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Development and validation of a prediction model for post-induction hypotension in elderly patients undergoing non-cardiac surgery: a prospective cohort study

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Abstract

Backgrounds Post-induction hypotension (PIH) is prevalent in elderly surgical patients and associated with adverse outcomes; however, predicting PIH remains challenging. We aimed to develop a feasible and practical PIH prediction model for elderly patients undergoing non-cardiac surgery.

Methods In this single-center prospective cohort study, 938 elderly patients undergoing non-cardiac surgery were enrolled from December 2022 to May 2023 ($n=657$ in the development cohort) and from June 2023 to August 2023 ($n=281$ in the temporal validation cohort), respectively. The study outcome was the occurrence of PIH, defined as hypotension during the first 15 min after anesthesia induction or until skin incision (whichever occurred first). Predictors were determined based on LASSO and logistic regression analyses. A nomogram and a dynamic application were used for model visualization. The internal and temporal validation were performed to evaluate the discriminability, calibration and clinical utility.

Results The median age was 71 years in both cohorts. The incidence of PIH was 51.6% and 50.5% in the development and validation cohorts, respectively. Cardiac function, baseline mean arterial pressure in the ward, etomidate use, and pre-induction mean arterial pressure were determined as predictors. The PIH prediction model was visualized as a nomogram and a dynamic application. The area under the receiver operating characteristic curve was 0.680 (95% confidence interval [CI]: 0.639 to 0.720) in internal validation and 0.697 (95% CI: 0.635 to 0.759) in temporal validation. The mean absolute errors were 0.012 and 0.029 for the internal and temporal validation calibration curves, respectively. The Brier score was 0.223. The decision curve analysis indicated that the model had a gain in predicting PIH.

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Conclusion A PIH prediction model with four predictors was developed and validated for elderly patients undergoing non-cardiac surgery. This model provides a foundation for future refinements to enhance its value of assisting clinical decision-making across diverse healthcare settings.

Trial registration This study was registered at the Chinese Clinical Trial Registry (ChiCTR2200066201).

Keywords Prediction model, Post-induction hypotension, Elderly patients, Non-cardiac surgery

Introduction

Post-induction hypotension (PIH) refers to hypotension occurring within 15 min after general anesthesia induction or until surgical incision (whichever occurs first) [1]. It is reported that PIH could account for approximately half of perioperative hypotension events in patients undergoing non-cardiac surgeries [2]. Hypotension is correlated with postoperative complications, prolonged length of hospitalization, and increased mortality, especially in elderly patients [3–5]. In comparison with intraoperative hypotension, PIH is more foreseeable because of its preoperative existing risk factors, such as advanced age, comorbidities, autonomic nervous system function, and volume status [6–8].

Several new predictors and models for PIH have emerged, including inferior vena cava ultrasound for intravascular volume, dynamic arterial elastance for arterial load, and dynamic pupillometry for autonomic function [9–11]. However, it may be difficult to use these tools in clinical practice due to the need for specific equipment or techniques. For the existing PIH prediction models, some were developed from retrospective studies with restricted data and factors, and some were derived from a specific type of surgery [12–14].

Therefore, we designed this prospective cohort study to establish a practical PIH prediction model for elderly patients undergoing non-cardiac surgery. We specifically focused on the elderly patients receiving general anesthesia with intravenous induction and tracheal intubation. With the use of this model, anesthesia providers can be more alert to PIH events and take appropriate precautions in advance.

Methods

Ethics statement

This single-center prospective cohort study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University (N° 2022 – 443, Chairperson Prof. Yitao Xu) on 8 November 2022 and registered at the Chinese Clinical Trial Registry (http://www.chictr.org.cn, identifier: ChiCTR2200066201) on 28 November 2022. To revise the scientific title for a better description of this study, we obtained an ethical approval update (N° 2023-012, Chairperson Prof. Yitao Xu) on 10 January 2023. The registration identifier remained unchanged. Informed consent to participate was obtained from all of the participants in the study. This study was reported following the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) checklist [15]. The study protocol has been published previously [16].

Study population

Between December 2022 and August 2023, we enrolled elderly patients aged ≥ 65 years with the American Society of Anesthesiologists physical status classifications I to III and scheduled for elective non-cardiac surgery (estimated duration ≥ 30 min) under general anesthesia with tracheal intubation. The exclusion criteria were as follows: (1) severe heart, brain, liver, kidney, or lung dysfunction which may lead to hemodynamic instability; (2) induction with volatiles, use of nerve blocks, spinal or epidural anesthesia; (3) tracheotomy, or pre-existing tracheal tube; or (4) refusal for participation. Additionally, patients who underwent two or more attempts of intubations were excluded from analysis.

Outcome measure

The study outcome was the occurrence of PIH, defined as hypotension during the first 15 min after anesthesia induction or until skin incision (whichever occurred first). The diagnosis of hypotension was based on a relative decrease in mean arterial pressure (MAP) ≥ 30% relative to baseline or an absolute MAP value ≤ 65 mmHg [4, 17, 18]. The baseline MAP was obtained in the ward preoperatively (using the average of multiple measurements to account for intra-individual variability). In the operating room, non-invasive cuff blood pressure was monitored on a single arm at a 1-min interval, aiming to ensure timely identification of PIH [16, 19]. During the data analysis phase, we utilized the traditional formula to calculate the MAP value at each time point: diastolic pressure + 0.33×pulse pressure [20].

Potential predictors

All candidate predictors were based on the published protocol (**supplemental file 1**) [16, 21]. On the day before surgery, a research assistant identified eligible patients and recorded preoperative potential predictors by reviewing electronic medical records and acquiring patients' self-report data. Demographics, ASA classifications, comorbidities, autonomic function, cardiac

function, vital signs, anxiety, and frailty status were collected. Demographic data included age, sex, and body mass index (BMI). Comorbidities included hypertension, diabetes mellitus, and age-adjusted Charlson Comorbidity index (aCCI) score. Autonomic and cardiac functions were assessed based on history, recent symptoms, and preoperative examination. Vital signs included baseline MAP and heart rate (HR) in the ward. Anxiety was assessed using the first four items of the Amsterdam Preoperative Anxiety and Information Scale (APAIS) [22]. Frailty status was evaluated using the FRAIL scale [23, 24].

On the day of surgery, the research assistant recorded the following potential predictors: duration of fasting (from 22:00 the day before surgery), preoperative volume of fluid infusion, regular MAP and HR values before induction, and anesthetics for induction (including propofol, ciprofol, etomidate, esketamine, fentanyl, and sufentanil).

Sample size Estimation

According to the existing literature [2, 25], the rate of PIH in elective non-cardiac surgery was approximately 35%. Based on the principle of at least 10 events per variable [26–28], 657 patients (multiply 23 by 10 and then divided by 35%) should be enrolled for the model construction and internal validation. In addition, 281 patients were continuously enrolled for temporal validation, in which the prediction model was evaluated in another time period [29]. Therefore, this study included a total of 938 patients.

Statistical analysis

Normally distributed variables were described as mean ± standard deviation (SD) and analyzed using the student t-test. Non-normally distributed variables are shown as median with interquartile range (IQR) and were analyzed using the Mann-Whitney U test. Categorical variables were presented as numbers (%) and were analyzed using the $\chi 2$ test or Fisher's exact test. We used absolute standardized differences (ASD) to compare the baseline characteristics between the two cohorts, and an ASD ≥ 0.14 indicated imbalance (i.e., $1.96\times \sqrt{(657+281)\,/\,(657\times\ 281)}$) [30]. Variables with ≤ 5% missing data were handled by multiple imputations, while variables with > 5% were excluded from the analysis.

For model development ($n=657$), we applied least absolute shrinkage and selection operator (LASSO) regression with 10-fold cross-validation for variable shrinkage and selection. Based on the best lambda value, we performed multivariable logistic regression analysis to exam the potential interactions (variance inflation factor [VIF] ≥ 10 means severe interactions) and to determine the predictors with statistical significance ($P<0.05$) for model construction. The final model was visualized as a nomogram, and a dynamic application was developed using the "Shiny" package. Internal validation was performed by bootstrapping method ($n=1000$). Temporal validation was performed in another cohort ($n=281$). Discriminative ability was assessed using the area under the receiver operating characteristic curve (AUC), and sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were also reported. The calibration was evaluated using the Hosmer-Lemeshow goodness-of-fit statistic, calibration curves and the Brier score. Calibration curves were used to measure the consistency between the predicted probability of the model and the actual observed results. In the calibration curves, the apparent curve represents the relationship between the predicted probability of the model and the actual observed probability, while the bias-corrected curve is the result of correcting the apparent curve [31, 32]. The Brier score reflects the mean squared difference between the observations and predictions, with lower values indicating higher accuracy (ranging from 0 to 100) [33]. Moreover, the clinical utility of the model was assessed using the decision curve analysis (DCA). DCA quantifies the net benefit of using the model and determines whether treating all or no patients is superior to the model, across the reasonable threshold probabilities [34, 35]. Statistical analyses were conducted using SPSS software (v 26.0, IBM SPSS, Chicago, Illinois, USA) and R software (v 4.2.2, www.R-project.org/).

Results

Patient characteristics

Among 1225 elderly patients screened, we enrolled a consecutive sample of 938 eligible patients undergoing noncardiac surgery, with 657 (70%) in the development cohort from December 2022 to May 2023 and 281 (30%) in the validation cohort from June 2023 to August 2023 (Fig. 1). All data were prospectively collected, and there were no missing data. Baseline data and candidate predictors are listed in Table 1.

The incidence of PIH

A total of 481 patients (51.3%) developed the PIH events, including 339 (51.6%) in the development cohort and 142 (50.5%) in the validation cohort (Table 2). In the post-hoc analysis, 42.2% of patients had MAP ≤ 65 mmHg, 44.8% of patients showed a relative decrease in MAP > 30% from baseline, and 44.8% of patients experienced PIH that lasted for 1 min. No significant differences were observed between the two cohorts in terms of the hypotension rates.

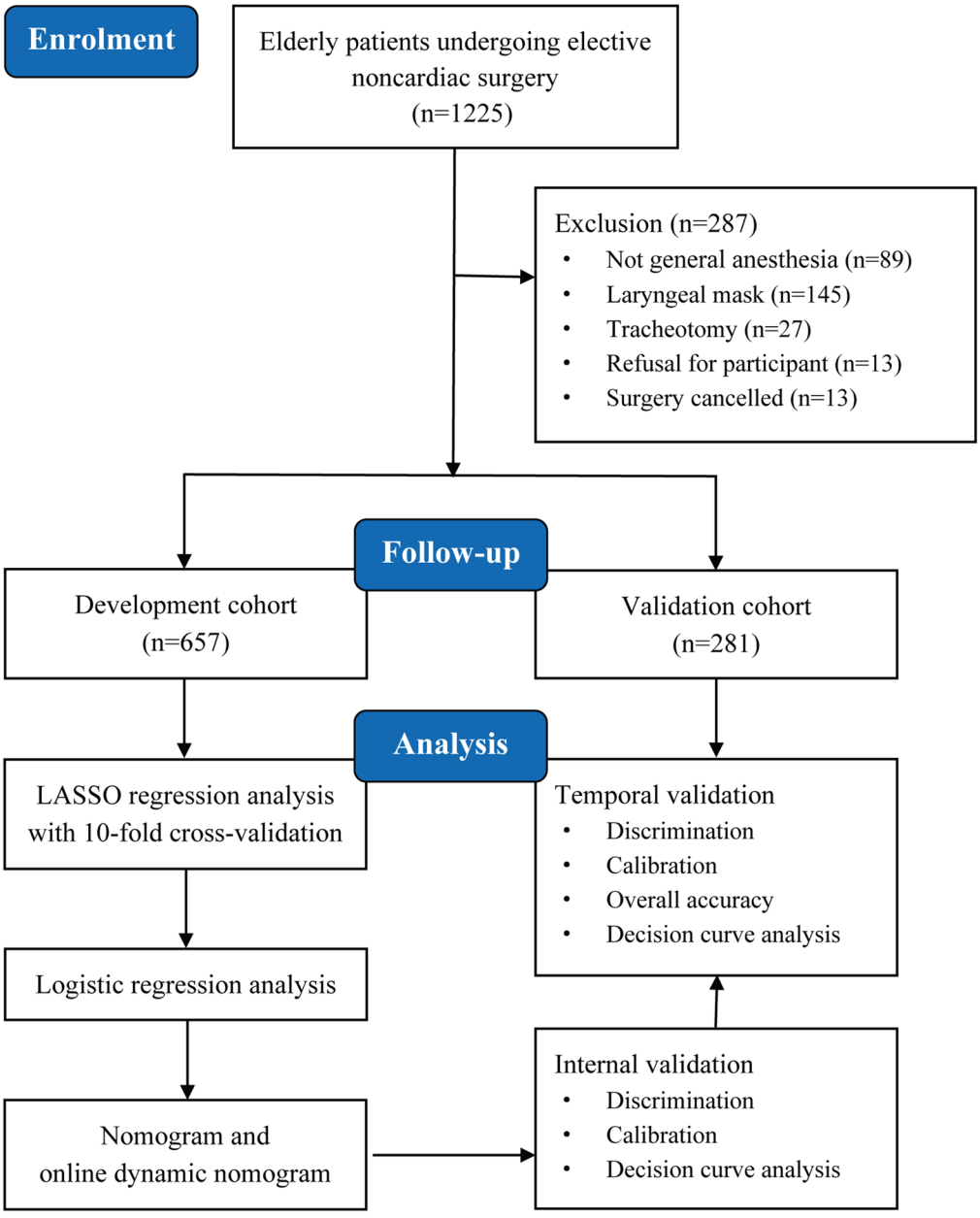

Fig. 1 Study flow chart. *Abbreviation*: LASSO, least absolute shrinkage and selection operator

Selection of predictors

Based on the LASSO regression (Fig. S1) and multivariate logistic regression analysis, we identified four variables (cardiac function, baseline MAP in the ward, etomidate, and pre-induction MAP) to establish the PIH prediction model (Table 3). All VIF values were approximately 1, representing low interactions.

Development and validation of the model

Based on these four predictors, a nomogram was developed (Fig. 2A). In addition, we developed an app to facilitate the use of this PIH prediction model in clinical scenarios (Fig. 2B). For a male elderly patient who had cardiac dysfunction, MAP of 90 mmHg in the ward and 85 mmHg before induction without the use of etomidate, his risk of PIH would be 77.2% (95% confidence interval [CI]: 69.5%–83.4%).

For internal validation, the AUC was 0.680 (95% CI: 0.639 to 0.720) (Fig. 3A), with sensitivity of 0.720 and specificity of 0.580 (PPV = 0.628 and NPV = 0.687). The value of the mean absolute error was 0.012 in the calibration curve (Fig. 3B), with a Hosmer-Lemeshaw goodness-of-fit statistic result of 0.652, suggesting a good agreement between the predicted and observed cases. The DCA curve showed that the prediction model had

Table 1 Comparison of characteristics between two cohorts

	Development cohort (*n* = 657)	Validation cohort (*n* = 281)	*P* value	ASD
Age, years	71 (68, 75)	71 (68, 76)	0.146	0.137
Male sex	351 (53.4%)	139 (49.5%)	0.266	0.078
BMI, $kg{\cdot}m^{-2}$	23 (21, 25)	23 (21, 25)	0.979	0.009
ASA classifications				
I	15 (2.3%)	8 (2.8%)	0.623	0.031
II	487 (74.1%)	214 (76.2%)		0.049
III	155 (23.6%)	59 (21%)		0.062
Comorbidities				
Hypertension	394 (60%)	180 (64.1%)	0.239	0.085
Diabetes mellitus	139 (21.2%)	58 (20.6%)	0.859	0.015
aCCI	5 (3, 6)	4 (3, 6)	0.017	0.171
Autonomic dysfunction	42 (6.4%)	17 (6%)	0.843	0.017
Cardiac dysfunction	453 (68.9%)	201 (71.5%)	0.431	0.057
MAP in the ward, mmHg	95 (88.5, 103)	96 (89, 101.5)	0.675	0.025
HR in the ward, bpm	74 (68, 78)	75 (70, 79)	< 0.001	0.263
Preoperative anxiety score	11 (8, 13)	12 (12, 16)	< 0.001	0.62
Preoperative frailty score	1 (1, 2)	0 (0, 1)	< 0.001	1.6
Fluid infusion, mL	200 (0, 500)	0 (0, 200)	0.001	0.337
Fasting duration, h [a]	13 (10, 16)	10 (10, 14)	< 0.001	0.399
Pre-induction MAP, mmHg	101 (94, 111)	103 (94, 113)	0.523	0.066
Pre-induction HR, bpm	72 (64, 80)	70 (63, 80)	0.332	0.002
Anesthetics				
Use of propofol	202 (30.7%)	53 (18.9%)	< 0.001	0.276
Use of ciprofol	315 (47.9%)	151 (53.7%)	0.104	0.116
Use of etomidate	400 (60.9%)	165 (58.7%)	0.535	0.045
Use of esketamine	44 (6.7%)	20 (7.1%)	0.815	0.016
Dose of sufentanil, μg	25 (20, 30)	20 (20, 25)	0.071	0.129

Data are presented as median (IQR) or number (%)

[a] Since 22:00 the day before surgery

Abbreviations: *BMI* body mass index, *ASA-PS* American Society of Anesthesiologists physical status classification, *aCCI* age-adjusted Charlson comorbidity index, *MAP* mean arterial pressure, *HR* heart rate, *ASD* absolute standardized differences

Table 2 Incidence of PIH

	Total (*n* = 938)	Development cohort (*n* = 657)	Validation cohort (*n* = 281)	*P* value
PIH [a]	481 (51.3%)	339 (51.6%)	142 (50.5%)	0.765
Post-hoc analysis				
MAP ≤ 65 mmHg	396 (42.2%)	278 (42.3%)	118 (42.0%)	0.927
Decrease in MAP > 30%	420 (44.8%)	292 (44.4%)	128 (45.6%)	0.755
PIH lasting for 1 min	420 (44.8%)	295 (44.9%)	125 (44.5%)	0.906

Data are presented as number (%)

[a] Defined as an absolute MAP ≤ 65 mmHg or a relative decrease in MAP > 30% of baseline (MAP in the ward)

Abbreviations: *PIH* post-induction hypotension, *MAP* mean arterial pressure

Table 3 Final predictors for the model

	VIF	β	SE	OR (95% CI)	*P* value
(Intercept)		1.530	0.849	4.616 (0.874 – 23.374)	0.072
Cardiac dysfunction	1.039	0.456	0.181	1.577 (1.106 – 2.250)	0.012
MAP in the ward	1.298	0.039	0.009	1.040 (1.022 – 1.059)	< 0.001
The use of etomidate	1.008	-0.608	0.170	0.544 (0.390 – 0.760)	< 0.001
Pre-induction MAP	1.265	-0.051	0.008	0.951 (0.936 – 0.966)	< 0.001

Abbreviations: *VIF* variance inflation factor, *SE* standard error, *OR* odds ratio, *CI* confidence interval, *MAP* mean arterial pressure

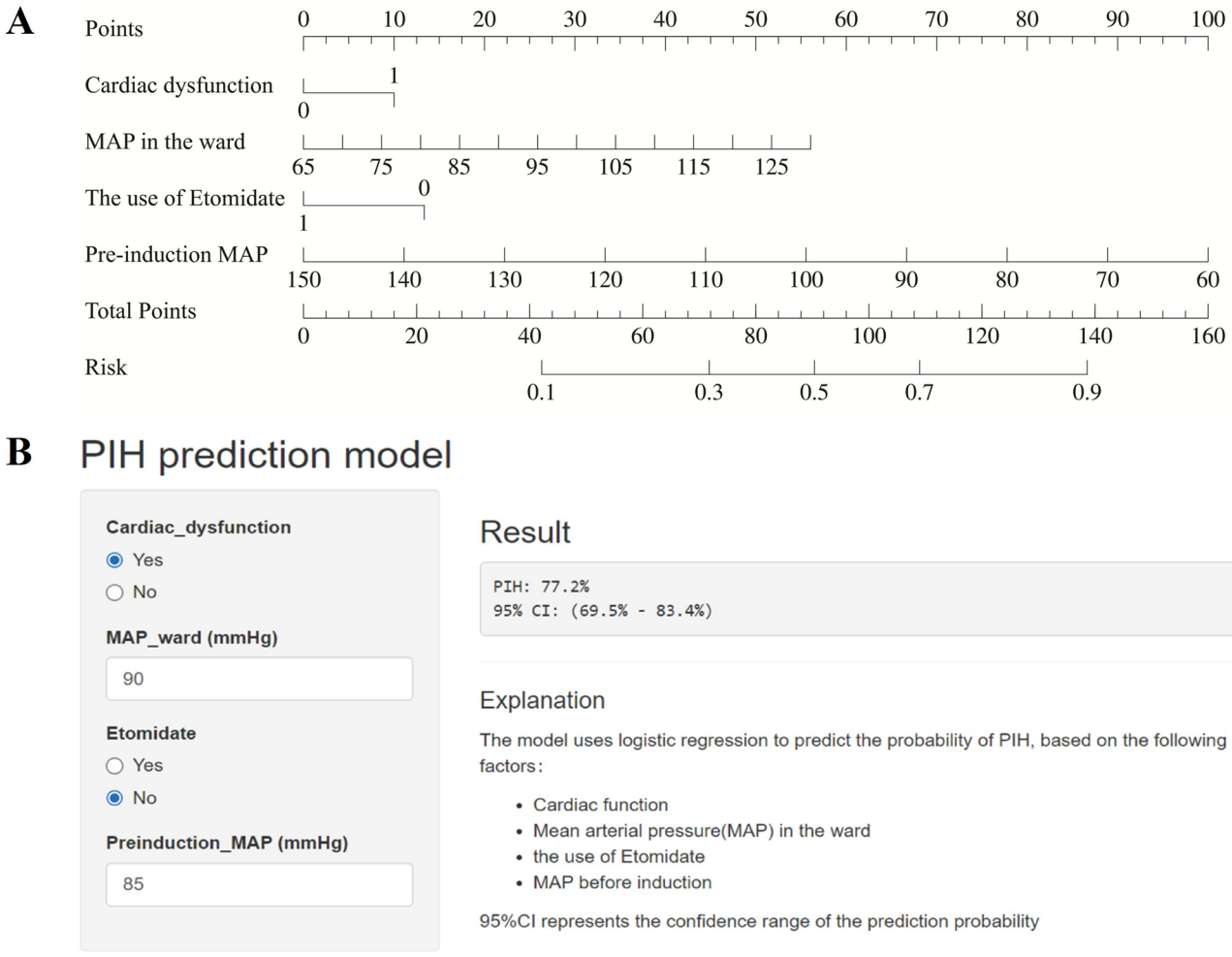

Fig. 2 Visualization for the prediction of post-induction hypotension. (**A**) Nomogram. Each predictor has a vertical line ("axis") labeled with its values (e.g., for cardiac dysfunction, the axis ranges from 0 to 1). First, for a specific value (e.g., cardiac dysfunction = 1), draw a vertical line upward to the Points axis to find the corresponding score. Repeat this for all predictors. Next, add all the points from the individual predictors to get the total points. Finally, draw a vertical line from the Total Points axis to the Risk axis to read the predicted probability; (**B**) The interface of dynamic app with an example patient. *Abbreviation*: MAP, mean arterial pressure

a gain in predicting PIH in most of the elderly patients (Fig. 3C).

For temporal validation, the AUC was 0.697 (95% CI: 0.635 to 0.759) (Fig. 3D), with sensitivity of 0.634 and specificity of 0.698 (PPV = 0.703 and NPV = 0.627). The value of the mean absolute error was 0.029 (Fig. 3E), with a Hosmer-Lemeshaw test result of 0.274 and a Brier score of 0.223. The DCA curve was similar to that of the internal validation (Fig. 3F).

Discussion

In this study, a preliminary prediction model for PIH was developed based on prospectively collected data, and this model was validated temporally. Cardiac dysfunction, high baseline MAP in the ward, etomidate not used for induction, and a relative low pre-induction MAP were risk factors for PIH. In both the internal and temporal validation cohorts, the model performance was consistent, suggesting there is no overfitting in the model training process. Both of the AUC values were approximately 0.7 with low mean absolute errors. A Brier score of 0.223 showed the model was well calibrated in that the predicted probabilities were close to the actual event rates. Furthermore, The DCA curves suggest that the application of this model can help in clinical decision-making.

There were three hemodynamic factors for PIH prediction in this model. Among them, cardiac dysfunction and a high MAP in the ward were the risk factors, whereas a high pre-induction MAP was a protecting factor. Recent studies found hypertension history and abnormal preoperative echocardiographic parameters contributed to a higher PIH rate during noncardiac surgery [36, 37]. In contrast, perioperative fluid therapy helped to prevent PIH [38, 39]. In light of the pathophysiological

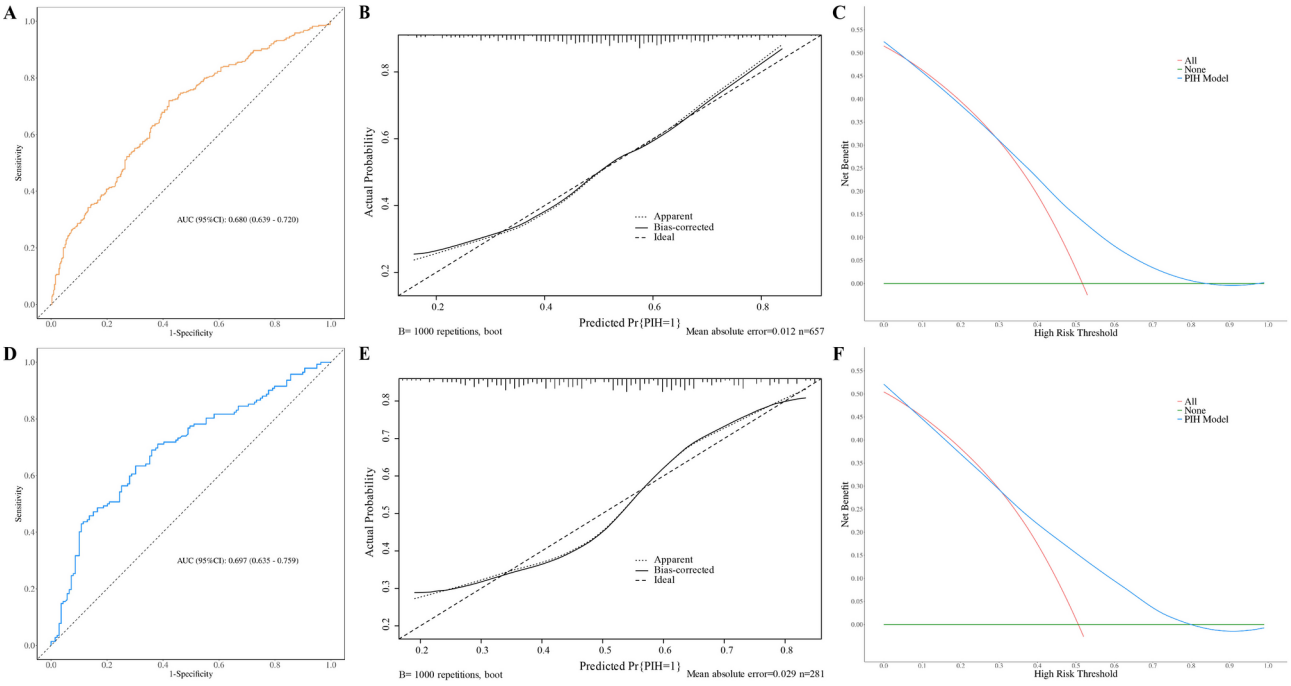

Fig. 3 Validation of the prediction model. (**A**) Receiver operating characteristic curve in the internal validation; (**B**) Calibration curve in the internal validation; (**C**) Decision curve analysis in the internal validation; (**D**) Receiver operating characteristic curve in the temporal validation; (**E**) Calibration curve in the temporal validation; (**F**) Decision curve analysis in the temporal validation

mechanisms, cardiovascular abnormalities are predominant, including suppression of myocardial contractility, preload reduction caused by venous dilatation, reduced vascular resistance after arterial dilation, and baroreceptor inhibition [40–42]. A high MAP in the ward often indicated poor blood pressure control and abnormal cardiac function, while a relatively higher pre-induction MAP may reflect an adequate volume status and an overall good condition of sympathetic activity. For our patients, the baseline MAP was determined in the ward, reflecting a normal condition and avoiding possible impact by the operating room environment and preoperative fasting [18]. The interval of blood pressure measurement was set at every 1 min to increase the ability to detect PIH. The observed incidence of PIH in our study was 51.3%, which is in line with the results of recent cohort studies and randomized controlled trials [18, 19, 39, 43].

It is noteworthy that severe cardiac dysfunction with existing hemodynamic instability was an exclusion criterion in this study because such patients usually had very low left atrial ejection fraction (< 30%) and were already at high risk of PIH. However, the 'cardiac dysfunction' factor of the model was evaluated through relative anamneses and preoperative examinations, especially for the asymptomatic patients. The use of anesthetics is a strong factor that influences the occurrence of PIH. For patients included in this study, propofol, ciprofol, etomidate, and esketamine were used for anesthesia induction. We found that the use of etomidate was associated with a decreased occurrence of PIH. It has been confirmed that etomidate has a superior hemodynamic profile in comparison with propofol for patients undergoing either noncardiac or cardiac surgery [44]. A recent trial showed that a target-controlled infusion of etomidate was noninferior to propofol in terms of overall major in-hospital morbidity [45]. Two studies based on the National Emergency Airway Registry found that etomidate caused less postintubation hypotension compared with ketamine [46, 47]. Nevertheless, the comparison between ciprofol and etomidate is yet to be studied. In our clinical practice, most patients (~ 60%) received etomidate during induction. Regarding the analgesics, studies have shown that sufentanil is not associated with an increased risk of PIH [21, 42].

The predictors identified in our study (e.g., baseline blood pressure, cardiac function) are indeed recognized by clinicians as risk factors for PIH. However, the novelty of this work lies in synthesizing these factors into a validated, user-friendly tool tailored for elderly non-cardiac surgical patients. Compared with previous studies [12–14], our predictive model was based on prospectively collected data and a published protocol [16]. To our knowledge, this is the first prospective model to explicitly focus on elderly patients in non-cardiac settings, a population with unique physiological vulnerabilities.

However, this study has some limitations. First, 23 candidate predictors were selected based on the literature, and only four of them were finally selected for model

development. On one hand, the potential interactions between predictors should be taken into consideration; on the other hand, it is also important to increase data diversity and precision (e.g. by including more laboratory examination results). Second, the endpoint event was only PIH. For elderly patients, intraoperative hypotension and related outcomes (such as acute kidney injury and myocardial injury) require further research. Third, the effects of anesthetics on blood pressure are dose-dependent. However, considering the various medication strategies, we only include the use of specific anesthetics as predictors. Fourth, the target population was elderly patients scheduled for general anesthesia with tracheal intubation, excluding the procedures with prior nerve blocks and the use of laryngeal mask. Finally, while our model provides a clinically feasible tool for PIH prediction, an AUC of ~0.7 underscores the need for further optimization. Future studies could integrate advanced machine learning algorithms (e.g., ensemble methods) and more preoperative data to improve performance. Multicenter collaborations may also help validate and refine the model across diverse populations, ensuring broader applicability.

Conclusion

PIH is prevalent among elderly patients undergoing non-cardiac surgery. Our study identified several key risk factors for PIH, including cardiac dysfunction, elevated preoperative MAP in the ward, no use of etomidate, and low pre-induction MAP. By utilizing prospectively collected clinical data, we have developed and validated a preliminary model for the early prediction of PIH. This model provides a foundation for future refinements and improvements, with the ultimate goal of enhancing its value of assisting clinical judgment across diverse healthcare settings.

Abbreviations

aCCI	Age-adjusted Charlson Comorbidity index
APAIS	Amsterdam Preoperative Anxiety and Information Scale
ASA-PS	American Society of Anesthesiologists Physical Status Classification
ASD	Absolute standardized differences
AUC	Area under the receiver operating characteristic curve
BMI	Body mass index
CI	Confidence interval
DCA	Decision curve analysis
LASSO	Least absolute shrinkage and selection operator
MAP	Mean arterial pressure
OR	Odds ratio
PIH	Post-induction hypotension
VIF	Variance inflation factor

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-03090-2.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3: Fig. S1 LASSO selection path diagram. (A) LASSO selection path plot: the left vertical dashed line indicates the minimum error (lambda.min), and the right dashed line indicates one standard error away from the minimum error (lambda.lse). (B) LASSO path plot: the curve of regression coefficients versus Log(lambda) as the coefficient scores are gradually decreasing. Abbreviation: LASSO, least absolute shrinkage and selection operator.

Supplementary Material 4

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Author contributions

Z. Bian, J. Hu and K. Peng: Study design; Z.Bian, W. Dou and H. Shi: Execution, acquisition of data; W. Dou and Y. Ying: Analysis and interpretation of data; Y. Ying: Preparing figures and tables; Z. Bian and J. Hu: Drafting the manuscript; F. Ji and K. Peng: Revising the manuscript and giving final approval of the version of the manuscript. All authors reviewed the manuscript.

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Data availability

The datasets and the preliminary dynamic app during the study are available from the corresponding authors on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and clinical study regulations from the Ethics Committee of the First Affiliated Hospital of Soochow University. This ethical approval of this study was obtained from the Ethics Committee of the First Affiliated Hospital of Soochow University (N° 2022 – 443, Chairperson Prof. Yitao Xu) on 8 November 2022. Then, this study was registered at the Chinese Clinical Trial Registry (http://www.chictr.org.cn, identifier: ChiCTR2200066201) on 28 November 2022. To revise the scientific title for a better description of this study, an ethical update was approved (N° 2023-012, Chairperson Prof. Yitao Xu) on 10 January 2023, but the registry identifier remained unchanged. Informed consent to participate was obtained from all of the participants in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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