

The Risk Factors and Predictive Nomogram for Length Of Stay More than 14 Days in Undergoing TKA Patients: A Secondary Analysis Based on a Cohort Study in Singapore

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Research Article

Keywords: total knee arthroplasty, length of stay, the risk factor, nomogram, secondary analysis, a cohort study

Posted Date: November 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1041995/v1>

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Abstract

Objective:

The aim was to explore the risk factors and establish a predictive nomogram of length of stay (LOS) more than 14 days in a undergoing Total knee arthroplasty (TKA) cohort .

Methods:

We used the raw data, a retrospective cohort study of 2622 patients undergoing TKA in Singapore, for secondary analysis. The LASSO regression was used to optimize feature selection for the LOS more than 14 days. The Multivariable logistic regression analysis was applied to build a predicting nomogram by using the feature selected in the LASSO regression model. In order to evaluate the prediction ability of the model, we calculated the C-index. Simultaneously, the ROC curve, the Calibration curve and the DCA curve was draw to assess the model. Finally, we used 1000 times bootstrap method to verify the accuracy of the model.

Results:

Finally, 100(3.81%) patients were hospitalized for more than 14 days and 2522 patients (96.19%) were less 14 days. Patient age, ASA status, type of anesthesia, operation duration, procedure description, DM, IHD, CHF, day of operation and blood transfusion were determined and incorporated into the diagnostic nomogram. The C-index was 0.797(95% CI: 0.755-0.839).The calibration curve showed that the model had good recognition ability.The DCA curve analysis showed that the risk nomogram of length of stay more than 14 days was clinically useful.The C-index is 0.763 through 1000 times bootstrapping validation.

Conclusion:

We used the age, ASA status, type of anesthesia, operation duration, procedure description, DM, IHD, CHF, day of operation and blood transfusion to establish the clinical prediction model , this method can conveniently predict the risk of individual patients with total knee arthroplasty length of stay for more than 14 days.

Introduction

Total knee arthroplasty (TKA) is one of the most common orthopedic surgeries, Studies have shown that over time, the prevalence rate has increased significantly and shifted to a younger age, and the prevalence rate in women is higher than that in men¹.The TKA was mainly used for the treatment of pain, mobility limitation and joint deformity caused by osteoarthritis, rheumatoid arthritis and knee trauma². It can help patients restore knee joint function and significantly improve the quality of life of patients³.The increased life expectancy and the aging population have led to a dramatic increase in the number of patients with knee disorders, and total knee arthroplasty (TKA) is currently the most important and

effective treatment for severe knee disorders, the demand for TKA will increase dramatically in the coming years^{4,5}. It is estimated that more than 700,000 TKA surgeries are performed in the United States every year, and this number will increase to nearly 3.5 million by 2030. Therefore, it is inevitable to perform TKA in an economical and effective way⁶.

The associated costs of surgical procedures, inpatient care, rehabilitation, and postoperative care have increased substantially due to enhanced intra - and perioperative management⁷. Meanwhile, as the epidemic of new coronary pneumonia spread, there was an obvious decline in the global economy, and the Medical insurance expenditure increased significantly. Some countries have removed the TKA from the List of Medicare Outpatient Payment System Rules⁸. The focus of reducing hospitalization cost is to reduce Length Of Stay(LOS). The shortening LOS will increase the turnover rate of inpatients, reduce medical costs and reduce the medical burden of the society⁹.

In addition, TKA surgery may be accompanied by serious complications, which will adversely affect the prognosis of patients and increase the possibility of disability and death¹⁰. However, the longer LOS is a risk factor for the postoperative complications. It is particularly important to reduce postoperative complications such as postoperative infection, thromboembolism, postoperative delirium and cognitive dysfunction¹¹. Therefore, how to determine the factors of LOS , reduce the incidence of surgical complications, decrease hospitalization expenses and save medical resources are the problems,which should be solved by the doctors .The purpose of this study was to explore the risk factors and establish a predictive nomogram of length of stay (LOS) more than 14 days in a undergoing Total knee arthroplasty (TKA) .

Patients And Methods

Patients Dates

Our study is a secondary analysis based on a single-center retrospective cohort study in Singapore. Patients who underwent TKA at Singapore General Hospital from January 2013 to June 2014 were selected¹². We download the raw data uploaded by Abdullah et al at the“DATADRYAD”web site (www.datadryad.org). Abdullah et al have authorized the ownership of the original data to the datadryad Web site; therefore, we could utilize these data for secondary analysis on a different hypothesis without violating the authors’rights.

The study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University. The Ethics Committee particularly approved that informed consent was not required because of being approved by the“DATADRYAD”Web site (www.datadryad.org) and data were analyzed anonymously.The ethics committee waived the requirement for informed consent from all patients.

Statistical analysis

Statistical analysis was performed using R software (version 3.1.1; <https://www.R-project.org>). Chi-squared tests (categorical variables) and one-way analysis of variance or K-W test (continuous variables of a normal distribution or skewed distribution) were appropriately performed to verify significant differences between different groups.

We used R package “glmnet” for doing lasso regression analysis. Lasso regression can perform variable screening and complexity adjustment while fitting the generalized linear model. Variable screening refers to not putting all variables into the model for fitting, but selectively putting variables into the model to get better performance parameters. Complexity adjustment is to avoid over fitting by controlling the complexity of the model through a series of parameters. Finally, we got the result of lasso's regression. All potential predictors were applied to develop a cohort model that predicted the risk of LOS more than 14 days.

Multivariate Logistic regression analysis was used to establish the prediction model combining the minimum absolute contraction and the selected features in the selection operator regression model. The accuracy of the prediction model was evaluated by the ROC curve. A decision curve analysis was performed by quantifying the net benefit at different threshold probabilities in the TKA cohort to determine the clinical usefulness of LOS more than 14 days risk nomogram. Furthermore, the calibration curves and decision curve analysis (DCA) curves were established for the assessment of the nomograms.

C-index, which is the consistency index, is used to evaluate the prediction ability of the model. We use 1000 bootstrap times to verify the accuracy of the model. There is a random sample put back in the original data, and the sample size remains unchanged. The obtained sample is called bootstrap sample.

Results

The Demographic characteristics of patients

Finally, 2622 patients who underwent TKA from January 2013 to June 2014, a retrospective cohort, were included in the study. 2622 patients (96.19%) were hospitalized for less than 14 days, however, 100 patients (3.81%) were hospitalized for more than 14 days. In Table 1, the proportion of patients with advanced age (≥ 70 years) was higher in the prolonged LOS group than in patients with normal LOS (< 70 years), and the difference was statistically significant ($P \leq 0.001$). There were no significant differences in BMI, race, and sex distribution between the 2 groups. However, patients in the LOS extended group had a high ASA score ($p \leq 0.001$), a long operation time ($p \leq 0.001$), a high ratio of bilateral knee replacement ($p \leq 0.001$), a high incidence of anemia and diabetes ($p \leq 0.001$), a history of cough ($p \leq 0.001$), a high risk of transfusion during operation ($p \leq 0.001$), repeated operation ($p \leq 0.001$) during hospitalization, and general anesthesia ($p \leq 0.001$).

The Feature Risk Factors Selection

This study was based on data on demographic, disease, and treatment characteristics of 2622 patients undergoing knee replacement in the cohort. 17 features were reduced to ten potential predictors on TKA patients in the cohort (Figure 1 A and B) and were with nonzero coefficients in the LASSO regression model, as shown in Figure 1. These characteristics included Age, ASA Status, type of anaesthesia, operation duration, procedure description, DM, IHD, CHF, day of operation and blood transfusion (Table 2).

The Development of Nomogram for LOS More Than 14 Days

We developed a model containing the above 10 independent predictors and expressed them as a nomogram (Figure 2).

The Validation of Prediction Nomogram

The ROC curve shows that the rosette has high predictive performance, and its AUC is 0.797 (Figure 3). This shows that the prediction model has strong prediction ability. The calibration curves used to predict LOS more than 14 days risk nomogram in knee patients in this study cohort showed good consistency (Figure 4). Similarly, the calibration curve also shows that the prediction ability of the model is strong.

To quantify the discrimination performance of the LOA more than 14 days nomogram, C-index was measured. The C-index for the prediction nomogram was 0.797 (95% CI: 0.755-0.839) for the cohort. The C-index is 0.763 through 1000 times bootstrapping validation. The DCA of LOS more than 14 days indicated that this nomogram can serve as an excellent diagnostic tool for patients undergoing TKA (Figure 5).

Discussion

The aim of our study was to develop and validate a LOS more than 14 days risk prediction model for TKA patients. The risk factors were Age, ASA status, type of anesthesia, operation duration, procedure description, DM, IHD, CHF, day of operation and blood transfusion. Ultimately, We built the nomogram using the above risk factors for LOS more than 14 days in TKA patients. The Nomogram transforms the complex regression equation into a visual graph, which makes the results of the prediction model more readable and convenient for patient evaluation. Because of the intuitive and easy to understand characteristic of nomogram, it has gradually been paid more and more attention and applied in medical research and clinical practice.

In the risk prediction nomogram with LOS more than 14 days in this study, the highest independent predictor score was blood transfusion, many studies have come to the same conclusion, and the transfusion rate was directly related to LOS¹³⁻¹⁵. Autologous blood transfusion is often required when the

blood loss is between 1000-1500 ml. research shows that the total blood loss after TKA may be as high as 2000 ml, and the proportion of blood transfusion may be as high as 67%^{16,17}. In a cohort of 228,316 TKA patients at 922 hospitals, the mean predicted probability of TKA transfusion was 7.9%, with 60% (95% CI, 36%-87%) patients with LOS more than 3 days¹³. In a cross-sectional study of 4,544,999 patients who received TKA between January 2000 and December 2009, blood transfusion were associated in-hospital mortality, LOS increased by 0.71±0.01 days¹⁴. In addition, Danninger et al.¹⁵ showed a significantly higher rate of major complications in patients receiving transfusion (19.1% vs 11.2%, P<0.0001), the mean length of hospital stay was significantly increased.

Our study found that the date of operation was a major factor in predicting the risk of LOS more than 14 days after blood transfusion. Similarly, studies demonstrated that operation procedure or factors related to doctors-nurses provide clinically relevant improvement in explaining length of stay in addition to patient-related risk factors⁸. In a prospective cohort study of 4,509 patients who underwent initial TKA at four hospitals between January 1, 2016 and September 30, 2017, surgery later in the day predicted a longer hospital stay, with patients who had surgery on Friday having a significantly longer LOS than patients who had surgery on Monday⁸. Our study showed that the risk prediction scores of operations on Monday, Tuesday and Friday were much higher than those on Thursday. The length of hospital stay was related to the date of operation. Possible reasons for this result include patients from different countries, surgical hospital system, doctors' mood and doctors' preferences.

This study found that the greater the variety of comorbid diseases, that is, the higher the comorbidity index, and the longer the hospital stay. Swain et al.¹⁸ showed that 67% of patients with osteoarthritis had at least one other chronic condition, 20% more than those without osteoarthritis. The results of this study suggest that co-morbidity CHF, DM, and IHD are independent predictors of LOS more than 14 days. Similarly, some previous studies suggested that the TKA patients with comorbidities had prolonged LOS¹⁹⁻²³. Higuera et al.²² showed that chronic heart failure was associated with longer hospital stays and increased rates of major postoperative complications in TKA patients. In a study of 15,321 TKA patients, 18.2% had a medical comorbidity DM, with a 300% increase in overall mortality. Belmont et al.²³ found that DM was an independent predictor of hospitalization of 4 days or more.

ASA status was also particularly important for predicting LOS more than 14 days of risk. Consistent with previous literature, ASA-status more than 3 is an independent risk factor for prolonged LOS and increased postoperative complications^{23,24}. The predicted risk score of bilateral total knee arthroplasty is higher than that of unilateral TKA, probably because bilateral patients suffer more blood loss, more severe hypotension, and more cardiac, respiratory, and neurological complications than unilateral patients^{25,26}. In this study, it was suggested that patients undergoing knee revision were also predictors of LOS more than 14 days of risk, and that revision arthroplasty was associated with longer hospital stays and higher rates of complications and mortality, similar to results confirmed in previous studies^{27,28}.

The type of anesthesia also played an important role in predicting the risk of LOS more than 14 days. In both primary and revised TKA patients, general anesthesia was associated with an increased risk of postoperative complications, such as thromboembolism and surgical incision infection, as well as increased the LOS, blood transfusion rates, postoperative opioid consumption, and surgical time, compared with epidural or spinal anesthesia²⁹⁻³³. In addition, age and operation duration were independent predictors of LOS more than 14 days risk, similar to previous finding^{23,34}. Limitations of this study include: as the included cases excluded patients with GA combined with RA and other anesthesia methods, the results of this study cannot be used to predict the risk of this population.

There are still some limitations in our study. Firstly, this study is a retrospective study, using clinical data from a single center. Therefore, there may be differences in treatment strategies, race, and so on. Second, because of differences in healthcare Settings and practices, predictive models developed in one country are unlikely to be directly applicable in another country, requiring external validation and updating of the predictive performance of models in other new patient. Finally, there may be some influencing factors not included in this paper, including patient income, medical expenses, medical insurance, hospital location, etc. Potential factors not included may also have some influence on the results.

Conclusion

We based on the variables, including age, ASA status, type of anesthesia, operation duration, procedure description, DM, IHD, CHF, day of operation and blood transfusion, established the risk prediction model of LOS more than 14 days in undergoing TKA patients. We found that the model had good predictive ability. Clinicians can use the model for hospitalized patients to reduce the length of hospital stay, reduce complications, and save medical resources.

Abbreviations

LOS: length of stay; TKA: total knee arthroplasty; ROC: receiver operating characteristic; OR: odds ratio; AUC: area under the curve; CI: confidence interval; DM: diabetes mellitus; IHD: ischemic heart disease; CHF: Congestive Hearts Failure; LASSO, least absolute shrinkage and selection operator; SE, standard error.

Declarations

Data availability statement

Availability of Data and Materials: Data can be down-loaded from "DATADRYAD" database. Dryad data package: Abdullah HR, Sim E, Hao Y, Lin G, Liew GHC, Lamoureux EL, Tan MH (2017). Data from: Association between preoperative anemia with length of hospital stay among patients undergoing primary total knee arthroplasty in Singapore: a single-center retrospective study. Dryad Digital Repository. <https://doi.org/10.5061/dryad.73250>.

Funding

This study was financially supported by the Department of Science Technology of Shandong Province for Key Technology Research and Development Program of Shandong (CN) NO. 2018GSF118080 and Qingdao Municipal Science and Technology Bureau for demotic science ar technology program (NO. 19-6-1-16-nsh)

Author contributions

BL performed the data analysis. BL, CX Z wrote the manuscript. BL, CX Z and YJ M contributed to the manuscript revise. YJ M contributed to literature search and data extraction. BL, CX Z and ZJ W conceived and designed the study. All authors have read and approved the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University. The Ethics Committee particularly approved that informed consent was not required because of being approved by the DRYAD and data were analyzed anonymously. The ethics committee waived the requirement for informed consent from all patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Baseline characteristics of selected participants

LOS more than 14 days?	No(n=2522)	Yes(n=100)	P-value
Gender			0.966
Male	610 (24.187%)	24 (24.000%)	
Female	1912 (75.813%)	76 (76.000%)	
Age(Years)			0.009
≤70	1064 (42.189%)	29 (29.000%)	
≥70	1458 (57.811%)	71 (71.000%)	
Race			0.095
Chinese	2119 (84.021%)	87 (87.000%)	
Indian	146 (5.789%)	4 (4.000%)	
Malay	185 (7.335%)	3 (3.000%)	
Others	72 (2.855%)	6 (6.000%)	
BMI			0.396
≤24	517 (20.500%)	24 (24.000%)	
≥24	2005 (79.500%)	76 (76.000%)	
ASA_Status			<0.001
1	180 (7.137%)	4 (4.000%)	
2	2196 (87.074%)	78 (78.000%)	
3	146 (5.789%)	18 (18.000%)	
Hb(g/dL)			0.003
≤12	479 (18.993%)	31 (31.000%)	
≥12	2043 (81.007%)	69 (69.000%)	
Type_of_Anaesthesia			0.001
GA	909 (36.043%)	52 (52.000%)	
RA	1613 (63.957%)	48 (48.000%)	
Operation_Duration			<0.001
≤100	1862 (73.830%)	58 (58.000%)	
≥100	660 (26.170%)	42 (42.000%)	
Procedure_Description			<0.001

Unilateral	2314 (91.753%)	80 (80.000%)	
Bilateral	188 (7.454%)	18 (18.000%)	
Revision	20 (0.793%)	2 (2.000%)	
Smoking			0.873
No	2283 (90.523%)	91 (91.000%)	
Yes	239 (9.477%)	9 (9.000%)	
OSA			0.270
No	2289 (90.761%)	94 (94.000%)	
Yes	233 (9.239%)	6 (6.000%)	
DM			0.012
No	2066 (81.919%)	72 (72.000%)	
Yes	456 (18.081%)	28 (28.000%)	
IHD			0.022
No	2399 (95.123%)	90 (90.000%)	
Yes	123 (4.877%)	10 (10.000%)	
CHF			<0.001
No	2504 (99.286%)	95 (95.000%)	
Yes	18 (0.714%)	5 (5.000%)	
CVA			0.353
No	2478 (98.255%)	97 (97.000%)	
Yes	44 (1.745%)	3 (3.000%)	
which Day of doing operation in a week?			0.002
Mon	410 (16.257%)	25 (25.000%)	
Tue	561 (22.244%)	28 (28.000%)	
Wed	435 (17.248%)	13 (13.000%)	
Thu	590 (23.394%)	10 (10.000%)	
Fri	395 (15.662%)	22 (22.000%)	
Sat	131 (5.194%)	2 (2.000%)	
Whether blood transfusion in the perioperation?			<0.001

No	2402 (95.242%)	67 (67.000%)
Yes	120 (4.758%)	33 (33.000%)

Results in the table: mean + SD / N (%)

Table 2 The Risk factors of LASSO Regression and Multivariate logistic Regression for LOS More Than 14 Days

Figures

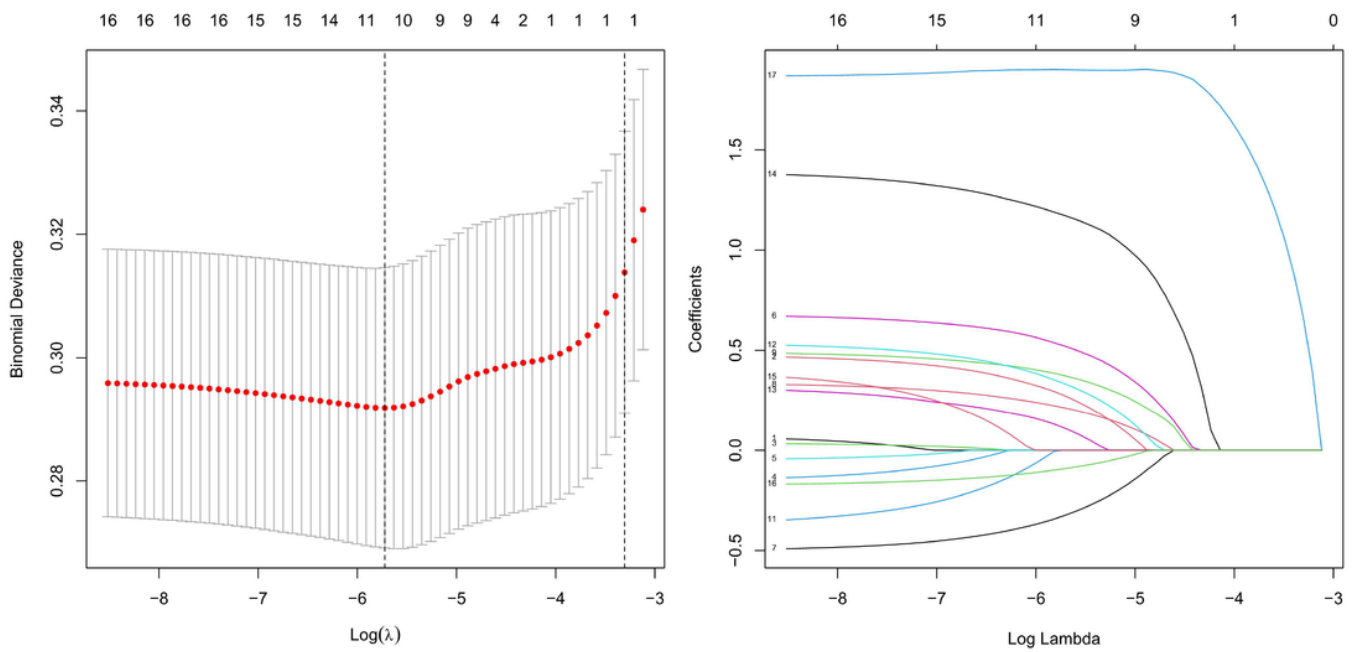


Figure 1

Demographic and clinical feature selection using the LASSO binary logistic regression model.

Variabel	Prediction Model		
	β	OR [95%CI]	P value
Age			
≤ 65	Ref	Ref	Ref
≥ 65	0.521	1.684(1.056,2.686)	0.029
ASA_Status			
1	Ref	Ref	Ref
2	0.293	1.341(0.468,3.839)	0.585
3	1.167	3.212(0.994,10.377)	0.051
Type_of_Anaesthesia			
GA	Ref	Ref	Ref
RA	-0.464	0.629(0.407,0.971)	0.037
Operation_Duration			
≤ 100	Ref	Ref	Ref
≥ 100	0.346	1.414(0.863,2.316)	0.169
Procedure_Description			
Unilateral	Ref	Ref	Ref
Bilateral	0.669	1.952(1.019,3.741)	0.044
Revision	0.917	2.501(0.53,11.811)	0.247
DM			
No	Ref	Ref	Ref
Yes	0.590	1.803(1.109,2.933)	0.017
IHD			
No	Ref	Ref	Ref
Yes	0.319	1.376(0.626,3.025)	0.427
CHF			
No	Ref	Ref	Ref
Yes	1.322	3.75(1.157,12.156)	0.028
Day_of_operation			

Mon	Ref	Ref	Ref
Tue	-0.072	0.931(0.513,1.689)	0.813
Wed	-0.756	0.470(0.227,0.971)	0.041
Thu	-1.327	0.265(0.122,0.579)	0.001
Fri	-0.112	0.894(0.476,1.680)	0.729
Sat	-1.212	0.298(0.067,1.317)	0.110

blood_transfusion			
No	Ref	Ref	Ref
Yes	1.846	6.335(3.868,10.373)	<0.001

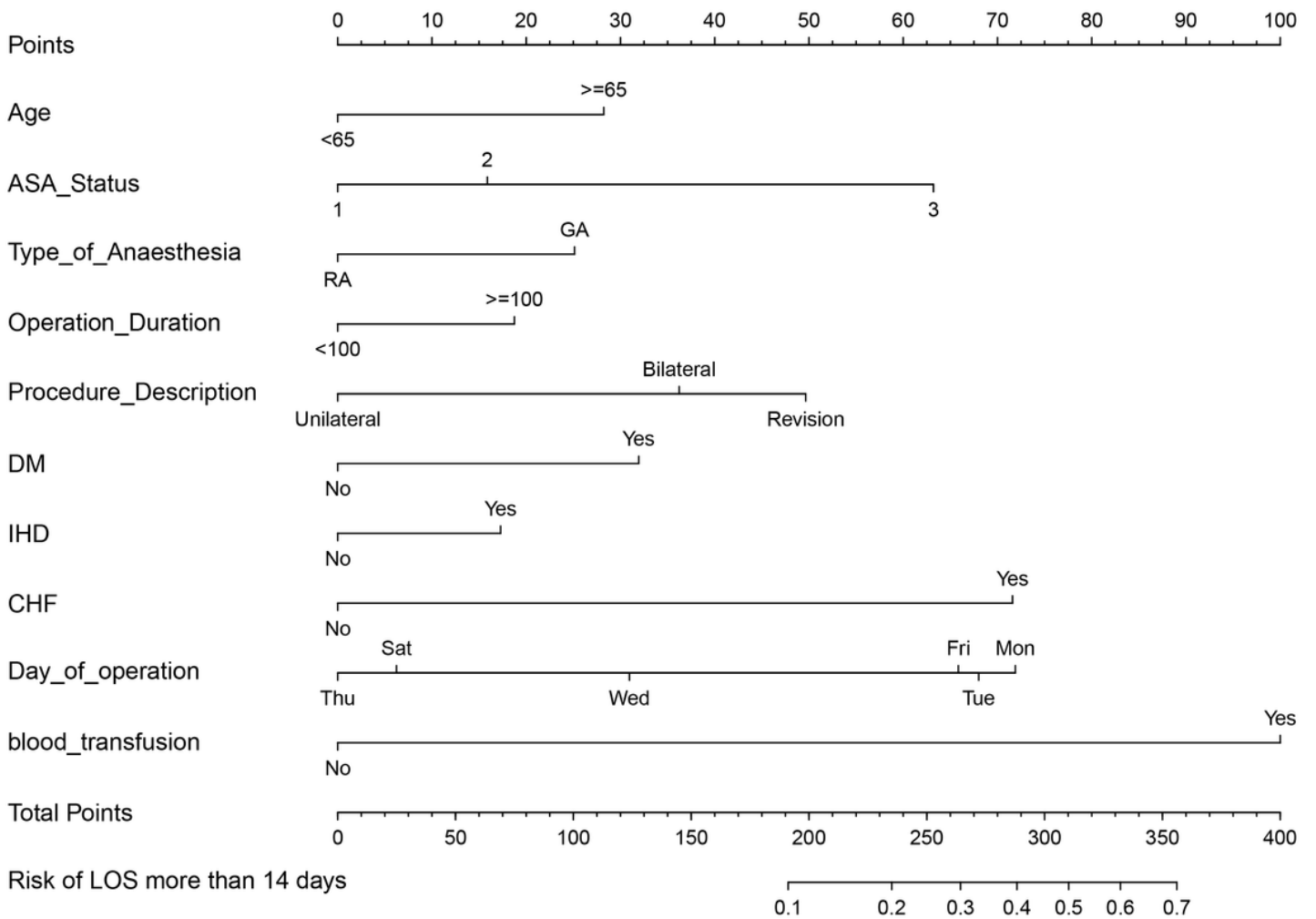


Figure 2

The Risk Nomogram for LOS More Than 14 days in Undergoing TKA Patients.

AUC= 0.797

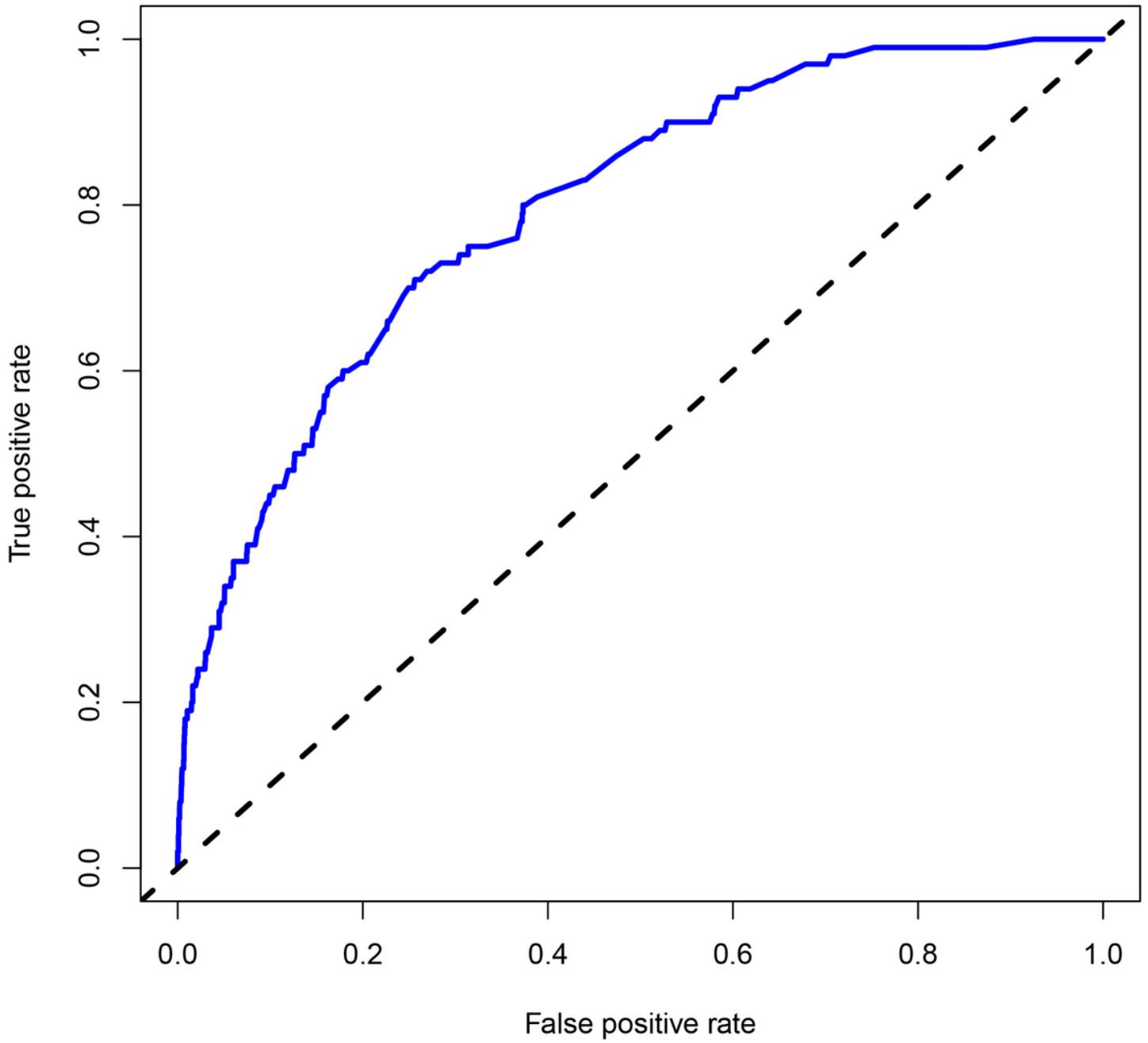


Figure 3

The ROC curves of the LOS more than 14 days in Undergoing TKA Patients.

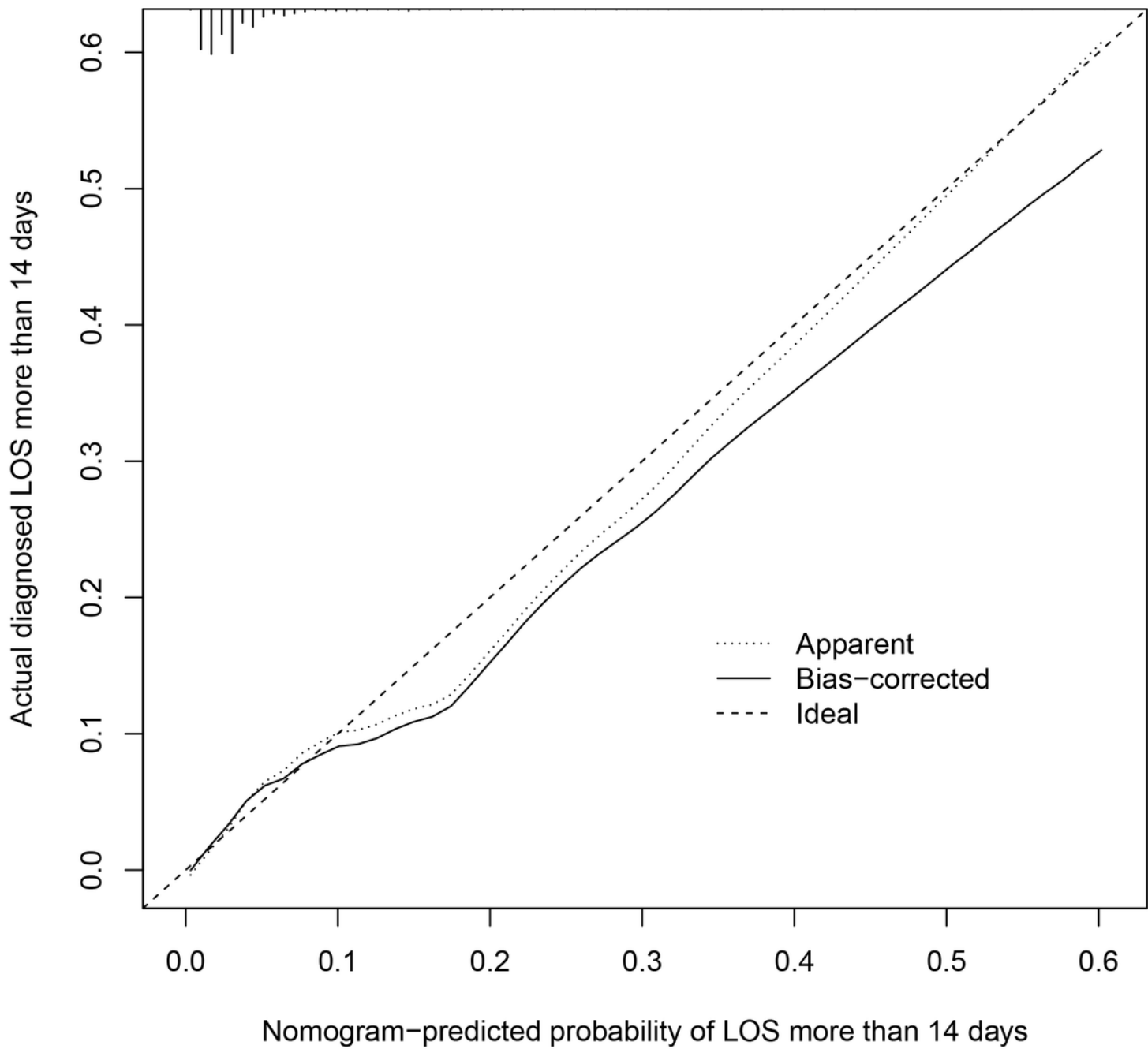


Figure 4

The Calibration curves of LOS More Than 14 days in Undergoing TKA Patients.

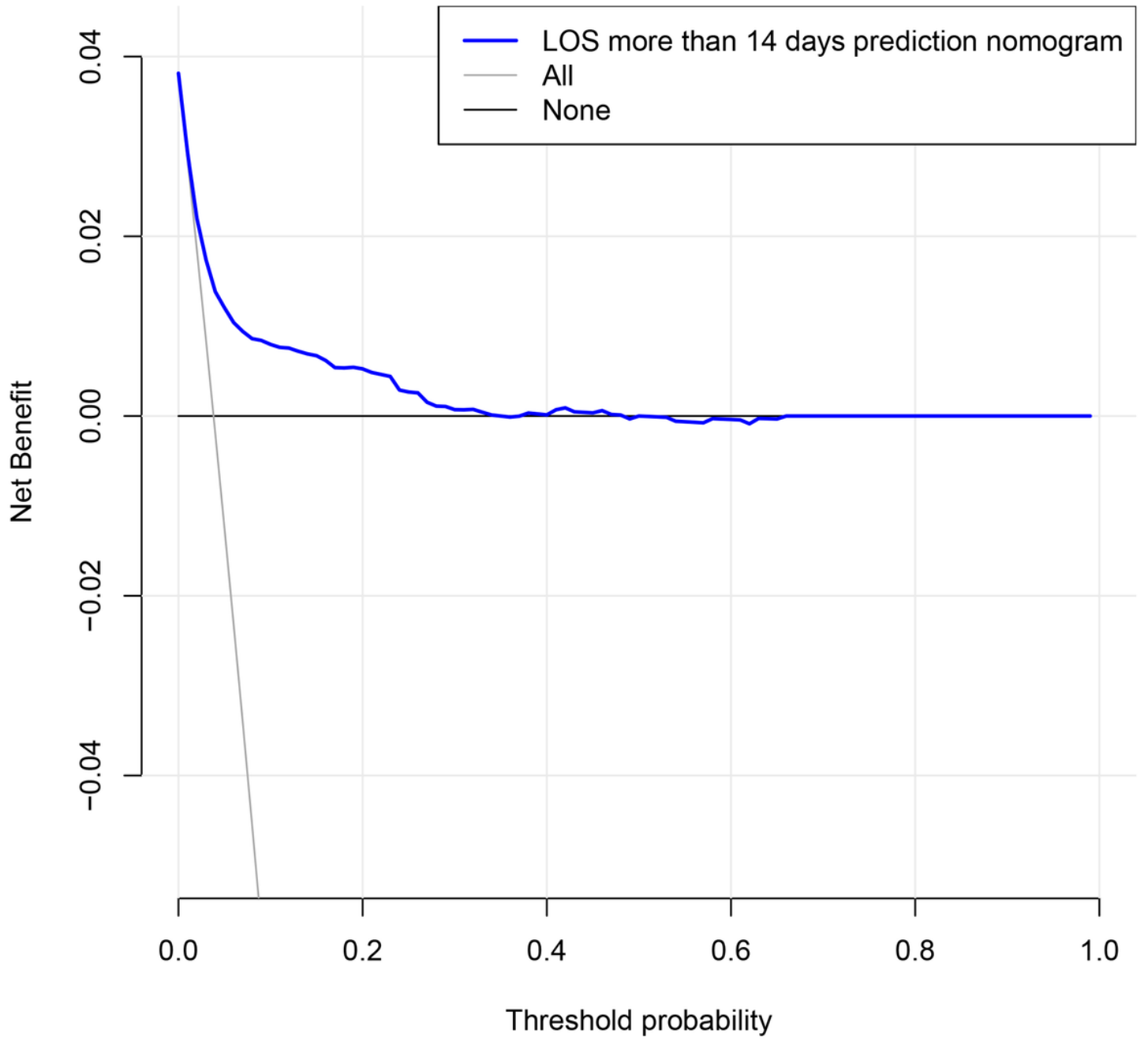


Figure 5

The Decision curve of LOS More Than 14 days in Undergoing TKA Patients.