# Clinical risk score for postoperative pneumonia following heart valve surgery

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**Abstract**

**Background:** Postoperative pneumonia (POP) is one of the most common infections following heart valve surgery (HVS) and is associated with a significant increase in morbidity, mortality, and health care costs. This study aimed to identify the major risk factors associated with the occurrence of POP following HVS and to derive and validate a clinical risk score.

**Methods:** Adults undergoing open HVS between January 2016 and December 2019 at a single institution were enrolled in this study. Patients were randomly assigned to the derivation and validation sets at 1:1 ratio. A prediction model was developed with multivariable logistic regression analysis in the derivation set. Points were assigned to independent risk factors based on their regression coefficients.

**Results:** POP occurred in 316 of the 3853 patients (8.2%). Multivariable analysis identified ten significant predictors for POP in the derivation set, including older age, smoking history, chronic obstructive pulmonary disease, diabetes mellitus, renal insufficiency, poor cardiac function, heart surgery history, longer cardiopulmonary bypass, blood transfusion, and concomitant coronary and/or aortic surgery. A 22-point risk score based on the multivariable model was then generated, demonstrating good discrimination (C-statistic: 0.81), and calibration (Hosmer-Lemeshow $\chi^2 = 8.234$, $P = 0.312$). The prediction rule also showed adequate discriminative power (C-statistic: 0.83) and calibration (Hosmer-Lemeshow $\chi^2 = 5.606$, $P = 0.691$) in the validation set. Three risk intervals were defined as low-, medium-, and high-risk groups.

**Conclusion:** We derived and validated a 22-point risk score for POP following HVS, which may be useful in preventive interventions and risk management.

**Trial Registration:** Chictr.org, ChiCTR1900028127; http://www.chictr.org.cn/showproj.aspx?proj=46932

**Keywords:** Postoperative pneumonia; Heart valve surgery; Risk factor; Prediction model; Risk score

## Introduction

Postoperative pneumonia (POP) is one of the most common infections following heart valve surgery (HVS) and is closely associated with a significant increase in morbidity, mortality, and treatment costs.[1,2] The incidence of POP after cardiac surgery varies widely between 2.1% and 21.6% in publications.[3,4]

Numerous studies attempted to identify the predictors of POP after cardiac surgery, and several risk factors have been recognized.[1,5] However, many reports were based on small sample sizes and were decades old.[4,6-8] Great progress in anesthesia and surgical techniques has been made, and the characteristics of patients undergoing heart surgery have changed over the years. Furthermore, the emergence and prevalence of some drug-resistant bacteria have markedly increased the risk of POP.[9] In addition, the majority of studies were completed in patients undergoing multiple types of surgery including coronary artery bypass graft (CABG), but a convincing prediction model specific to POP following HVS is still lacking.[10-12] Therefore, a better understanding of factors that influence the occurrence of POP following HVS is essential, and a validated prediction rule is still in urgent need.

The purpose of this observational study was to identify independent predictors for the occurrence of POP following HVS in adult patients and to derive and validate a clinical risk score.

## Methods

### *Ethical approval*

The study was conducted according to the ethics statement of the *Declaration of Helsinki*, and it was approved by the Ethics Committee of Tongji Medical

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College of Huazhong University of Science and Technology (No. IORG0003571). Written informed consent was not required due to the retrospective, observational nature of this study.

### Study population

We conducted a retrospective, single-center, observational study incorporating consecutive patients who underwent HVS between January 2016 and December 2019. Exclusion criteria were as follows: (1) aged <18 years; (2) pneumonia within 2 weeks before surgery; (3) immunosuppression, immunodeficiency, or organ transplantation; (4) discharge or death within 48 h after surgery; and (5) incomplete medical records.

### Data collection

We acquired data from the electronic medical record system of our hospital. Factors that may associate with the development of POP were collected and analyzed. Preoperative variables included age, sex, body mass index, smoking and drinking history, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), cerebrovascular and peripheral vascular disease, renal insufficiency, gastrointestinal tract disease, atrial fibrillation, general and cardiac surgical history, New York Heart Association (NYHA) class, pulmonary artery hypertension, pericardial effusion, left ventricular ejection fraction, and laboratory values. Operative variables included type of surgery, cardiopulmonary bypass (CPB) time, aortic cross clamp time, and blood transfusion. Postoperative variables included reintubation, mortality, and the length of mechanical ventilation (MV), intensive care unit (ICU), and hospital stay.

### Definitions

The diagnosis of POP was according to the American guidelines.[13,14] In this study, POP referred to pneumonia from the first postoperative day to discharge. POP was diagnosed when new and/or progressive pulmonary infiltrates presented on chest radiograph combined with two or more of the following criteria: (1) fever (>38°C) without other explanations, (2) leucocytosis ($>12 \times 10^9$/L) or leucopenia ($<4 \times 10^9$/L), and (3) purulent secretions. Semi-quantitative cultures from endotracheal aspiration of lower respiratory tract secretions or sputum with an initial microscopic examination combined with quantitative bacterial cultures were mainly used to identify the microbiological etiology of POP.

### Statistical analysis

Statistical analysis was completed using SPSS (IBM SPSS Statistics, version 24, Armonk, NY, USA). Results were expressed as means ± standard deviations or counts followed by percentages. In the derivation set, univariate analysis was performed to initially screen potential predictors for POP after HVS. Continuous data were analyzed using unpaired Student's *t* test, and categorical data were analyzed using chi-square test or Fisher exact test.

Variables with $P < 0.100$ were then entered into a multivariable logistic regression model to identify the independent risk factors. Collinearity was tested using variance inflation factors procedure before the construction of the model. Continuous variables were initially incorporated into the multivariable model in a continuous manner. Those significant factors were then dichotomized to assign risk points and have a better clinical application. Optimal thresholds were determined according to the Youden index combined with the cutoff values used in published reports. Points were assigned to the independent risk factors in the final multivariable model with each regression coefficient divided by the smallest one and rounded to the nearest integer. A composite point-based risk score was then generated by summing the score of each risk factor. Finally, risk stratification was carried out for identifying a higher-risk subgroup of developing POP.

The discriminative performance of the prediction model in the derivation set was evaluated by the area under the receiver operating characteristic (ROC) curve. Calibration was assessed through the Hosmer-Lemeshow goodness-of-fit test. A similar process was performed in the validation set, and the area under the two ROC curves was compared. Decision curve analysis was used to assess the clinical utility of our model, with graphical decision and clinical impact curves.

## Results

A total of 3853 adults undergoing HVS fulfilled the inclusion criteria and were incorporated into this study, including 2077 male patients, with a mean age of 51.3 ± 12.6 years. The baseline characteristics and comorbidities were similar between the derivation and validation sets [Table 1].

Of the 3853 operations, 75.2% were performed for isolated valve surgery, 12.5% for concomitant CABG, 10.7% for concomitant aortic surgery, and 1.6% for concomitant CABG and aortic surgery. The mean CPB time was 118.0 ± 49.6 min, and blood products were transfused in 84.1% of the cases. Operative variables were comparable between the derivation and validation sets [Table 1].

The most common microorganism isolated in this study was *Acinetobacter baumannii* (37.9%), followed by *Klebsiella pneumoniae* (20.9%), *Staphylococcus aureus* (12.6%), and *Pseudomonas aeruginosa* (12.2%). Polymicrobial POP was detected in 26.9% of cases.

The rate of POP was 8.2%, in which 88.0% occurred within the first postoperative week, with a median of 3 days. The overall mortality was 2.9%, with a rate in patients with POP of 28.2% *vs.* 0.7% in those without POP ($P < 0.001$). Duration of MV was longer in patients with POP than those without POP (7.4 ± 7.6 days *vs.* 1.3 ± 1.2 days; $P < 0.001$), and similar results were also seen for ICU stay (13.7 ± 11.3 days *vs.* 3.2 ± 2.2 days; $P < 0.001$) as well as hospital stay (28.1 ± 14.4 days *vs.* 14.8 ± 6.1 days; $P < 0.001$). Comparisons between the derivation and validation sets are depicted in Figure 1.

**Table 1: Comparison of characteristics between the derivation and validation sets.**

| Characteristics | Derivation set ($n = 1926$) | Validation set ($n = 1927$) | *P* value |
|---|---|---|---|
| Demographics | | | |
| Age (years) | 51.23 ± 12.50 | 51.30 ± 12.62 | 0.850 |
| Male | 1028 (53.4) | 1049 (54.4) | 0.508 |
| Body mass index (kg/m$^2$) | 23.05 ± 3.30 | 23.03 ± 3.30 | 0.849 |
| Smoking history | 522 (27.1) | 512 (26.6) | 0.709 |
| Drinking history | 398 (20.7) | 378 (19.6) | 0.417 |
| Underlying conditions | | | |
| Hypertension | 463 (24.0) | 472 (24.5) | 0.742 |
| Diabetes mellitus | 100 (5.2) | 121 (6.3) | 0.147 |
| COPD | 250 (13.0) | 243 (12.6) | 0.731 |
| Cerebrovascular disease | 670 (34.8) | 688 (35.7) | 0.552 |
| Peripheral vascular disease | 803 (41.7) | 809 (42.0) | 0.855 |
| Renal insufficiency | 154 (8.0) | 166 (8.6) | 0.487 |
| Gastrointestinal tract disease | 157 (8.2) | 159 (8.3) | 0.910 |
| Atrial fibrillation | 438 (22.7) | 452 (23.5) | 0.599 |
| General surgery history | 577 (30.0) | 563 (29.2) | 0.614 |
| Heart surgery history | 149 (7.7) | 159 (8.3) | 0.556 |
| NYHA class III–IV | 346 (18.0) | 351 (18.2) | 0.840 |
| Pulmonary artery hypertension | 606 (31.5) | 623 (32.3) | 0.564 |
| Pericardial effusion | 306 (15.9) | 296 (15.4) | 0.652 |
| Ejection fraction (%) | 61.10 ± 7.70 | 61.12 ± 7.88 | 0.957 |
| Laboratory values | | | |
| White blood cell ($\times 10^9$/L) | 5.97 ± 2.20 | 5.96 ± 2.10 | 0.904 |
| Red blood cell ($\times 10^{12}$/L) | 4.29 ± 0.57 | 4.28 ± 0.56 | 0.559 |
| Hemoglobin (g/L) | 128.45 ± 18.00 | 128.12 ± 18.38 | 0.573 |
| Platelet ($\times 10^9$/L) | 180.98 ± 58.06 | 181.55 ± 58.48 | 0.763 |
| Creatinine (μmol/L) | 78.07 ± 46.09 | 77.55 ± 40.96 | 0.712 |
| Albumin (g/L) | 40.32 ± 3.93 | 40.24 ± 3.92 | 0.522 |
| Globulin (g/L) | 24.60 ± 4.29 | 24.75 ± 4.55 | 0.311 |
| Operative variables | | | |
| Type of surgery | | | 0.987 |
| Isolated valve surgery | 1445 (75.0) | 1452 (75.3) | |
| Concomitant CABG | 244 (12.7) | 237 (12.3) | |
| Concomitant aortic surgery | 206 (10.7) | 206 (10.7) | |
| Concomitant CABG and aortic surgery | 31 (1.6) | 32 (1.7) | |
| CPB time (min) | 118.71 ± 50.06 | 117.22 ± 49.17 | 0.351 |
| Aortic cross clamp time (min) | 77.49 ± 34.88 | 75.84 ± 35.94 | 0.149 |
| Blood transfusion | 1632 (84.7) | 1609 (83.5) | 0.293 |

Data are expressed as mean ± standard deviation or *n* (%). COPD: Chronic obstructive pulmonary disease; CABG: Coronary artery bypass graft; CPB: Cardiopulmonary bypass; NYHA: New York Heart Association.

### Risk score derivation

Univariate analysis of risk factors for POP in the derivation group is displayed in Table 2. With the use of multivariable logistic regression analysis, we identified ten significant predictors of POP including age >60 years, smoking history, diabetes mellitus, renal insufficiency, COPD, NYHA class III–IV, heart surgery history, CPB time >120 min, and blood transfusion [Figure 2A]. Point values were assigned to these independent risk factors of POP according to their regression coefficients in the multivariable model [Table 3]. Odds ratios and corresponding 95% confidence intervals (CIs) were also calculated. A simplified risk score of 22 possible points was then generated by summing the point values of all the predictors. In the derivation group, scores ranged from 0 to 20 with a median of 5. Predicted probability of POP based on the risk score is presented in Figure 2B.

The occurrence of POP after HVS was significantly predicted in our multivariable model ($\chi^2 = 202.6$, $P < 0.001$). The area under the ROC curve was 0.81 (95% CI, 0.79–0.83; Figure 2C), demonstrating reasonable discrimination. The correlation between the observed and expected events of POP was high ($r = 0.99$), indicating good calibration (Hosmer-Lemeshow $\chi^2 = 8.234$, $P = 0.312$; Figure 2D).

### Risk score validation

When our prediction rule for POP was applied to the validation set, risk scores ranged from 0 to 16 with a median of 5. The discriminatory ability of the risk score was robust as the area under the ROC curve was 0.83

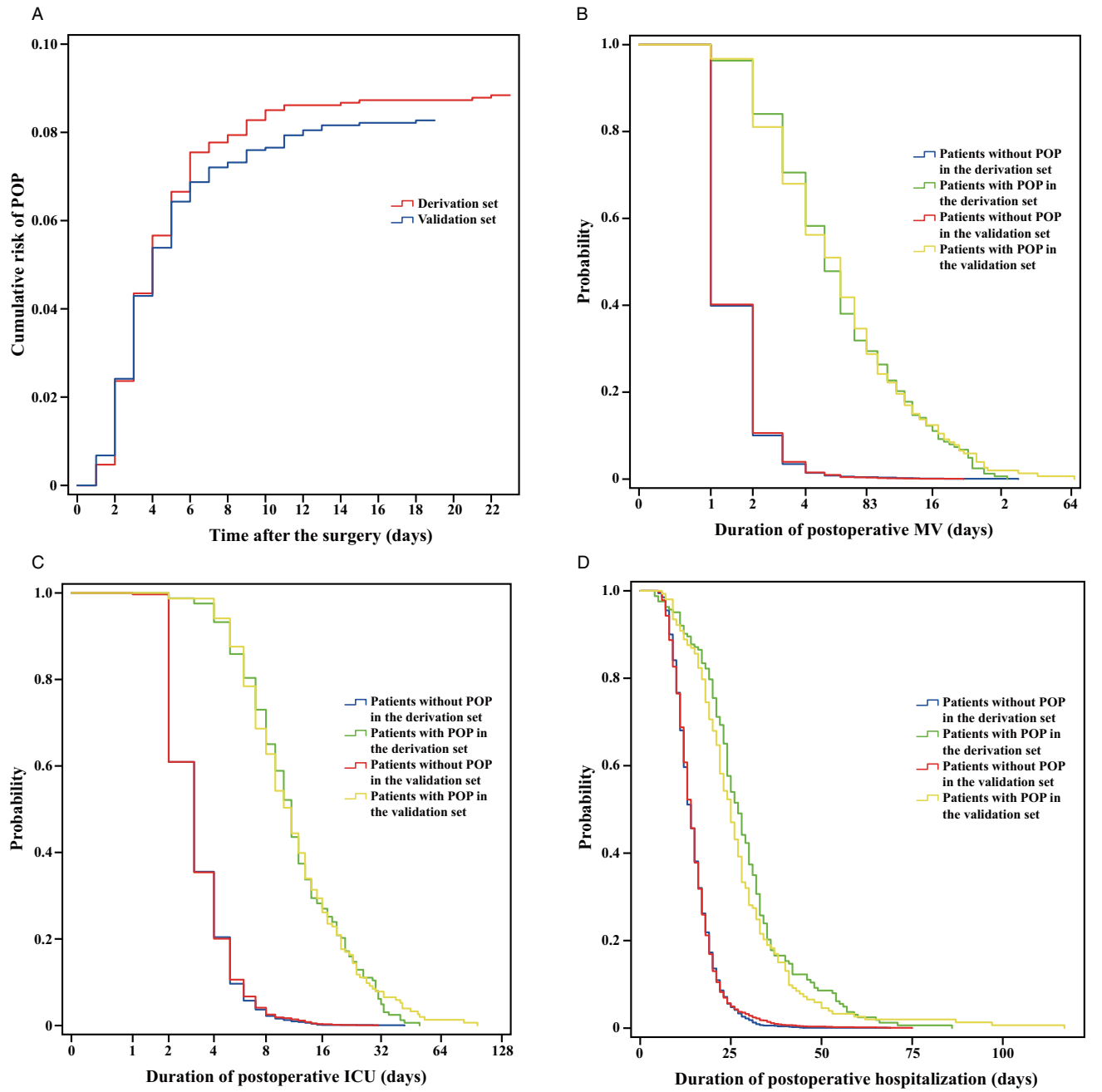


**Figure 1:** Kaplan-Meier curve showing the cumulative risk of POP over time (A), and the changing probability of patients with MV (B), staying in the ICU (C), and staying in the hospital (D) among patients with and without POP in the derivation and validation sets over time. ICU: Intensive care unit; MV: Mechanical ventilation; POP: Postoperative pneumonia.

(95% CI, 0.81–0.85). No significant difference was found between the derivation and validation groups ($P = 0.478$; Figure 2C). In addition, the clinical risk score outperformed Kilic risk score (C-statistic: 0.69; 95% CI, 0.66–0.72) and Allou risk score (C-statistic: 0.60; 95% CI, 0.57–0.63) in predicting POP in our analysis ($P < 0.001$; Figure 2C). The rule also indicated good calibration in the validation set (Hosmer-Lemeshow $\chi^2 = 5.606$, $P = 0.691$; Figure 2D).

### *Risk stratification*

Comparison of predicted and observed probability in the derivation and validation sets by the calculated risk score is presented in Figure 3. Three risk intervals were identified as low-, medium-, and high-risk groups corresponding to scores of 0 to 6, 7 to 9, and ≥10. Approximately two-thirds of the patients were categorized at low risk, nearly a quarter at medium risk, and only about one-tenth at high risk. The population composition of each risk group and their corresponding observed POP rates in the derivation and validation groups are listed in Table 4.

Compared with the low-risk group, the odds ratios for the occurrence of POP were 6.99 (95% CI, 4.49–10.89; $P < 0.001$) for the medium-risk group and 18.98 (95% CI, 11.98–30.06; $P < 0.001$) for the high-risk group in the

**Table 2: Univariate analysis of risk factors for POP following HVS in the derivation set.**

| Characteristics | No POP ($n = 1763$) | POP ($n = 163$) | $\chi^2/t$ | *P* value |
|---|---|---|---|---|
| Demographics | | | | |
| Age (years) | 50.62 ± 12.43 | 57.79 ± 11.28 | 7.098 | <0.001 |
| Male | 922 (52.3) | 106 (65.0) | 9.721 | 0.002 |
| Body mass index (kg/m$^2$) | 23.02 ± 3.26 | 23.32 ± 3.68 | 1.090 | 0.276 |
| Smoking history | 458 (26.0) | 64 (39.3) | 13.329 | <0.001 |
| Drinking history | 361 (20.5) | 37 (22.7) | 0.450 | 0.502 |
| Underlying conditions | | | | |
| Hypertension | 392 (22.2) | 71 (43.6) | 37.152 | <0.001 |
| Diabetes mellitus | 79 (4.5) | 21 (12.9) | 21.400 | <0.001 |
| COPD | 213 (12.1) | 37 (22.7) | 14.892 | <0.001 |
| Cerebrovascular disease | 592 (33.6) | 78 (47.9) | 13.400 | <0.001 |
| Peripheral vascular disease | 709 (40.2) | 94 (57.7) | 18.696 | <0.001 |
| Renal insufficiency | 115 (6.5) | 39 (23.9) | 61.430 | <0.001 |
| Gastrointestinal tract disease | 140 (7.9) | 17 (10.4) | 1.234 | 0.267 |
| Atrial fibrillation | 397 (22.5) | 41 (25.2) | 0.590 | 0.443 |
| General surgery history | 525 (29.8) | 52 (31.9) | 0.321 | 0.571 |
| Heart surgery history | 123 (7.0) | 26 (16.0) | 16.835 | <0.001 |
| NYHA class III–IV | 298 (16.9) | 48 (29.4) | 15.933 | <0.001 |
| Pulmonary artery hypertension | 556 (31.5) | 50 (30.7) | 0.051 | 0.821 |
| Pericardial effusion | 272 (15.4) | 34 (20.9) | 3.293 | 0.070 |
| Ejection fraction (%) | 61.22 ± 7.60 | 59.79 ± 8.65 | 2.275 | 0.023 |
| Laboratory values | | | | |
| White blood cell ($\times 10^9$/L) | 5.91 ± 2.10 | 6.64 ± 3.06 | 2.978 | 0.003 |
| Red blood cell ($\times 10^{12}$/L) | 4.30 ± 0.57 | 4.16 ± 0.60 | 3.074 | 0.002 |
| Hemoglobin (g/L) | 128.71 ± 17.94 | 125.61 ± 18.48 | 2.109 | 0.035 |
| Platelet ($\times 10^9$/L) | 181.83 ± 57.34 | 171.83 ± 64.88 | 1.900 | 0.059 |
| Creatinine (μmol/L) | 76.61 ± 44.91 | 93.89 ± 55.00 | 3.894 | <0.001 |
| Albumin (g/L) | 40.40 ± 3.90 | 39.52 ± 4.24 | 2.734 | 0.006 |
| Globulin (g/L) | 24.61 ± 4.28 | 24.55 ± 4.49 | 0.166 | 0.868 |
| Operative variables | | | | |
| Type of surgery | | | 116.502 | <0.001 |
| Isolated valve surgery | 1375 (78.0) | 70 (42.9) | | |
| Concomitant CABG | 189 (10.7) | 55 (33.7) | | |
| Concomitant aortic surgery | 178 (10.1) | 28 (17.2) | | |
| Concomitant CABG and aortic surgery | 21 (1.2) | 10 (6.1) | | |
| CPB time (min) | 114.75 ± 43.45 | 161.48 ± 85.05 | 6.931 | <0.001 |
| Aortic cross clamp time (min) | 75.60 ± 32.72 | 97.86 ± 48.53 | 5.736 | <0.001 |
| Blood transfusion | 3891 (81.2) | 510 (96.2) | 75.435 | <0.001 |

Data are expressed as mean ± standard deviation or *n* (%). COPD: Chronic obstructive pulmonary disease; CABG: Coronary artery bypass graft; CPB: Cardiopulmonary bypass; HVS: Heart valve surgery; NYHA: New York Heart Association; POP: Postoperative pneumonia.

derivation set. The corresponding values in the validation set were 6.23 (95% CI, 3.91–9.92; $P < 0.001$) and 20.27 (95% CI, 12.73–32.26; $P < 0.001$), respectively. The fact that predicted probabilities were within the 95% CI of observed probabilities of POP also demonstrated a good calibration.

### *Clinical utility assessment*

To evaluate the clinical utility of the risk score, we further conducted decision curve analysis. Graphical decision and clinical impact curves are presented in Figure 4. The decision curve showed the threshold risk against the standardized net benefit and the clinical impact curve showed the number of estimated high risk and true positives among 1000 patients. The decision curves of the model in the derivation and validation sets indicated that the risk score could obtain more clinical net benefits within a large range of risk thresholds compared with "no intervention" or "intervention for all" strategies. The clinical impact curves also demonstrated that the model had good clinical utility and excellent predictive power.

## Discussion

In this study, we derived and validated a prediction rule for POP utilizing data from 3853 patients undergoing HVS at our institution. A composite 22-point risk score was generated incorporating ten readily obtainable predictors and three risk intervals were defined. The risk score demonstrated good discrimination and calibration, and was well-validated. Decision curve analysis of the model indicated good clinical utility.

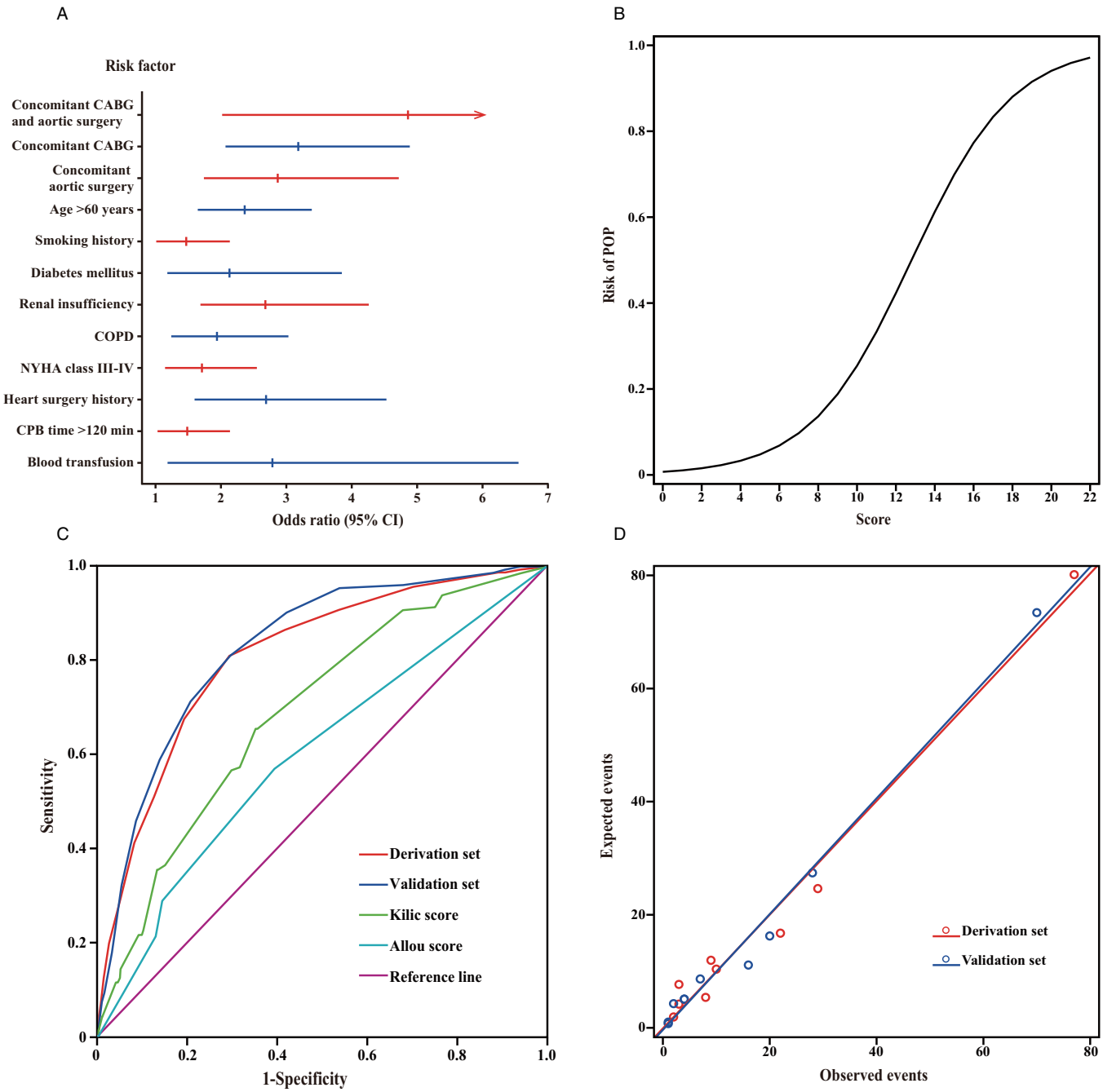


**Figure 2:** Derivation, validation, and evaluation of the clinical risk score. (A) Independent risk factors for POP following HVS identified by multivariable logistic regression analysis; (B) predicted risk of POP based on the 22-point risk score; (C) ROC curves drawn using the risk score in the derivation set (C-statistic: 0.81; 95% CI, 0.79–0.83) and validation set (C-statistic: 0.83; 95% CI, 0.81–0.85), and the comparison with Kilic risk score (C-statistic: 0.69; 95% CI, 0.66–0.72) and Allou risk score (C-statistic: 0.60; 95% CI, 0.57–0.63). (D) Observed *vs.* expected events by predicted risk category in the derivation set (Hosmer-Lemeshow $\chi^2 = 8.234$, $P = 0.312$; $r = 0.99$) and validation set (Hosmer-Lemeshow $\chi^2 = 5.606$, $P = 0.691$; $r = 0.99$). CABG: Coronary artery bypass graft; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CPB: Cardiopulmonary bypass; HVS: Heart valve surgery; NYHA: New York Heart Association; POP: Postoperative pneumonia; ROC curve: Receiver operating characteristic curve.

### *POP and outcomes*

The overall POP rate in this study was 8.2%, falling within the range previously reported.[1] Prolonged ICU and hospital stay as well as a higher mortality rate were observed in patients with POP, which was consistent with the results in published papers.[15] The poor outcomes associated with POP highlight the need to identify significant predictors and high-risk patients.

### *Risk factors*

Several risk factors identified in our analysis have been reported in previous studies. Advanced age[10-12,16-19] and

**Table 3: Multivariable analysis of independent risk factors for POP following HVS, with corresponding point values.**

| Characteristics | Odds ratio (95% CI) | *P* value | Coefficient | Point value |
|---|---|---|---|---|
| Isolated valve surgery | Reference | Reference | Reference | |
| Concomitant CABG | 3.175 (2.068–4.876) | <0.001 | 1.155 | 3 |
| Concomitant aortic surgery | 2.862 (1.740–4.708) | <0.001 | 1.051 | 3 |
| Concomitant CABG and aortic surgery | 4.848 (2.016–11.659) | <0.001 | 1.579 | 4 |
| Age >60 years | 2.359 (1.645–3.382) | <0.001 | 0.858 | 2 |
| Smoking history | 1.468 (1.010–2.133) | 0.044 | 0.384 | 1 |
| Diabetes mellitus | 2.129 (1.181–3.841) | 0.012 | 0.756 | 2 |
| Renal insufficiency | 2.676 (1.685–4.250) | <0.001 | 0.984 | 3 |
| COPD | 1.937 (1.240–3.026) | 0.004 | 0.661 | 2 |
| NYHA class III–IV | 1.708 (1.145–2.546) | 0.009 | 0.535 | 1 |
| Heart surgery history | 2.686 (1.597–4.519) | <0.001 | 0.988 | 3 |
| CPB time >120 min | 1.485 (1.032–2.136) | 0.033 | 0.395 | 1 |
| Blood transfusion | 2.781 (1.184–6.531) | 0.019 | 1.023 | 3 |
| Intercept | 0.007 | <0.001 | −4.918 | |

COPD: Chronic obstructive pulmonary disease; CABG: Coronary artery bypass graft; CI: Confidence interval; CPB: Cardiopulmonary bypass; HVS: Heart valve surgery; NYHA: New York Heart Association; POP: Postoperative pneumonia.

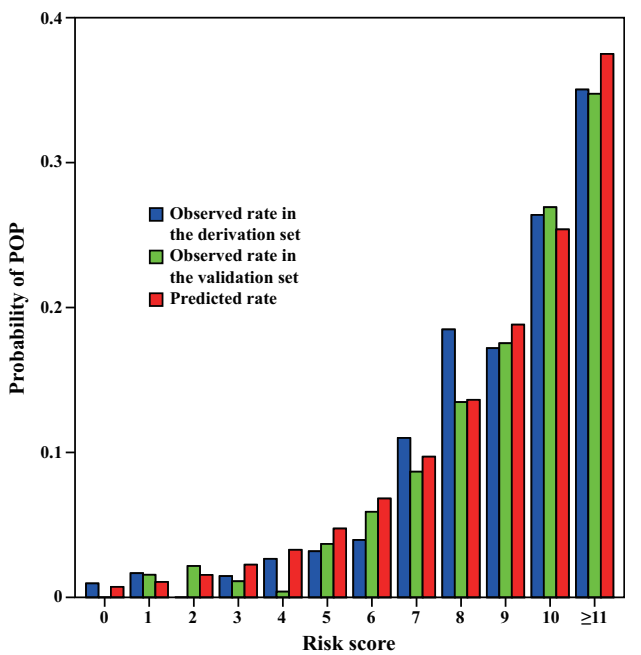


**Figure 3:** Predicted and observed probability of POP in the derivation and validation sets by risk score. POP: Postoperative pneumonia.

COPD[3,11,12,16,18-20] have been well-acknowledged as risk factors for POP, which was reaffirmed by our study. Smoking history is another preoperative predictor for POP that is frequently reported,[3,11] despite some studies reaching an inconsistent conclusion.[18] Renal insufficiency, whether acute or chronic, is often considered to be associated with the occurrence of POP.[3,10,11,20] Diabetes mellitus as a significant predictor for POP is also verified in previous studies.[6,11]

Not surprisingly, poor cardiac function is closely related to the occurrence of POP. Strobel *et al*[11] reported that ejection fraction was negatively correlated with the occurrence of POP and the need for preoperative intra-aortic balloon pump had 1.59-fold increased odds of POP. Hortal *et al*[10] found that intraoperative inotropic support appeared as a significant predictor for POP in the multivariable analysis, and NYHA class IV was incorporated as an independent variable into the risk score. Similar results have also been found in other work.[12,16,20,21] In addition, previous heart surgery has also been confirmed as a risk factor for POP in several reports.[3,10]

Combined surgery was identified as an independent risk factor for POP in the multivariable analysis. As far as we know, it is reported here that concomitant CABG and/or aortic surgery can significantly increase the risk of POP following HVS. This can possibly be explained by the fact that combined surgery is more complicated and time-consuming, and thus may result in greater damage.

CPB may account for pulmonary dysfunction presenting as decreased pulmonary compliance and increased likelihood of atelectasis and POP by inducing a systemic inflammatory response.[22] As expected, prolonged CPB time was identified as an independent predictor for POP in this study, which has been well-established in the literature.[12,16,20] Therefore, more efforts are needed to shorten the length of CPB and reduce the damage from circulatory support techniques to improve the prognosis.[23,24]

Blood transfusion has been recognized as a significant risk factor in the majority of published reports,[3,12,16,17,20,25] which is consistent with our results. Blood products are routinely transfused in traditional heart surgery; however, growing evidence suggesting that this clinical practice may have adverse effects,[26-28] and a dose-effect relationship, was observed in some studies.[10,18,29-31] Changes in immune function can partially explain the relationship between blood transfusion and POP.[32,33] In addition, storage time of blood products may relate to the occurrence of POP.[34-36] Consequently, a restrictive transfusion strategy should be performed to reduce the POP rate and improve the prognosis, and efforts aiming to seek alternative therapies should be encouraged.[37-40]

**Table 4: POP risk score: distribution of patients and rates of POP by intervals.**

| Characteristics | Derivation set ($n = 1926$) | | | Validation set ($n = 1927$) | | |
|---|---|---|---|---|---|---|
| | Low risk (0–6 points) | Medium risk (7–9 points) | High risk (≥10 points) | Low risk (0–6 points) | Medium risk (7–9 points) | High risk (≥10 points) |
| Patients, *n* (%) | 1278 (66.4) | 439 (22.8) | 209 (10.8) | 1280 (66.4) | 428 (22.2) | 219 (11.4) |
| Predicted rate of POP, % (95% CI) | 3.2 (3.1–3.3) | 11.7 (11.3–12.0) | 33.6 (31.8–35.5) | 2.9 (2.8–3.0) | 11.6 (11.1–12.2) | 30.3 (28.4–32.2) |
| Observed rate of POP, % (95% CI) | 2.4 (1.6–3.3) | 14.8 (11.5–18.1) | 32.1 (25.7–38.4) | 2.3 (1.5–3.1) | 12.6 (9.5–15.8) | 32.0 (25.7–38.2) |

CI: Confidence interval; POP: Postoperative pneumonia.

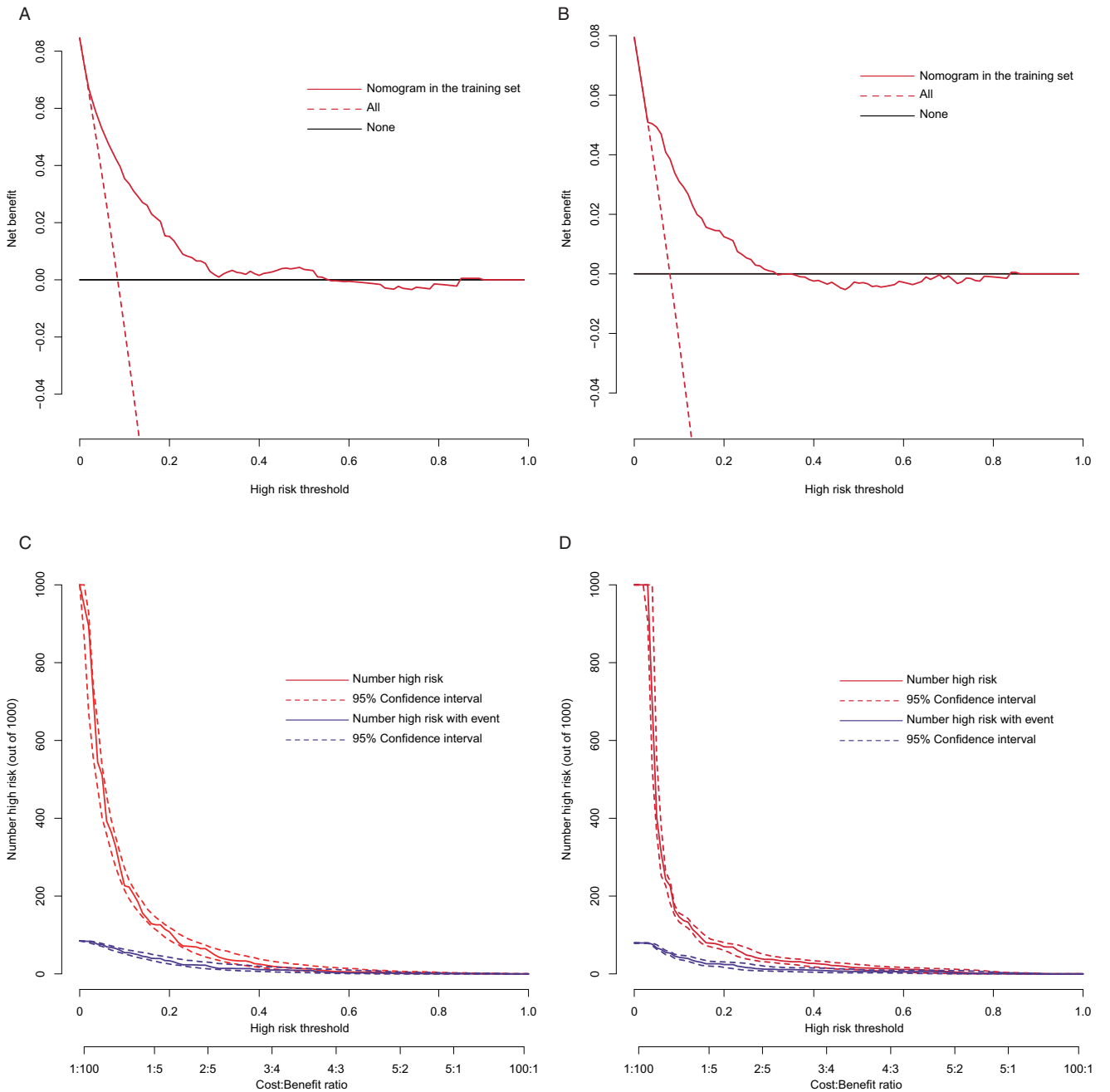


**Figure 4:** Decision curve analysis of the clinical risk score. Decision curves of the model in the derivation (A) and validation sets (B), and clinical impact curves in the derivation (C) and validation sets (D).

There were several risk factors identified in other studies but not in our analysis, in which prolonged MV is most commonly reported.[10,17,18,29] Endotracheal intubation may damage the defense mechanism of the respiratory system and thus the risk of POP may increase if MV extends.[41] Therefore, MV should be stopped as soon as conditions permit.[42,43] The duration of MV differed greatly in patients with and without POP in this study, but we did not include it into the multivariable analysis because it was a postoperative variable and cannot be obtained early. Reintubation is another postoperative predictor for POP that is frequently reported.[20,21,44,45] However, we found it difficult to discern whether POP emerged before or after the operation, which was another reason why we did not include it in our model. In addition, underweight,[3,19] peripheral vascular disease,[11,12] cerebrovascular disease,[11] and anemia[18] were also reported as predictors for POP in some results.

Despite the majority of risk factors for POP being non-modifiable, several preventive measures have been reported to be effective. Respiratory physiotherapy,[46] oropharyngeal nursing,[47] silver-coated endotracheal tubes,[48] subglottic secretion drainage,[49,50] and selective digestive decontamination can be mentioned as examples of such preventive methods.[51] However, it cannot be a good strategy to apply these techniques to patients without selection as some are laborious, costly, and time-consuming. The 22-point risk score may be helpful in risk evaluation and stratification. Appropriate preventive measures targeting higher-risk patients identified by the score may be more efficient.

Several limitations should be mentioned in this study. First, the prediction rule originated from a retrospective study of a small population in a single institution, which may limit its generalizability. Second, some factors that may relate to the occurrence of POP, such as drug use, were not included in this study. Third, all continuous variables were dichotomized to facilitate score assignment in the final model, which may cause the loss of individual information. Fourth, long-term follow-up after discharge was not performed due to the difficulty of implementation, which may underestimate the real incidence of POP after HVS.

Despite limitations, the study achieved its aims. Although several risk scores for POP following cardiac surgery have been developed,[3,10,12] to our knowledge, the work we report is validated clinical risk score specific to POP following HVS. Particularly, similar studies have been mainly conducted in the United States and Europe, but few are available in China.

## Conclusions

We derived and validated a 22-point risk score for POP following HVS using ten significant predictors in this study. The rule performed well in both discrimination and calibration, and three risk intervals were created. Decision curve analysis of the model showed reasonable clinical utility and we believe the risk score is applicable at the bedside as it is easily calculable and the factors incorporated are readily available. It may also have utility in risk stratification and preventive interventions.

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## Conflicts of interest

None.

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