantation. Additionally, the nomogram's validation on a separate cohort underscores its generalizability and reliability.

Despite the strengths, our study has certain limitations that warrant acknowledgment. Firstly, the study is based on data from a single center, which may limit the external validity of the nomogram. Secondly, while the AUC values indicate good discrimination, there is room for further improvement in predictive accuracy. Lastly, the model's performance in diverse populations with different comorbidities and genetic backgrounds needs to be evaluated in future studies.

Future research should focus on multicenter validation of the nomogram to enhance its applicability across different patient populations. Additionally, incorporating genetic and molecular biomarkers, such as neutrophil gelatinase-associated lipocalin, may further refine the predictive accuracy of the model [13]. Longitudinal studies to monitor the nomogram's predictive performance over time are also recommended.

In conclusion, our study presents a novel nomogram for predicting the risk of postoperative AKI after liver transplantation. The nomogram's development represents a significant advancement in the personalized risk assessment of postoperative complications in liver transplantation.

Disclosure

Relevant data was collected from the Chinese Liver Transplant Registry and the hospital information system.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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