ANNALS OF MEDICINE
2025, VOL. 57, NO. 1, 2487636
https://doi.org/10.1080/07853890.2025.2487636

RESEARCH ARTICLE

Predicting postoperative complications after pneumonectomy using machine learning: a 10-year study

Yaxuan Wang[a*], Shiyang Xie[b*], Jiayun Liu[a*], He Wang[a], Jiangang Yu[a], Wenya Li[c], Aika Guan[d], Shun Xu[c], Yong Cui[a] and Wenfei Tan[a]

[a]Department of Anesthesiology, the First Hospital of China Medical University, China; [b]Department of Radiation Oncology, the First Hospital of China Medical University, China; [c]Department of Thoracic Surgery, the First Hospital of China Medical University, China; [d]Queen' University, Kingston, Canada

ABSTRACT

Background: Reducing postoperative cardiovascular and neurological complications (PCNC) during thoracic surgery is the key to improving postoperative survival.

Objective: We aimed to investigate independent predictors of PCNC, develop machine learning models, and construct a predictive nomogram for PCNC in patients undergoing thoracic surgery for lung cancer.

Methods: This study used data from a previous retrospective study of 16,368 patients with lung cancer (training set: 11,458; validation set: 4,910) with American Standards Association physical statuses I–IV who underwent surgery. Postoperative information was collected from electronic medical records to help build models based on cause-and-effect and statistical data, potentially revealing hidden dependencies between factors and diseases in a big data environment. The optimal model was analyzed and filtered using multiple machine-learning models (Logistic regression, eXtreme Gradient Boosting, Random forest, Light Gradient Boosting Machine and Naïve Bayes). A predictive nomogram was built and receiver operating characteristics were used to assess the validity of the model. The discriminative power and clinical validity were assessed using calibration and decision-making curve analyses.

Results: Multivariate logistic regression analysis revealed that age, surgery duration, intraoperative intercostal nerve block, postoperative patient-controlled analgesia, bronchial blocker use and sufentanil use were independent predictors of PCNC. Random forest was identified as the optimal model with an area under the curve of 0.898 in the training set and 0.752 in the validation set, confirming the excellent prediction accuracy of the nomogram. All the net benefits of the five machine-learning models in the training and validation sets demonstrated excellent clinical applicability, and the calibration curves showed good agreement between the predicted and observed risks.

Conclusion: The combination of machine-learning models and nomograms may contribute to the early prediction and reduction in the incidence of PCNC.

ARTICLE HISTORY
Received 29 August 2024
Revised 15 January 2025
Accepted 22 March 2025

KEYWORDS
Lung cancer, nomogram; machne learning; postoperative cardiovascular and neurological complications; thoracic surgery; video-assisted thoracoscopic surgery

Introduction

Cardiovascular and neurological complications following thoracic surgery are critical postoperative concerns that significantly affect patient prognosis, quality of life, duration of hospital stay, and mortality [1]. Due to the proximity of the surgical site to the heart and hypoxia caused by single-lung ventilation during pneumonectomy, postoperative cardiovascular and neurological complications (PCNC) are more likely to occur. Current research mostly focuses on major adverse cardiovascular and neurological events, including death, acute ischemic stroke, or myocardial infarction, with an incidence rate of 0.8–3% [2,3]. Nevertheless, minor PCNC, such as postoperative atrial fibrillation and transient cerebral ischemia, whose incidence can be as high as 30% [4], which is significantly higher than that of other noncardiac and thoracic

CONTACT Wenfei Tan winfieldtan@hotmail.com Department of Anesthesiology, the First Hospital of China Medical University, Nanjingbei Street 155#, Shenyang, China, 110001
*These authors contributed equally to this work.

Supplemental data for this article can be accessed online at https://doi.org/10.1080/07853890.2025.2487636.

surgeries, are independent risk factors for severe postoperative cardiovascular and neurological adverse events and death [5]. Therefore, patients with PCNC should be closely monitored, regardless of their severity.

In previous studies, video-assisted thoracoscopic surgery (VATS) lobectomy has been shown to correlate with reduced pain, minimized complications, and improved quality of life without affecting oncologic outcomes in patients with lung cancer [6,7]. However, based on data obtained from our hospital's information system, PCNC (including minor complications) after VATS have an incidence of approximately 20% [8–11], which is not lower than that of open surgery. Furthermore, data from a European research group indicated that a longer surgical duration correlated with an increased incidence of postoperative complications [12]. Moreover, the operating time and anaesthetic technique may also influence the outcomes of cardiovascular and neurological complications.

Reducing the occurrence of PCNC in thoracic surgery remains a key issue in improving the quality of postoperative survival. Current methods for predicting PCNC have significant limitations. Previous studies have mostly relied on traditional risk scores or the judgment of clinicians, which can lead to limited accuracy and an inability to consider interactions between complex variables. Machine learning is a type of artificial intelligence that can provide more accurate predictions without explicit programming; moreover, it may be able to analyse the underlying mechanisms of various complications [13]. Recently, multiple machine-learning models, such as random forest, eXtreme Gradient Boosting (XGboost), Light Gradient Boosting Machine (LightGBM), and Naive Bayes, have been used to construct information models based on big data and effectively reveal the potential relationship between multiple clinical predictors and outcomes. Gradient boosting is an integrated learning method that constructs a predictive model with improved performance by integrating multiple simple models. Our implementation of XGBoost is a regularized implementation of gradient boosting, which is effective in preventing overfitting [14]. Random forest is an ensemble learning algorithm that constructs multiple decision trees and votes or averages their results to obtain the final prediction. It excels in handling nonlinear problems and improving prediction accuracy and generalization ability [15]. Naïve Bayes estimated parameters are less sensitive to missing data and have a relatively simple algorithm. Therefore, this study selected these five machine-learning models that can process big data, manage complex interactions between variables, and provide powerful predictive performance in medical research. Previous studies have used machine-learning methods in clinical settings with great success [14–16]. The nomogram has become increasingly familiar to clinical doctors as an intuitive and concise predictive method [17,18]. Hence, this study aimed to develop a predictive model for PCNC by linking machine-learning models to actionable clinical decisions, such as preoperative risk stratification or targeted preoperative interventions to reduce the incidence of PCNC.

Materials and methods

Ethics declaration

This study was approved by the Ethics Committee of the First Hospital of China Medical University (approval number: 2022-449; approval date: November 4, 2022). This was a retrospective observational cohort study that did not contain personally identifiable information; therefore, written informed consent was not required by the Ethics Committee of the First Hospital of China Medical University. Trial Registration: Chinese Clinical Trial Registry, 2023.08.01, No. ChiCTR2300074188 (https://www.chictr.org.cn/showproj.html?proj=200744), and the principal investigator was Wen-fei Tan. This was a retrospective observational cohort study with no requirement for patients to register before enrolment. This study adhered to the principles in the Declaration of Helsinki.

Patients

The data of patients who underwent thoracic surgery for lung tumours at divisions A and B of the hospital between September 2012 and September 2022 were reviewed. Patients in the Zhongshan Division comprised the training set, whereas patients in the Hunnan division comprised the validation set. The study samples and treatment data were obtained from the hospital's electronic information system. Patients who (1) were pathologically diagnosed with malignant lung cancer and (2) underwent lung tumour resection were enrolled in the study. In contrast, patients (1) in whom lung cancer was not the only primary malignancy, (2) with insufficient medical record data, and (3) with a previous history of cardiovascular and neurological diseases were excluded (as this study focused on patients with new-onset PCNC, which is often overlooked preoperatively, increasing the likelihood of medical disputes once new-onset postoperative complications occur). PCNC were described based on evidence shown on postoperative electrocardiogram (ECGs), computed tomography (CT) scans, or cranial magnetic resonance imaging (MRIs); findings following a consultation with a cardiologist or neurologist; or a diagnosis of new-onset cardiovascular or neurological-related diseases including: (1) cardiac-related (atrial flutter, atrial fibrillation, supraventricular tachycardia, rapid ventricular arrhythmias, sustained ventricular tachycardia, coronary artery disease, congestive heart failure; percutaneous coronary intervention or coronary artery bypass grafting, obstructive coronary artery disease, myocardial ischemia [presence or absence of clinical symptoms of ECG abnormalities] or myocardial infarction [suppression of tumorigenicity [ST] segment elevation, non-ST segment elevation, or troponin elevation]) or (2) neurological-related (transient ischemic attack, stroke, cerebral embolism, ischaemic/haemorrhagic cerebral infarction, or cerebral artery stenosis [intracranial arteries or carotid arteries] during the postoperative period).

Data collection

Data on sex, age, body mass index, history of smoking, alcohol consumption, chemotherapy, previous surgery, and disease history were collected from the hospital's electronic medical record system. Data on the time of surgery, operative technique, interoperative intercostal nerve block, postoperative patient-controlled analgesia (PCA), method of intubation, and dosage of anaesthetic drugs were obtained from the electronic records of the surgical anaesthesiologists.

Statistical analysis

Categorical variables are expressed using counts and percentages, and the Pearson chi-squared (χ^2) test or Fisher exact test was used for the comparison of data between groups. Continuous variables are expressed as means ± standard deviations, and data between groups were compared using the Student's *t*-test or Mann–Whitney U-test.

The principle for interpolating missing data in electronic medical records is the 80% rule [19]. If the percentage of missing values was greater than 20%, the values were excluded from the final dataset. If the percentage of missing values was less than 20%, interpolation was performed using the mean method.

The hyperparameters of the model were selected through the utilization of 10-fold cross-validation in the training dataset. Tenfold cross-validation involves dividing the dataset into 10 partitions. Utilising 90% of the data for model development, with the residual 10% allocated as a designated test dataset, ensured a systematic evaluation of the model's performance. This process was repeated to ensure that each partition was employed only once as the test dataset and nine times as the training dataset. This approach to model selection is known as cross-validation and its primary function is to provide a more accurate assessment of model performance by averaging metrics across multiple iterations.

A logistic regression analysis was performed to predict the incidence of PCNC. Significant candidate predictors and factors related to the dose of anaesthetic drugs were selected using univariate logistic regression analysis and included in the multivariate logistic regression analysis. All the candidate predictors were checked for collinearity using a variance inflation factor (VIF). These characteristics are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was set at a p-value of less than 0.05.

Multiple machine learning models, including Logistic regression, XGBoost, Random forest, LightGBM and Naïve Bayes were built using R software. The models repeated 10 samples for training and validation to analyse the importance of the training and validation set metrics, and the optimal models were selected.

The performance of the predictive nomogram was validated in both the training and test sets, and calibration curves were used to assess the calibration accuracy of the predictive model. Calibration plots with 1,000 bootstrap weights were used to assess the model's calibration accuracy. The nomogram's specific performance was quantified by calculating the area under the curve (AUC) value of the receiver operator characteristics (ROC) curve and by calculating the specificity, sensitivity, accuracy, positive predictive value (PPV), and negative predictive value (NPV). The clinical utility and net benefit of the nomogram were determined using decision curve analysis (DCA). The x-axis of the decision curve represents the threshold for the predicted probability. The net benefit to patients in terms of clinical decisions based on the classification of outcomes at this threshold is shown on the y-axis. All statistical analyses were performed using SPSS version 25 (IBM Corporation, Armonk, NY, USA) and R software version 4.3.1 (http://www.rproject.org).

Results

Patient characteristics

Between September 2012 and September 2022, 16,368 patients who underwent thoracic surgery for lung tumors at the hospital's Department of Thoracic Surgery were enrolled in the study (Supplemental Table 1). A total of 3,528 patients with missing electronic medical records and 2,106 patients with a history of cardiovascular or neurological diseases before surgery were excluded. Of the included patients, 3,398 developed PCNC. The age of patients in the PCNC group (64.10 ± 10.63) was remarkably high compared with the non-PCNC group (59.84 ± 11.60); the same trend was observed regarding history of smoking and alcohol consumption. Additionally, the average duration of surgery was also noticeably higher in patients in the PCNC group (136.36 ± 73.06) compared with that in patients in the non-PCNC group (116.28 ± 63.19); moreover, there were also statistically significant differences between the two groups regarding PCA and anesthetic drug dose of sufentanil. A total of 11,458 patients from Hospital Division A comprised the training set, whereas 4,910 patients from Hospital Division B comprised the validation set (Supplemental Figure 1). The external data as validation set is being actively advanced. All indicators were equally distributed between the two groups (Supplemental Table 2).

Feature selection

To achieve feature selection and reduce the dimensionality of the data, univariate logistic regression was initially used to filter all variables. Among all assessed variables, the univariate logistic regression analysis revealed that age, alcohol consumption history, duration of surgery, intraoperative intercostal nerve block, postoperative PCA, and method of anaesthetic intubation were significantly associated with the occurrence of PCNC (Supplemental Table 3). Following univariate logistic regression, which identified the above six variables, we added variables related to the dosage of anaesthetic drugs (such as sufentanil) which anaesthetists pay particular attention to. Together with the above variables, we used multivariate logistic regression to further screen the candidate variables. After screening, only six variables were individually relevant to PCNC: age (OR:1.030; 95% CI:1.026–1.035; p<.001), duration of surgery (OR:1.003; 95% CI:1.003–1.004; p<.001), intraoperative intercostal anaesthesia (OR:0.091, 95% CI:0.072–0.115; p<.001), type of PCA (epidural PCA: OR:0.452; 95% CI:0.402–0.508; intravenous PCA: OR:0.452, 95% CI:0.398–0.513; p<.001), method of intubation (endobronchial blocker tube: OR:0.553; 95% CI:0.470–0.651; p<.001), and dose of sufentanil (OR:0.988; 95% CI:0.984–0.992; p<.001) (Table 1). All the above variables were tested for multicollinearity and the VIF was less than 10. Ultimately, these six independent factors were used to construct the predictive models for PCNC.

Model evaluation and comparison

Several machine-learning models (Logistic regression, XGBoost, Random forest, Light GBM, and Naïve Bayes), which are widely used in the medical field, were trained to model the PCNC and were repeated 10 times. The effectiveness of the models in the training and validation sets was evaluated by calculating the AUC values of the ROC, as well as the specificity, sensitivity, accuracy, PPV, and NPV (Figure 1) (Supplemental Table 4). In the training set, Random forest showed the best performance, with an AUC value of 0.898, 95% CI of 0.892–0.904, sensitivity of 0.905, specificity of 0.712, PPV value of 0.451, and NPV value of 0.966. In the testing set, both the Random forest and Light GBM showed good effectiveness, with an AUC value of 0.752. In the validation set, both the Random forest and Light GBM showed good effectiveness, with an AUC value of 0.752. XGBoost and logistic regression showed that Naïve Bayes had the lowest AUC value but also exceeded 0.7, demonstrating that all models performed satisfactorily. We also constructed calibration plots for the five models and found that the line for each model was near the ideal line in both the training and validation sets (Figure 2). The Brier values in the training set were as follows: logistic regression, 0.148; XGBoost, 0.150; Random forest, 0.114; Light

Table 1 Multivariate logistic regression analysis for the PCNC risk factors.

Intercept and variables	Prediction model		
	β	OR (95%CI)	*P*-value
Intercept	−2.474	0.084 (0.061-0.117)	<0.001
Age, years	0.030	1.030 (1.026-1.035)	<0.001
History of alcohol	−0.095	0.909 (0.806-1.026)	0.122
Duration of surgery, min	0.003	1.003 (1.003-1.004)	<0.001
Intraoperative intercostal nerve block	−2.402	0.091 (0.072-0.115)	<0.001
Type of PCA			
None	Reference		
Epidural PCA	−0.795	0.452 (0.402-0.508)	<0.001
Intravenous PCA	−0.794	0.452 (0.398-0.513)	<0.001
Method of intubation			
Double-lumen endobronchial tubes	Reference		
Bronchial blockers	−0.592	0.553 (0.470-0.651)	<0.001
Dose of Sufentanil, μg	−0.012	0.988 (0.984-0.992)	<0.001

Abbreviation: PCNC: postoperative cardiovascular and neurological complications; PCA: patient-controlled analgesia.

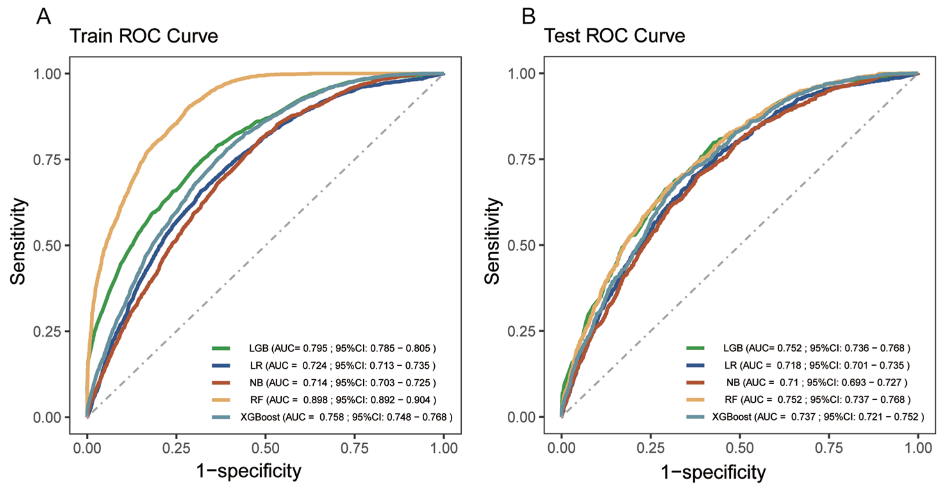

Figure 1. ROC Curves of the predictive nomogram for PCNC. A: Training set; B: Validation set. Abbreviations: ROC: receiver operator characteristics; PCNC: postoperative cardiovascular and neurological complications.

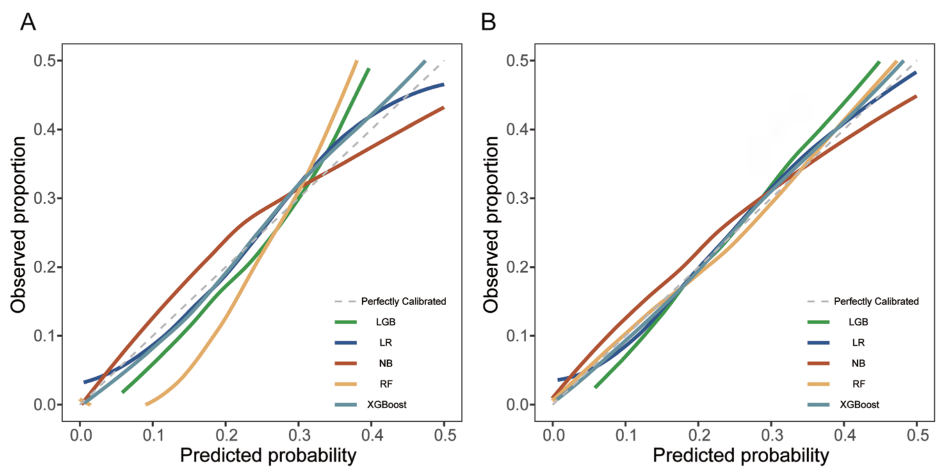

Figure 2. Calibration curves for assessing the accuracy of the predictive nomogram for PCNC. A: Training set; B: Validation set. Abbreviation: PCNC: postoperative cardiovascular and neurological complications.

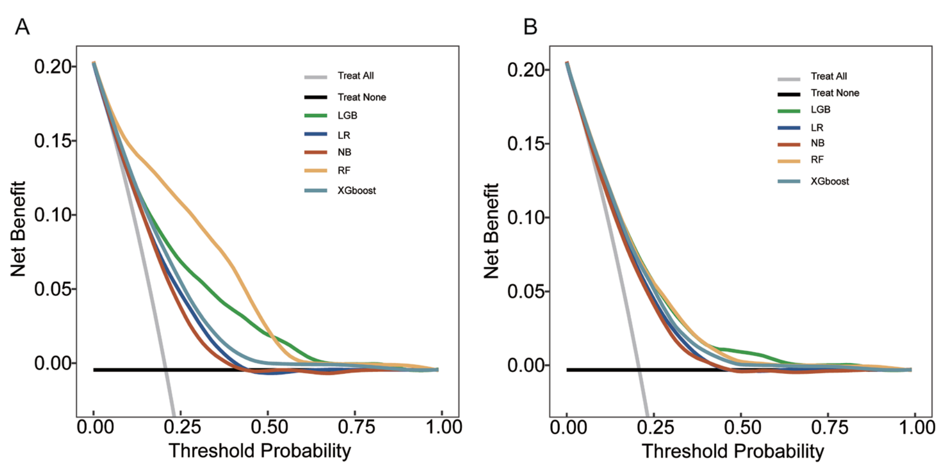

Figure 3. The DCA used to evaluate the clinical benefit of the predictive nomogram for PCNC. A: Training set; B: Validation set. Abbreviation: PCNC: postoperative cardiovascular and neurological complications; DCA, decision curve analysis.

GBM, 0.132; and Naïve Bayes, 0.142. In the validation set, the Brier values were as follows: logistic regression, 0.149; XGBoost, 0.145; Random forest, 0.142; Light GBM, 0.142; and Naïve Bayes, 0.151. The DCA curves exhibited excellent clinical applicability to all five machine-learning models (Figure 3).

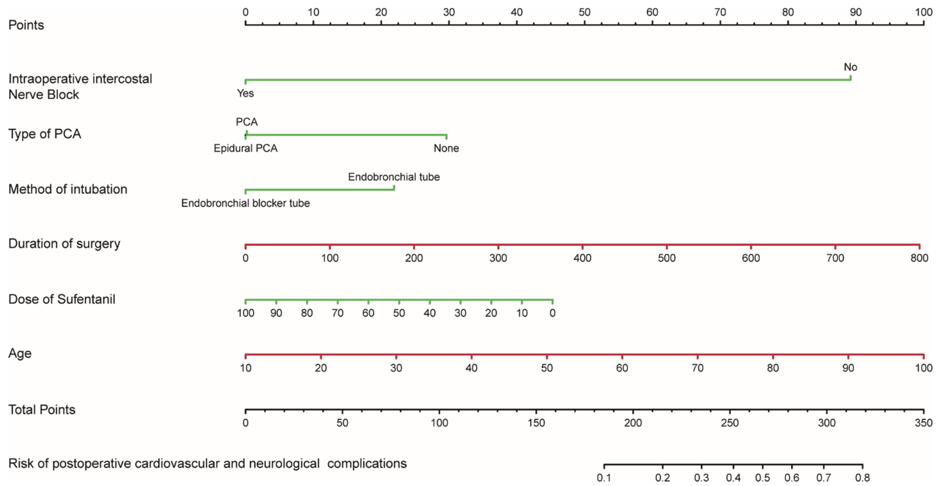

Figure 4. Nomogram for predicting the incidence of postoperative cardiovascular and neurological complications.

Development of the nomogram

As the predictive nomogram based on logistic regression is more intuitive and broadly used in clinics, this study developed a nomogram of PCNC in addition to multiple machine-learning models for the convenience of clinicians (Figure 4).

Discussion

In this retrospective study, the multivariate logistic regression analysis demonstrated that age and surgery duration were independent risk factors for PCNC. In contrast, PCA, intraoperative intercostal nerve block, anaesthetic intubation method, and sufentanil use were independent protective factors. The five machine-learning models constructed from these candidate indicators demonstrated excellent predictive efficacy in both the training and validation sets. As a big data study, our research differs from previous studies which are often limited by small sample sizes [20,21]. Therefore, the predictive model of our study may have a good generalizability. Consequently, it may be highly applicable in the clinical setting. Accurately identifying protective and disruptive factors using machine-learning models and nomograms may reduce the incidence of PCNC and improve the quality of life of postoperative patients.

In the present study, the main concern was PCNC, which differ from previous studies that only focused on major cardiovascular and cerebrovascular events such as perioperative acute ischemic stroke and acute myocardial infarction [2,3,22]. The incidence of major cardiovascular and cerebrovascular events is generally 3%, which may lead to serious postoperative outcomes. However, cardiovascular and neurological events, such as postoperative atrial fibrillation and transient cerebral ischemia, have also been shown in previous studies to be independent risk factors for severe postoperative cardiovascular and neurological adverse events and death [5]. Studies have shown that the incidence of atrial fibrillation after thoracic surgery can be as high as 30% [23,24]. Therefore, our study differed from previous studies by including all perioperative cardiovascular and neurological complications, resulting in an incidence rate of approximately 20%. Regardless of severity, the outcome variables to be explored in the study were analysed to derive the independent factors affecting the outcome. The criteria for defining PCNC in this study included a diagnosis of new-onset cardiovascular or neurological diseases during the postoperative period through evidence on ECG, CT scans, or cranial MRI, or following consultation with a cardiologist or neurologist. The inclusion criteria included the observation of almost all additional PCNC-related diseases, making the study more detailed and comprehensive.

Age has been confirmed to play a critical role as a risk indicator for PCNC [25–28]. Additionally, several studies have confirmed that the duration of surgery is associated with a high incidence of postoperative complications [12,29,30]. These conclusions align with the results of the present study.

With the recent increase in opioid-free anaesthesia, many anaesthesiologists consider the opioid analgesics used in the past to be un-ideal and potentially counterproductive, contributing to the severity of postoperative pain and being strongly associated with adverse postoperative outcomes [31–34]. Previous studies have provided contradictory evidence regarding the use of opioids [35,36]. However, most studies have examined whether focusing on opioid-related adverse outcomes, such as nausea and vomiting alone [37–39], while ignoring postoperative adverse cardiovascular and neurological events, may adversely affect patient survival and prognostic outcomes. In real-world practice, experienced anaesthesiologists prefer to use a higher dose of sufentanil when a patient's hemodynamic state becomes unstable. Moreover, the duration of surgery is positively correlated with the incidence of PCNC, and as the duration of surgery increases, the dosage of sufentanil also increases, which may lead to serious bias as a higher dose of sufentanil may be related to the occurrence of PCNC. In contrast, our data showed that sufentanil was an independent protective factor rather than a risk factor for PCNC. Hence, we are more concerned with the conclusion that appropriate intraoperative administration of sufentanil helps improve patient prognosis during the early postoperative period from the anaesthesiologist's point of view. This may be because maintaining perioperative hemodynamic stability improves perioperative cardiovascular and neurological complications.

In thoracic surgical procedures, an intraoperative intercostal nerve block is an intercostal nerve block performed by thoracic surgeons under direct thoracoscopic view. Compared with the traditional intercostal nerve blocks performed under ultrasound guidance with a more defined block extent, intercostal nerve blocks performed by thoracic surgeons under a direct thoracoscopic view have not been fully implemented. In this study, intraoperative intercostal nerve block was shown to be an independent protective factor for PCNC and accounted for a larger predictive score in the nomogram; therefore, it had a stronger influence on the risk of PCNC. Therefore, this method can be recommended to thoracic surgeons for reducing postoperative pain, accelerating recovery, and reducing the incidence of PCNC.

As a standard postoperative analgesic modality used in recent years for individualized, on-demand, and self-controlled drug delivery, PCA [40] has been receiving increasing attention and popularity among patients. However, postoperative patient-controlled epidural analgesia (PCEA) is associated with adverse postoperative outcomes such as hypotension [41]. Additionally, patient-controlled intravenous analgesia (PCIA) may markedly increase the incidence of nausea and vomiting [42,43]. Although the impact of PCA on PCNC remains unclear, it is possible that both PCEA and PCIA are protective because PCA reduces postoperative pain. All three perioperative analgesic modes exerted a significant protective effect on PCNC; thus, we hypothesized that by alleviating perioperative pain, the aim of maintaining stable perioperative haemodynamics and improving perioperative cardiovascular and neurological complications could be achieved [44].

Achieving lung separation in thoracic surgery primarily involves the use of double-lumen endobronchial tubes (DLTs) or bronchial blockers (BBs). DLTs can be easily and precisely inserted, whereas BBs reduce the incidence and degree of airway injury [45,46]. However, no study has investigated the association between these intubation methods and PCNC. The present study confirmed that BB were more protective in reducing the risk of PCNC than DLT. In contrast to the results of previous studies, we hypothesized that the inflammatory response due to the more severe airway injury caused by DLTs may be responsible for the higher susceptibility to PCNC [46]. The outcomes of VATS pneumonectomy were comparable to those of the open approach.

Although this study developed machine-learning models and predictive nomograms for PCNC, it has limitations. First, a relatively small sample size was used in this study. The inclusion of more patients in future studies may reduce bias and increase the accuracy and effectiveness of the prediction model. Second, this 10-year retrospective study introduces a time bias that affects the occurrence, detection, and management of complications, and thus, the data used to train the model. Advances in surgical and anaesthetic techniques over a 10-year period may have resulted in a reduction in PCNC and thus changed the risk profile of later patients compared with earlier patients. Advances in perioperative monitoring or postoperative care may also have resulted in the earlier detection and prevention of complications, thus reducing the applicability of the model in real-world and modern settings. Third, because this study is based on data exported from the hospital information system for further cleaning and research, the missing data in electronic medical record processing adopts the 80% rule, which results in more patients being excluded. This limits the exposure of the prediction model to all clinical situations, which, in turn, biases the prediction model and may lead to an underestimation of the risk in real-world populations. A smaller sample size reduces the statistical power of the model and increases the possibility of overfitting. Fourth, this study grouped complications broadly as cardiovascular or neurological, resulting in a lack of precise and consistent classification of the results which may have reduced their accuracy and interpretability. This may have reduced the credibility of the study and limited its predictive ability for specific complications. Fifth, in a strict sense, the training and validation sets established in this study cannot be called external validation sets. Without testing the model with independent data from other institutions or settings, it is unclear whether the model performance metrics truly reflect its predictive ability. This may undermine the reliability of the model for broader clinical applications. Therefore, multicenter studies are warranted to fill this gap.

Conclusions

This study established machine-learning models and nomograms for predicting PCNC and showed promising predictive performance. It has been demonstrated that the risk of PCNC in elderly patients may be reduced through the efforts by surgeons and anesthesiologists. However, regarding the limitations of the study such as external validation, data exclusion and ambiguity in complication categorization, the opportunity for further refinement is appreciated in the future.

Acknowledgments

Not applicable.

Consent for publication

This study did not contain personal identifiers; Therefore, there was no requirement to obtain individual patient consent.

Author contributions

CRediT: **Yaxuan Wang**: Conceptualization, Data curation, Funding acquisition, Methodology, Project administration, Software, Writing – original draft; **Shiyang Xie**: Funding acquisition, Investigation, Resources, Supervision, Visualization, Writing – review & editing; **Jiayun Liu**: Formal analysis, Investigation, Methodology, Validation; **He Wang**: Formal analysis, Investigation, Methodology, Software; **Jiangang Yu**: Conceptualization, Data curation, Formal analysis, Investigation, Supervision; **Wenya Li**: Data curation, Formal analysis, Resources, Supervision, Validation; **Aika Guan**: Data curation, Formal analysis, Methodology, Software, Validation, Visualization; **Shun Xu**: Conceptualization, Data curation, Supervision, Validation; **Yong Cui**: Methodology, Project administration, Supervision, Visualization, Writing – review & editing. **Wenfei Tan**: Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing.

Competing interests

No potential conflict of interest was reported by the author(s).

Preprint

This manuscript has been stored on a preprint server with relevant links(https://doi.org/10.21203/rs.3.rs-4164223/v1).

Funding

This work was supported by a grant from the National Natural Science Foundation of China (No. 82171187 to T.W.), the Wu Jieping Foundation (No.320.6750.2024-05-14 to T.W.), the Natural Science Foundation of Liaoning Province of China (No. 2022-MS-191 to S.X.) and the Natural Science Foundation of Liaoning Province of China (No. 2022-MS-222 to Y.W.).

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

References

[1] Smilowitz NR, Gupta N, Ramakrishna H, et al. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. JAMA Cardiol. 2017;2(2):181–187. Feb 1PMID: 28030663. doi: 10.1001/jamacardio.2016.4792.

[2] Smilowitz NR, Gupta N, Guo Y, et al. Perioperative acute myocardial infarction associated with non-cardiac surgery. Eur Heart J. 2017;38(31):2409–2417. Aug 14PMID: 28821166. doi: 10.1093/eurheartj/ehx313.

[3] Bateman BT, Schumacher HC, Wang S, et al. Perioperative acute ischemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. Anesthesiology. 2009;110(2):231–238. FebPMID: 19194149. doi: 10.1097/ALN.0b013e318194b5ff.

[4] Bessissow A, Khan J, Devereaux PJ, et al. Postoperative atrial fibrillation in non-cardiac and cardiac surgery: an overview. J Thromb Haemost. 2015;13(Suppl 1):S304–S12. JunPMID: 26149040. doi: 10.1111/jth.12974.

[5] Lin MH, Kamel H, Singer DE, et al. Perioperative/postoperative atrial fibrillation and risk of subsequent stroke and/or mortality. Stroke. 2019;50(6):1364–1371. JunPMID: 31043148. doi: 10.1161/STROKEAHA.118.023921.

[6] Lim E, Harris RA, McKeon HE, et al. Impact of video-assisted thoracoscopic lobectomy versus open lobectomy for lung cancer on recovery assessed using self-reported physical function: VIOLET RCT. Health Technol Assess. 2022;26(48):1–162. DecPMID: 36524582. doi: 10.3310/THBQ1793.

[7] Alban J, Kennedy K, Hulbert A, et al. Surgery for early-stage lung cancer with video-assisted thoracoscopic surgery versus open thoracotomy: a narrative review. Semin Oncol. 2022;49Aug 28. PMID: 36088130(3-4): 261–264. doi: 10.1053/j.seminoncol.2022.06.012.

[8] Riddersholm S, Tayal B, Kragholm K, et al. Incidence of stroke after pneumonectomy and lobectomy. Stroke. 2019;50(5):1052–1059. PMID: 31009351. d May. doi: 10.1161/STROKEAHA.118.024496.

[9] Giambrone GP, Wu X, Gaber-Baylis LK, et al. Incidence and implications of postoperative supraventricular tachycardia after pulmonary lobectomy. J Thorac Cardiovasc Surg. 2016;151(4):982–988. AprPMID: 26778376. doi: 10.1016/j.jtcvs.2015.11.057.

[10] Frendl G, Sodickson AC, Chung MK, et al. AATS guidelines for the prevention and management of perioper-

ative atrial fibrillation and flutter for thoracic surgical procedures. J Thorac Cardiovasc Surg. 2014;148(3):e153–93. 2014 SepPMID: 25129609. doi: 10.1016/j.jtcvs.2014.06.036.

[11] Vaporciyan AA, Correa AM, Rice DC, et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg. 2004;127(3):779–786. MarPMID: 15001907. doi: 10.1016/j.jtcvs.2003.07.011.

[12] Gómez-Hernández MT, Forcada C, Varela G, et al. Spanish Group of Video-assisted Thoracic S. Operating time: an independent and modifiable risk factor for short-term complications after video-thoracoscopic pulmonary lobectomy. Eur J Cardiothorac Surg. 2022;62(6) Nov :3. PMID: 36264130. doi: 10.1093/ejcts/ezac503.

[13] Mathis MR, Kheterpal S, Najarian K. Artificial intelligence for anesthesia: what the practicing clinician needs to know: more than black magic for the art of the dark. Anesthesiology. 2018; Oct129(4):619–622. PMID: 30080689. doi: 10.1097/ALN.0000000000002384.

[14] Hernesniemi JA, Mahdiani S, Tynkkynen JA, et al. Extensive phenotype data and machine learning in prediction of mortality in acute coronary syndrome - the MADDEC study. Ann Med. 2019;51(2):156–163. MarPMID: 31030570. doi: 10.1080/07853890.2019.1596302.

[15] Ren Y, Loftus TJ, Datta S, et al. Performance of a machine learning algorithm using electronic health record data to predict postoperative complications and report on a mobile platform. JAMA Netw Open. 2022;5(5):e2211973. May 2PMID: 35576007. doi: 10.1001/jamanetworkopen.2022.11973.

[16] Hu X-Y, Liu H, Zhao X, et al. Automated machine learning-based model predicts postoperative delirium using readily extractable perioperative collected electronic data. CNS Neurosci Ther. 2022;28(4):608–618. AprPMID: 34792857. doi: 10.1111/cns.13758.

[17] Li W, Liu Y, Liu W, et al. Machine learning-based prediction of lymph node metastasis among osteosarcoma patients. Front Oncol. 2022;12:797103. PMID: 35515104. doi: 10.3389/fonc.2022.797103.

[18] Li W, Dong S, Wang H, et al. Risk analysis of pulmonary metastasis of chondrosarcoma by establishing and validating a new clinical prediction model: a clinical study based on SEER database. BMC Musculoskelet Disord. 2021;22(1):529. Jun 9PMID: 34107945. doi: 10.1186/s12891-021-04414-2.

[19] Bijlsma S, Bobeldijk I, Verheij ER, et al. Large-scale human metabolomics studies: a strategy for data (pre-) processing and validation. Anal Chem. 2006;78(2):567–574. Jan 15PMID: 16408941. doi: 10.1021/ac051495j.

[20] Salati M, Migliorelli L, Moccia S, et al. A machine learning approach for postoperative outcome prediction: surgical data science application in a thoracic surgery setting. World j Surg. 2021;45(5):1585–1594. 2021 MayPMID: 33594578. doi: 10.1007/s00268-020-05948-7.

[21] Kadomatsu Y, Emoto R, Kubo Y, et al. Development of a machine learning-based risk model for postoperative complications of lung cancer surgery. Surg Today. 2024;54(12):1482–1489. Dec9. PMID: 38896280. doi: 10.1007/s00595-024-02878-y.

[22] Ramamoorthy V, Chan K, Appunni S, et al. Prevalence and trends of perioperative major adverse cardiovascular and cerebrovascular events during cancer surgeries. Sci Rep. 2023;13(1):2410. Feb 10PMID: 36765154. doi: 10.1038/s41598-023-29632-7.

[23] Bhave PD, Goldman LE, Vittinghoff E, et al. Incidence, predictors, and outcomes associated with postoperative atrial fibrillation after major noncardiac surgery. Am Heart J. 2012;164(6):918–924. DecPMID: 23194493. doi: 10.1016/j.ahj.2012.09.004.

[24] Danelich IM, Lose JM, Wright SS, et al. Practical management of postoperative atrial fibrillation after noncardiac surgery. J Am Coll Surg. 2014;219(4):831–841. OctPMID: 25127508. doi: 10.1016/j.jamcollsurg.2014.02.038.

[25] Vlisides P, Mashour GA. Perioperative stroke. Can J Anaesth. 2016; Feb63(2):193–204. PMID: 26391795. doi: 10.1007/s12630-015-0494-9.

[26] Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, nonneurologic surgery. Anesthesiology. 2011; Jun114(6):1289–1296. PMID: 21478735. doi: 10.1097/ALN.0b013e318216e7f4.

[27] Wilcox T, Smilowitz NR, Xia Y, et al. Cardiovascular risk factors and perioperative myocardial infarction after noncardiac surgery. Can J Cardiol. 2021;37(2):224–231. FebPMID: 32380229. doi: 10.1016/j.cjca.2020.04.034.

[28] Smilowitz NR, Berger JS. Perioperative cardiovascular risk assessment and management for noncardiac surgery: a review. JAMA. 2020; 324(3):279–290. PMID: 32692391. doi: 10.1001/jama.2020.7840.

[29] Heise D, Bednarsch J, Kroh A, et al. Operative time, age, and serum albumin predict surgical morbidity after laparoscopic liver surgery. Surg Innov. 2021;28(6):714–722. DecPMID: 33568020. doi: 10.1177/1553350621991223.

[30] Surace P, Sultan AA, George J, et al. The association between operative time and short-term complications in total hip arthroplasty: an analysis of 89,802 surgeries. J Arthroplasty. 2019;34(3):426–432. MarPMID: 30528133. doi: 10.1016/j.arth.2018.11.015.

[31] Bugada D, Lorini LF, Lavand'homme P. Opioid free anesthesia: evidence for short and long-term outcome. Minerva Anestesiol. 2021; Feb87(2):230–237. PMID: 32755088. doi: 10.23736/S0375-9393.20.14515-2.

[32] Massoth C, Schwellenbach J, Saadat-Gilani K, et al. Impact of opioid-free anaesthesia on postoperative nausea, vomiting and pain after gynaecological laparoscopy - A randomised controlled trial. J Clin Anesth. 2021;75Dec;75::110437. PMID: 34229292. doi: 10.1016/j.jclinane.2021.110437.

[33] Ziemann-Gimmel P, Goldfarb AA, Koppman J, et al. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. Br J Anaesth. 2014;112(5):906–911. MayPMID: 24554545. doi: 10.1093/bja/aet551.

[34] Cozowicz C, Olson A, Poeran J, et al. Opioid prescription levels and postoperative outcomes in orthopedic surgery. Pain. 2017; Dec158(12):2422–2430. PMID: 28891865. doi: 10.1097/j.pain.0000000000001047.

[35] D'Amico F, Barucco G, Licheri M, et al. Opioid free anesthesia in thoracic surgery: a systematic review and meta analysis. J Clin Med. 2022;11(23):6955. Nov 25PMID: 36498529. doi: 10.3390/jcm11236955.

[36] Shanthanna H, Ladha KS, Kehlet H, et al. Perioperative opioid administration. Anesthesiology. 2021;134(4):645–659. PMID: 32991672. doi: 10.1097/aln.0000000000003572.

[37] Frauenknecht J, Kirkham KR, Jacot-Guillarmod A, et al. Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis. Anaesthesia. 2019; 74(5):651–662. PMID: 30802933. doi: 10.1111/anae.14582.

[38] Szczepaniak A, Machelak W, Fichna J, et al. The role of kappa opioid receptors in immune system - An overview. Eur J Pharmacol. 2022;933:175214. Oct 15PMID: 36007608. doi: 10.1016/j.ejphar.2022.175214.

[39] Wang Q, Liu Z, Tang S, et al. Morphine suppresses the immune function of lung cancer by up-regulating MAEL expression. BMC Pharmacol Toxicol. 2022;23(1):92. PMID: 36476246. doi: 10.1186/s40360-022-00632-z.

[40] Grass JA. Patient-controlled analgesia. Anesth Analg. 2005; Nov101(5 Suppl):S44–S61. PMID: 16334492. doi: 10.1213/01.ANE.0000177102.11682.20.

[41] Salicath JH, Yeoh EC, Bennett MH. Epidural analgesia versus patient-controlled intravenous analgesia for pain following intra-abdominal surgery in adults. Cochrane Database Syst Rev. 2018; 8(8):CD010434. PMID: 30161292. doi: 10.1002/14651858.CD010434.pub2.

[42] Kissin I. Patient-controlled-analgesia analgesimetry and its problems. Anesth Analg. 2009; 108(6):1945–1949. PMID: 19448227. doi: 10.1213/ane.0b013e3181a1a481.

[43] Momeni M, Crucitti M, De Kock M. Patient-controlled analgesia in the management of postoperative pain. Drugs. 2006;66(18):2321–2337. PMID: 17181375. doi: 10.2165/00003495-200666180-00005.

[44] van Boekel RLM, Warlé MC, Nielen RGC, et al. Relationship between postoperative pain and overall 30-day complications in a broad surgical population: an observational study. Ann Surg. 2019; May269(5):856–865. PMID: 29135493. doi: 10.1097/SLA.0000000000002583.

[45] Knoll H, Ziegeler S, Schreiber JU, et al. Airway injuries after one-lung ventilation: a comparison between double-lumen tube and endobronchial blocker: a randomized, prospective, controlled trial. Anesthesiology. 2006;105(3):471–477. PMID: 16931978. doi: 10.1097/00000542-200609000-00009.

[46] Clayton-Smith A, Bennett K, Alston RP, et al. A comparison of the efficacy and adverse effects of double-lumen endobronchial tubes and bronchial blockers in thoracic surgery: a systematic review and meta-analysis of randomized controlled trials. J Cardiothorac Vasc Anesth. 2015;29(4):955–966. AugPMID: 25753765. doi: 10.1053/j.jvca.2014.11.017.