

# Development and Validation of a Nomogram for Determining Patients Requiring Prolonged Postanesthesia Care Unit Length of Stay After Laparoscopic Cholecystectomy

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## Research article

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# Abstract

**Background:** Laparoscopic Cholecystectomy (LC) is a common surgical procedure for managing gallbladder disease. Prolonged length of stay (LOS) in the postanesthesia care unit (PACU) may lead to overcrowding and a decline in medical resource utilization. In this work, we aimed to develop and validate a predictive nomogram for identifying patients who require prolonged PACU LOS.

**Methods:** Data from 913 patients undergoing LC at a single institution in China between 2018 and 2019 were collected, and grouped into a training set (cases during 2018) and a test set (cases during 2019). Using the least absolute shrinkage and selection operator regression model, the optimal feature was selected, and multivariable logistic regression analysis was used to build the prolonged PACU LOS risk model. The *C*-index, calibration plot, and decision curve analysis were used in assessing the model calibration, discrimination, and clinical application value, respectively. For external validation, the test set data was evaluated.

**Results:** The predictive nomogram had 8 predictor variables for prolonged PACU LOS, including age, ASA grade, active smoker, gastrointestinal disease, liver disease, and cardiovascular disease. This model displayed efficient calibration and moderate discrimination with a *C*-index of 0.662 (95% confidence interval, 0.603 to 0.721) for the training set, and 0.609 (95% confidence interval, 0.549 to 0.669) for the test set. Decision curve analysis demonstrated that the prolonged PACU LOS nomogram was reliable for clinical application when an intervention was decided at the possible threshold of 7%.

**Conclusions:** We developed and validated a predictive nomogram with efficient calibration and moderate discrimination, and can be applied to identify patients most likely to be subjected to prolonged PACU LOS. This novel tool may shun overcrowding in PACU and optimize medical resource utilization.

## Introduction

Laparoscopic Cholecystectomy (LC) is among the most commonly performed procedures in general surgery [1] [2]. Compared with open cholecystectomy (OC), LC is highly preferred as it is associated with less blood loss, less pain, and confer better cosmetic outcomes [3] [4] [5] [6]. Of note, reports from many studies have indicated a reduction of mortality and wound infection rates as well as improved quality of life after LC [7] [8] [9] [10]. The postanesthesia care unit (PACU) is an integral component of the perioperative workflow. PACU length of stay (LOS) impacts on operating room (OR) efficiency and present health burden to patients [11] [12] [13]. Extended PACU LOS can result in PACU backlog, decelerating the surgical schedule, this implies a reduced quality of care for other surgical patients [13]. Further, overcrowding in the PACU and prolonged PACU LOS may lead to poor clinical outcomes [11] [12] [14] [15].

Predictors for prolonged PACU LOS such as specific anesthesia type, surgical specialty, scheduled surgery duration, postoperative opioid administration, morbid obesity, hypertension, obstructive sleep apnoea have been described in different populations [16] [17] [18] [19] [20] [21] [22]. The studies in most cases assessed outpatients [16] [21], pediatric populations [17] [18] [19], or all adult surgical patients

undergoing general anesthesia or regional anesthesia [20] [22]. However, no existing literature has reported a nomogram for prolonged PACU LOS of LC patients. Therefore, developing a predictive tool can be valuable in determining LC patients who require prolonged PACU LOS.

In this study, we collected data from a single tertiary-care medical institution in China and constructed a predictive nomogram. We purposed to provide a convenient predictive tool to anesthesiologists, nurses, or other care providers in PACU, to aid in the identification of patients requiring prolonged PACU LOS. This improves OR efficiency thereby minimizing healthcare burden.

## Methods

### Study sample

This study protocol was approved by Sun Yat-sen Memorial Hospital of Sun Yat-sen University Ethics Committee (approval number: SYSEC-KY-KS-2020-104). The resulting dataset remained unidentified and did not contain sensitive health information of patients as defined by the Human Research Protections Program in our institution, therefore, informed consent requirement by our Institutional Review Board was waived. For this retrospective analysis, two separate anesthesiologists from the Sun Yat-sen Memorial Hospital of Sun Yat-sen University manually obtained data from the electronic medical record system. All data from patients undergoing LC between January 1, 2018 and December 31, 2019 were extracted. This manuscript adheres to the applicable Equator guidelines for quality improvement studies.

Patients aged above 18 years, scheduled for LC, were included in the study dataset. We only chose patients who had received general anesthesia (i.e. balance anesthesia) as our institution did not administer neuraxial anesthesia (spinal or epidural) and combine with regional analgesia (Transversus Abdominis Plane blocks) to LC patients. Anesthesiologist selected endotracheal intubation (ETI) or laryngeal mask airway (LMA) as an airway management tool, based on personal preference. During the study period, the staffing and discharge criteria of the PACU remained unchanged in our hospital. All surgeries were performed by highly experienced surgeons using a standard procedure. In this study, we used short-acting opioids (e.g. remifentanyl) and nonsteroidal anti-inflammatory drugs (NSAIDs, e.g. flurbiprofen axetil) to treat intraoperative and postoperative pain. We defined PACU LOS as the duration between admission to discharge from PACU, whereas prolonged PACU LOS was defined as time greater than or equal to the 75th percentile in each cohort, as described by previous studies [21]. Thus, we treated prolonged PACU LOS as a binary outcome rather than as continuous variables. Data of each patient derived from the electronic medical record system included: minutes in the PACU, sex, age (dichotomized to  $\geq 65$  vs.  $< 65$  years of age to account for geriatric patients), body mass index (BMI) (dichotomized to  $\geq 28$  vs.  $< 28$  kg/m<sup>2</sup> to account for obesity in Chinese [23]), American Society of Anesthesiologists (ASA) grade, airway management device (ETI vs. LMA), surgery duration (dichotomized to  $< 60$  vs.  $\geq 60$  min). Besides, information on comorbidities including, diabetes mellitus, hypertension, active smoker, alcohol abuse, gastrointestinal disease, liver disease, cardiovascular disease, asthma, and allergic history was obtained. All the above data were considered as categorical variables. Of note, patients who were directly

admitted to an intensive care unit, completely bypassed the PACU, Converted from Laparoscopic to Open Cholecystectomy during surgery, or missed values of any covariates were excluded in the analysis.

## Statistical analysis

R software (R version 4.0.0) for statistical computing was used to perform all statistical analyses. After examining the data, patients with missing information were excluded before the model was constructed. This was followed by categorizing the data set into a training set (cases during 2018) and a test set (cases during 2019).

Using the least absolute shrinkage and selection operator (LASSO) regression methods, the optimal predictive features were selected [24] [25]. Then, features with nonzero coefficients in the LASSO regression were selected to construct a predicting model, as we incorporated the multivariable logistic regression analysis. These features represented the odds ratio (OR) having a 95% confidence interval (CI) and as P-value. All statistical significance levels were two-sided. Although there was no statistical significance in the training set, sex and BMI were still included in this model, as it has been the case with previous studies [12] [19] [21]. The nomogram was built to provide a convenient tool to predict probability of prolonged PACU LOS for each LC patients.

Calibration curves, in combination with the Hosmer-Lemeshow test [26], were plotted to evaluate the calibration of this predictive nomogram. Harrell's *C*-index was calculated to assess the discrimination performance of our nomogram [27]. Besides, the performance of the nomogram was determined using the test data set. We employed the Decision curve analysis (DCA) to assess the clinical application value of the prolonged PACU LOS risk nomogram [28]. In the training data set, quantification of the net benefits was undertaken at different threshold probabilities.

## Results

### Clinical characteristics

Among the 1,375 patients who underwent LC between January 1, 2018 and December 31, 2019 from our institution. However, due to the missing data of any of the covariates, 462 patients were excluded. A final total of 913 were included for the analyses after meeting the inclusion criteria, where, 456 and 457 patients were grouped in the training set and test set, respectively. All the characteristics of patients in each data set are highlighted in Table 1.

In the training set, the mean (standard deviation) and median (25%-75% interquartile range) PACU LOS were 57.13 minutes (20.87 minutes) and 55 minutes (44-66 minutes), respectively. In the test set, the mean (standard deviation) and median (25%-75% interquartile range) PACU LOS were 59.04 minutes (22.57 minutes) and 55 minutes (45-72 minutes), respectively. Therefore, considering our previous description, we defined prolonged PACU LOS as greater than 66 minutes in the training set and 72 minutes in the test set.

## Feature selection

Out of the clinical features, 15 features were reduced to six potential predictors based on 913 patients in the cohort (Fig. 1A and B). These predictors were featured with non-zero coefficients in the LASSO regression model.

The features included age, ASA grade, active smoker, gastrointestinal disease, liver disease, and cardiovascular disease (Table 2). Based on the previous studies, we also included sex and BMI in the model [12] [19] [21].

## Developing an individualized prediction model

Following the logistic regression analysis, the results obtained are as shown in Table 2, which included sex, age, BMI, ASA grade, active smoker, gastrointestinal disease, liver disease, and cardiovascular disease. We developed a model in which the above independent predictors were incorporated and was presented as the nomogram (Fig. 2).

## Apparent performance and validation of the prolonged PACU LOS nomogram

The calibration curve of the prolonged PACU LOS nomogram revealed reliable consistency between prediction and observation in the training set (Fig. 3). The *C*-index for the predictive nomogram was 0.662 (95% CI, 0.603 to 0.721) for the training set whereas, in the test set, the *C*-index of the nomogram for prediction was 0.609 (95% CI, 0.549 to 0.669). In the prolonged PACU LOS nomogram, apparent performance addressed a certain prediction potential.

## Clinical use

The DCA for the prolonged PACU LOS nomogram showed that if the threshold probability of a patient and a doctor is >7 and <52%, respectively, using this nomogram to predict prolonged PACU LOS risk is highly beneficial compared to either the intervention-all-patients scheme or the intervention-none-patients scheme (Fig. 4). Within this range, the net benefit was comparable with several overlaps, based on the prolonged PACU LOS nomogram.

## Discussion

Here we developed and validated a predictive nomogram for prolonged PACU LOS for LC patients. The predictors including sex, age, BMI, ASA grade, active smoker, gastrointestinal disease, liver disease, and cardiovascular disease were incorporated in our model. Usually, extended time spent in the PACU is both onerous to the patients and costly to the institution [11] [12] [29]. The nomogram suggested that younger (Age <65) male patients, with obesity (BMI >28 kg/m<sup>2</sup>), ASA grade I, does not smoke, has no gastrointestinal disease, cardiovascular disease, or liver disease are 10% less likely to undergo prolonged PACU LOS. In this study, we provide a novel prediction nomogram vital in helping care providers (anesthesiologists, nurses) in PACU to identify patients with higher chances of being subjected to

prolonged PACU LOS. Within institutions such as community hospitals and clinics with fewer ORs, this predictive tool is highly suitable and beneficial. It is worth noting that all predictors included in this model can be determined preoperatively.

Previously, several studies have revealed risk factors for prolonged PACU LOS in various surgical populations [16] [17] [18] [19] [20] [21] [22]. These studies suggest the need to focus on a special subset of patients as a way of reducing research bias [21], rather than focusing on all patients scheduled for surgery with general anesthesia [20]. To the best of our knowledge, so far, no study has investigated the application of a nomogram to predict prolonged PACU LOS of LC patients.

Consistent with previous studies, we revealed that age is associated with prolonged PACU LOS [19] [20]. The geriatric population may be associated with many postoperative complications and poor drug metabolism, in this case, longer recovery time is required after the operation. Likewise, patients with higher ASA grades are more likely to undergo prolonged PACU LOS. Also, we found that active smoking may result in longer PACU duration, which may be associated with a higher risk of respiratory complications. Elsewhere, a study by Coccolini *et al.* [8] demonstrated that LC had decreased odds for respiratory complications (such as airway obstruction and pneumonia) when compared with OC. Interestingly, we observed that patients with gastrointestinal diseases, such as chronic gastritis, gastric and duodenal ulcers, showed increased odds for prolonged PACU LOS. This is because such patients, in most cases, have electrolyte disorders, anemia, and high risk of postoperative nausea and vomiting (PONV), they should be carefully monitored, thus require longer stay in PACU [30]. Due to the postoperative cardiovascular complications, it can strongly be suggested that cardiovascular disease is associated with prolonged PACU LOS.

On the contrary, patients who preoperatively had liver disease may be at a lower risk of extended time in PACU. This is closely linked to the use of anesthetic and anesthesia management of LC. For example, when handling the surgery patients with liver disease, drugs that are not metabolized by the liver (e.g. cisatracurium, remifentanyl, and sevoflurane) are administered while the dosage of an anesthetic is reduced to protect liver function. Also, inconsistent with previous findings [19] [21], we found that higher BMI may result in a lower probability of prolonged PACU LOS. Based on our institution practice, we routinely selected short-acting anesthetics to induce general anesthesia and timely stopped drug infusion among obesity patients. A previous study revealed that the airway management device (i.e. LMA) was associated with prolonged PACU LOS [31], however, no statistical difference was found in this study. Moreover, Abdi *et al.* [32] reported that LMA, with less pharyngolaryngeal discomfort and pain, showed low risks for prolonged PACU LOS compared to ETI.

This study had several limitations. First, the retrospective design of this study implies that the selection bias and information bias is unavoidable. Second, the accuracy of the analysis relies on data records, storage, and retrieval from the medical system. Some factors include nonclinical and social issues, and difficult to extract from our electronic records. Therefore, other factors that may be associated with prolonged PACU LOS exist, and their exclusion may affect the discriminating ability in our model. Third,

we included patients with specific surgery and anesthesia type, thus, the generalizability was uncertain for other patients with different types of surgical procedures and anesthesia. Finally, we report on a single-institution experience, therefore, this predictive nomogram for patients undergoing LC need to be further evaluated in the other institution and countries.

## **Conclusion**

We developed a predictive nomogram with a relatively moderate accuracy to aid in identifying which LC patients are more likely to be subjected to prolonged PACU LOS. These predictors may contribute to prior planning in PACU for bed space and allow for optimization of the OR efficiency.

## **Abbreviations**

LC: laparoscopic cholecystectomy; PACU: postanesthesia care unit; LOS: length of stay; OC: open cholecystectomy; OR: operating room; ETI: endotracheal intubation; LMA: laryngeal mask airway; BMI: body mass index; ASA: American Society of Anesthesiologists; LASSO: least absolute shrinkage and selection operator; OR: odds ratio; CI: confidence interval; DCA: decision curve analysis; PONV: postoperative nausea and vomiting

## **Declarations**

### **Acknowledgments**

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### **Authors' contributions**

Study conception and design [BBC, LL, WBG]; Methodology: [BBC, WBG, XFS]; Formal analysis and investigation: [BBC, XFS]; Writing—original draft preparation: [LL, XFS]; Writing—review and editing: [BBC, LL, JFZ]; Funding acquisition: [JFZ]; Resources: [BBC, LL]; Supervision: [JFZ, WBG].

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### **Availability of data and materials**

The data that support the findings of this study are available from the corresponding author upon request.

### **Ethics approval**

This study was performed in line with the principles of the Declaration of Helsinki. The study protocol was approved by Sun Yat-sen Memorial Hospital of Sun Yat-sen University Ethics Committee (approval number: SYSEC-KY-KS-2020-104).

### **Informed Consent**

The resulting dataset remained unidentified and did not contain sensitive health information of patients as defined by the Human Research Protections Program in our institution, therefore, informed consent requirement by our Institutional Review Board was waved.

### **Consent for publication**

Not applicable.

### **Competing interests**

Not applicable.

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## Tables

**Table 1.** Clinical Characteristics in the Training Versus Test Data Sets.

	<b>Training Data Set N (%)</b>	<b>Test Data Set N (%)</b>
Total	456	457
Median PACU LOS (25%, 75% IQR)	55 (44,66)	55(34,72)
Prolonged PACU LOS	113(24.78)	114(24.95)
Age ≥ 65-years old	122(26.75)	107(23.41)
Male sex	222(48.68)	213(46.61%)
BMI ≥ 28 kg/m <sup>2</sup>	49(10.75)	39(8.53)
<b>ASA Physical Status</b>		
Ⅰ	29(6.36)	29(6.35)
Ⅱ	326(71.49)	337(73.74%)
Ⅲ	97(21.27)	90(19.69%)
Ⅳ	4(0.88)	1(0.22)
<b>Airway management device</b>		
ETI	382(83.77)	296(64.77)
LMA	74(16.23)	161(35.23)
<b>Surgery duration (min)</b>		
< 60	141(30.9)	143(31.3)
≥ 60	315(69.1)	314(68.7)
<b>Comorbidities</b>		
Diabetes melitus	41(8.99)	44(9.63)
Hypertension	93(20.39)	98(21.44)
Cardiovascular disease	24(5.26)	17(3.72)
Liver disease	39(8.55)	30(6.56)
Gastrointestinal disease	17(3.73)	4(0.66)
Active smoker	58(12.72)	35(7.66)
Asthma	5(1.10)	3(0.66)
Alcohol abuse	19(4.17)	3(0.66)
Allergic history	48(10.53)	41(8.97)

Prolonged PACU LOS was defined as time greater than or equal to the 75th percentile in each cohort.

*PACU* postanesthesia care unit, *LOS* length of stay, *IQR* interquartile range, *BMI* body mass index, *ASA* American Society of Anesthesiologists, *ETI* endotracheal intubation, *LMA* laryngeal mask airway.

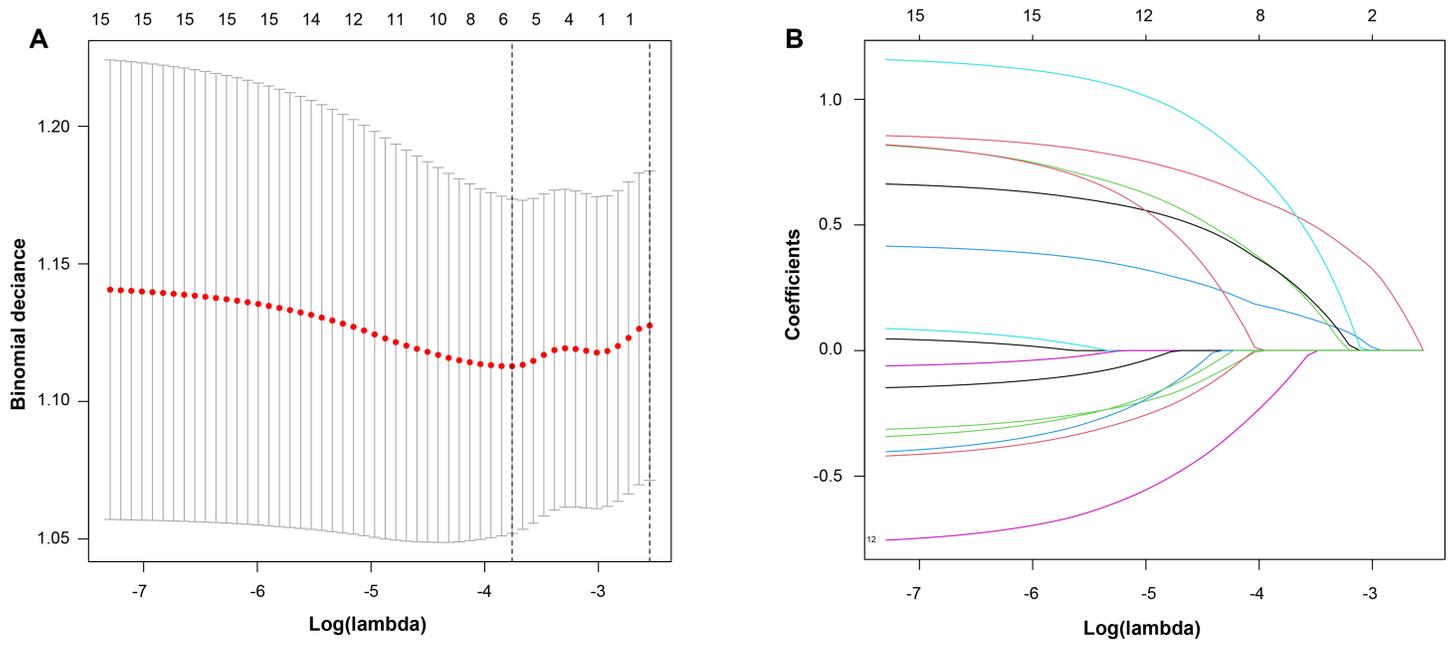
**Table 2** Prediction Factors for Prolonged PACU LOS Built on the Training Set.

	$\beta$	OR (95% CI)	<i>P</i>
Intercept	-2.241	0.106(0.029-0.368)	< .001
Sex	0.058	1.059(0.650-1.736)	.818
Age	0.757	2.131(1.269-3.571)	.004
BMI	-0.395	0.673(0.299-1.395)	.310
ASA grade	0.318	1.374(0.863-2.195)	.181
Active smoker	0.739	2.093(1.067-4.057)	.029
Gastrointestinal disease	1.142	3.134(1.122-8.629)	.026
Liver disease	-0.719	0.487(0.173-1.172)	.135
Cardiovascular disease	0.637	1.891(0.756-4.669)	.166

$\beta$  is the regression coefficient.

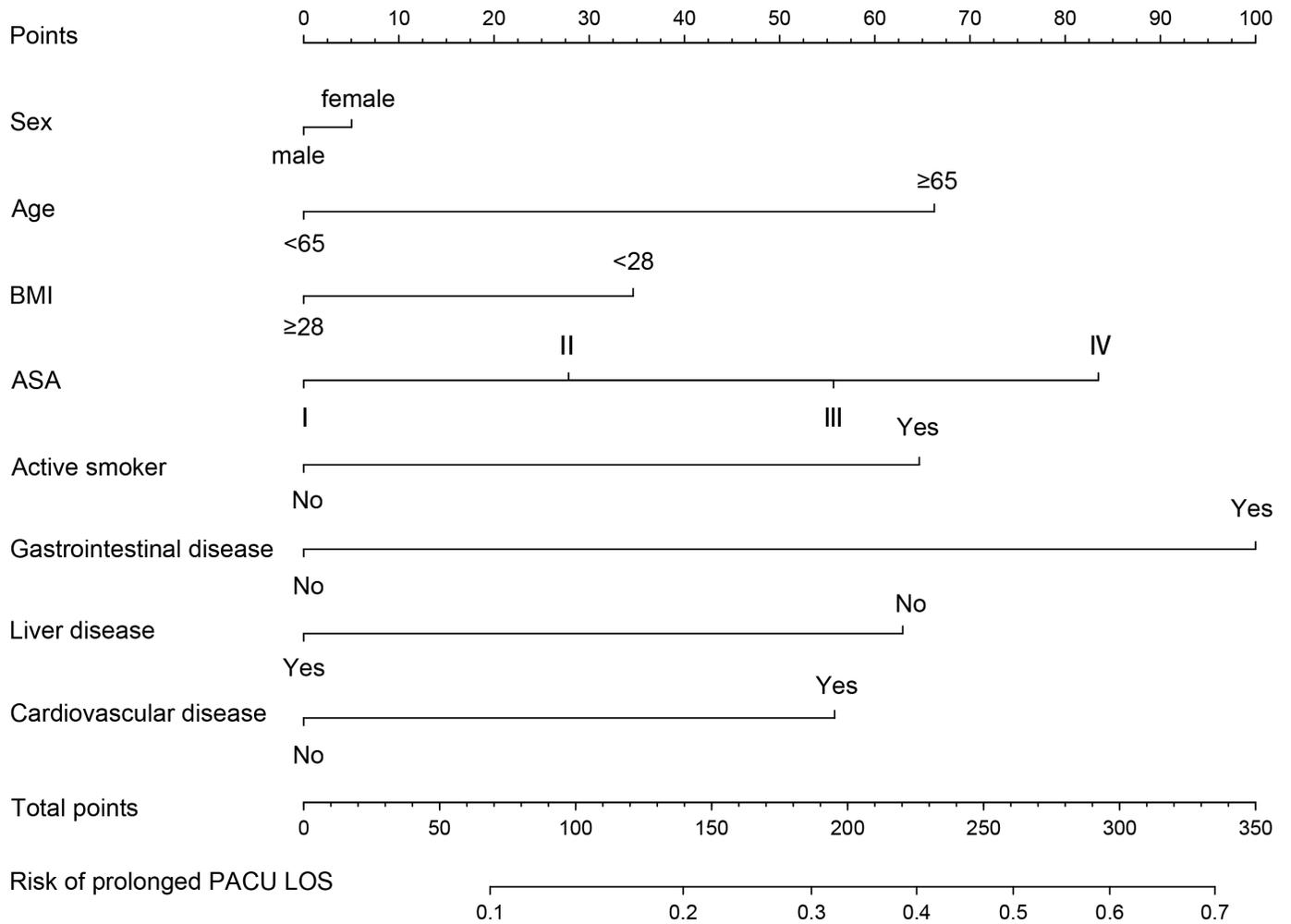
*PACU* postanesthesia care unit, *LOS* length of stay, *BMI* body mass index, *ASA* American Society of Anesthesiologists, *OR* odds ration, *CI* confidence interval.

## Figures



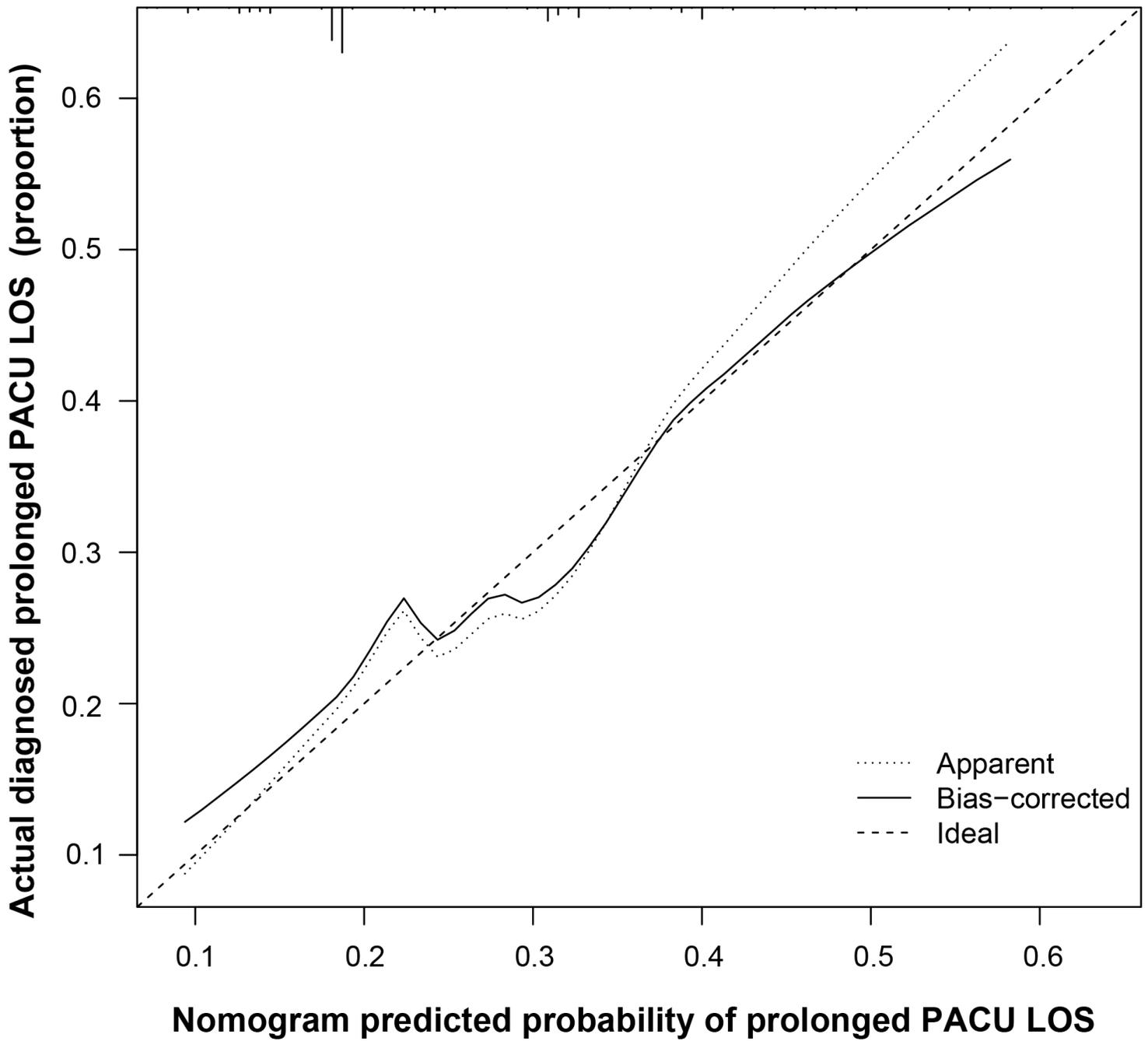
**Figure 1**

Patient feature selection using the LASSO regression model. A, Optimal parameter ( $\lambda$ ) selection. B, LASSO coefficient profiles of the 15 texture features. Abbreviations: LASSO, least absolute shrinkage and selection operator.



**Figure 2**

Developed prolonged PACU LOS nomogram. This nomogram was developed on the training set, with the sex, age, BMI, ASA grade, active smoker, gastrointestinal disease, liver disease and cardiovascular disease. Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; PACU, postanesthesia care unit; LOS, length of stay.



**Figure 3**

Calibration curves of the prolonged PACU LOS nomogram prediction on the training set. The x-axis represents the predicted prolonged PACU LOS risk. The y-axis represents the actual diagnosed prolonged PACU LOS.

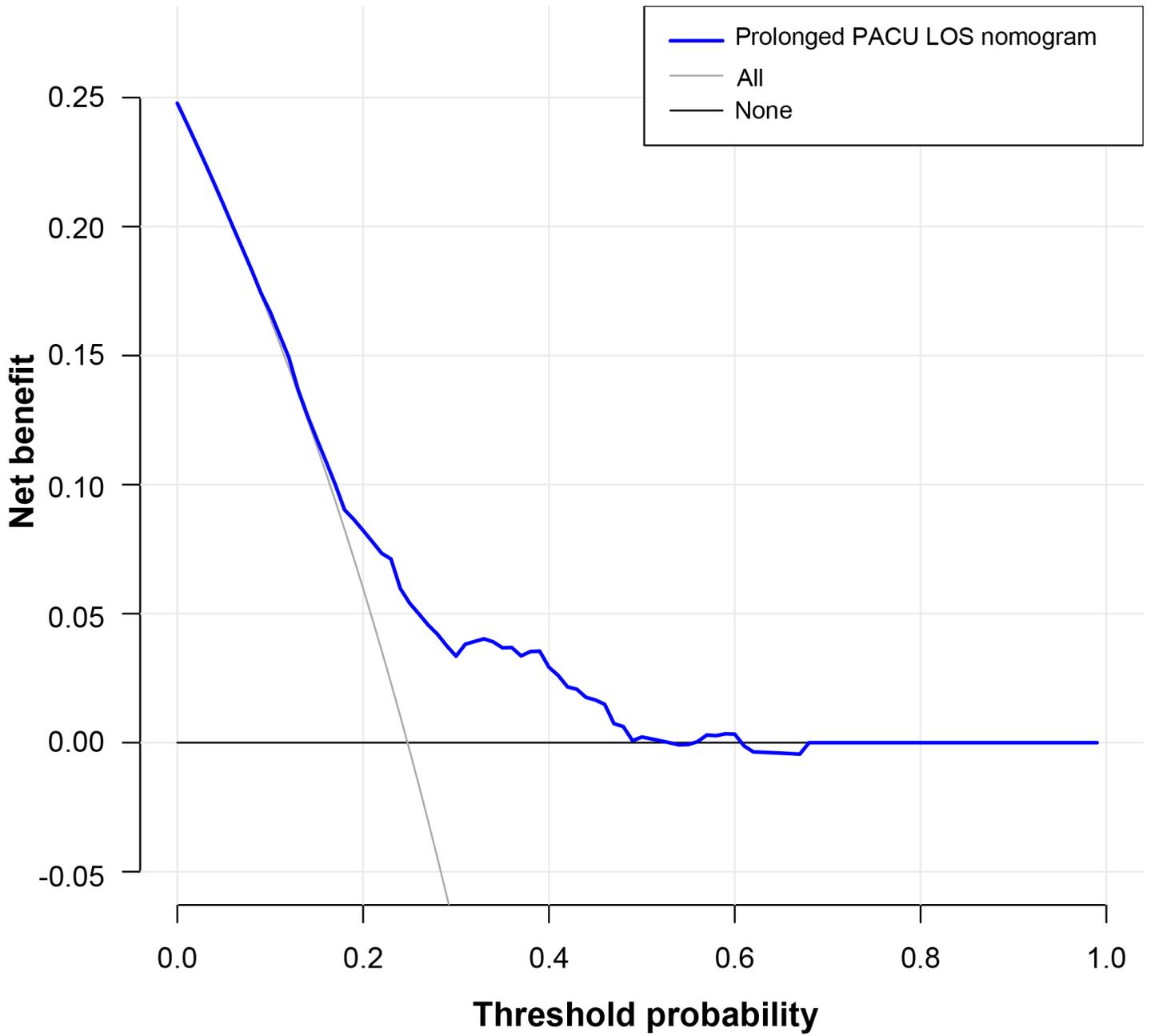


Figure 4

Decision curve analysis for the prolonged PACU LOS nomogram.