

# A Novel Patient-Specific Model for Predicting Postoperative SIRS in Elderly Patients: A Retrospective Cohort Study

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## Research

**Keywords:** Nomogram, Postoperative SIRS, Elderly patients, Predicting model

**Posted Date:** May 17th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-490948/v1>

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# Abstract

## Background

Postoperative systemic inflammatory response syndrome (SIRS) is common in surgical ICU patients especially in elderly patients, and the geriatric population with SIRS is more susceptible to sepsis, MODS, and death. There have been no reliable and accurate methods to predict SIRS in the elderly. Therefore, we aimed to develop and validate a novel effective model for predicting postoperative SIRS in elderly patients.

## Methods

Data of 16141 patients aged  $\geq 65$  years who underwent surgery in two centers of Third Affiliated Hospital of Sun Yat-sen University from January 2015 to September 2020 were retrieved and analyzed. We developed a predictive model for postoperative SIRS based on a retrospectively cohort study of 5904 patients spanning from January 2015 to December 2019. The discriminative performance of this model was determined by area under the receiver operating characteristics curve (AUC). We also used the model to validate outcomes in 1105 patients who underwent surgery at the same institutions from January 2020 to September 2020, and to perform a stratified analysis.

## Results

A total of 5904 patients were enrolled in the training cohort and 1105 patients comprised the validation cohort, in which incidence rates of postoperative SIRS were 24.6% and 20.2%, respectively. Patients with SIRS had more postoperative complications and a worse in-hospital survival rate than patients without SIRS. Six feature variables including preoperative fever, preoperative serum albumin level, ASA classification, total intraoperative infusion volume, surgical duration, and postoperative intensive care unit admission were identified as valuable predictors to construct the nomogram, with high AUCs in both the training and validation cohorts (0.800 [0.787, 0.813] and 0.823 [0.791, 0.855], respectively).

## Conclusions

We constructed an effective nomogram using 6 routinely obtained variables to assist clinicians to predict postoperative SIRS in elderly patients.

## Background

Systemic inflammatory response syndrome (SIRS) occurs in one-third of all hospitalized patients and in more than 50% of all intensive care unit (ICU) patients. Furthermore, over 80% of surgical ICU patients develop postoperative SIRS(1) and are at considerable risk for severe complications and death.

Approximately one-third of SIRS patients develop severe sepsis and septic shock (1), causing complications that include multiple organ dysfunction syndrome (MODS) and increased postoperative mortality (2, 3). Notably, the incidence of SIRS is significantly higher in patients older than 75 years than in those younger than 40 years of age (4), and the geriatric population with SIRS is more susceptible to sepsis, MODS, and death due to various age-related organ dysfunctions, preexisting comorbidities, and limited physiologic reserve to cope with SIRS-related hemodynamic and metabolic changes(5). The early diagnosis of sepsis is critical because each one-hour delay in treatment increases mortality by 7.6%(6). Because the consensus definition of severe sepsis requires signs that meet criteria for SIRS (7), the proactive prediction and early diagnosis of postoperative SIRS in elderly patients may enable clinicians to provide timely treatment to prevent sepsis and organ failure.

Multiple risk factors have been identified to facilitate the prediction of postoperative SIRS. These include preoperative high-sensitive C-reactive protein/albumin ratio, C-reactive protein level, erythrocyte sedimentation rate, and platelet-to-lymphocyte ratio(8–10). A nomogram for the prediction of SIRS after transrectal ultrasound-guided prostate biopsy has also been developed (11). However, most of these factors focus on a single organ system or solitary event, or are established from clinical trials not designed to study the geriatric population. An effective risk stratification and prediction model for postoperative SIRS in elderly surgical patients has not yet been available.

The goal of our study was to develop and externally validate an accurate but simple prediction model for postoperative SIRS in elderly patients. We aimed to use routinely measured perioperative variables to create a predictive model that could be easily implemented in clinical practice to support clinicians in the prevention of severe sepsis, septic shock, and postoperative morbidity in elderly patients.

## Methods

### Patients

In this retrospective study, data of 16141 patients aged  $\geq 65$  years who underwent surgery in two centers of the Third Affiliated Hospital of Sun Yat-sen University (Guangzhou, Guangdong, China) from January 2015 to September 2020 were retrieved from the Electronic Health Record (EHR) systems. During the retrospective enrollment, patients with preoperative SIRS; those who underwent topical, local, nerve block, or combined spinal epidural anesthesia; and those whose total intraoperative infusion volumes, fluid losses, or ASA classifications were not recorded were excluded.

In the EHR systems of our hospital, a database platform was established by extracting medical records from the hospital information system (HIS), laboratory information system, and Docare Anesthesia System (2005–2020 Medalsystem Co. Ltd., Suzhou, China). This platform enabled access to comprehensive data collected during hospital admissions, inpatient stays, and post-hospital follow-up visits that included demographic characteristics, daily documentation, laboratory and imaging results, anesthesia records, and other clinical characteristics.

# Definition of SIRS

A case definition of SIRS was met when a patient exhibited two of the following four criteria as we reported previously (12) : (1) body temperature  $\geq 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$ , (2) heart rate  $\geq 90$  beats/min, (3) respiratory rate  $\geq 20$  breaths/min or arterial carbon dioxide tension  $< 32$  mmHg and (4) leucocyte count  $\geq 12 \times 10^9/\text{L}$  or  $< 4 \times 10^9/\text{L}$ . The incidence of SIRS within three postoperative days was recorded.

## Variable definition

We used descriptive statistics to characterize patients in the training and validation cohorts, both with and without SIRS (Table 1). Twenty variables were selected from the electronic health records based on previously published literature(13–15) and clinical experience. These included demographic variables such as age and gender; comorbid conditions, including diabetes and hypertension; smoking history; preoperative fever; preoperative laboratory variables; preoperative condition, including intubation before surgery; ASA classification; surgical grade; intraoperative events including total infusion volume, total fluid loss, blood loss, surgical duration, and postoperative ICU admission. For continuous variables, data were placed on a scale of approximate symmetry of distribution using the Yeo-Johnson transformation and were data-centered and normalized.

Table 1  
Patient characteristics of non-SIRS and SIRS groups

Variables	Development Cohort <sup>1</sup>		Validation Cohort <sup>1</sup>	
	Non-SIRS	SIRS	Non-SIRS	SIRS
	<b>4453 (75.4)</b>	<b>1451 (24.6)</b>	<b>882(79.8)</b>	<b>223(20.2)</b>
Age <sup>2*</sup> , y	70.0 [67.0,75.0]	71.0 [67.0,76.0]	70.0 [67.0,74.0]	71.0 [67.0,75.5]
Gender <sup>1*</sup>				
Female	2034 (45.7)	542 (37.4)	358 (40.6)	87 (39.0)
Male	2419 (54.3)	909 (62.6)	524 (59.4)	136 (61.0)
Preoperative intubation <sup>1*</sup>				
No	4388 (98.5)	1282 (88.4)	878 (99.5)	203 (91.0)
Yes	65 (1.46)	169 (11.6)	4 (0.45)	20 (8.97)
Hypertension <sup>1#</sup>				
No	1756 (39.4)	590 (40.7)	436 (49.4)	114 (51.1)
Yes	2697 (60.6)	861 (59.3)	446 (50.6)	109 (48.9)
Diabetes mellitus <sup>1*</sup>				
No	2997 (67.3)	860 (59.3)	823 (93.3)	198 (88.8)
Yes	1456 (32.7)	591 (40.7)	59 (6.69)	25 (11.2)
History of smoking <sup>1*</sup>				
No	3927 (88.2)	1215 (83.7)	850 (96.4)	215 (96.4)
Yes	526 (11.8)	236 (16.3)	32 (3.63)	8 (3.59)
ASA classification <sup>1*</sup>				
I/II	3204 (72.0)	663 (45.7)	608 (68.9)	83 (37.2)
III/IV/V	1249 (28.0)	788 (54.3)	274 (31.1)	140 (62.8)
Preoperative fever <sup>1*</sup>				
No	3971 (89.2)	1067 (73.5)	870 (98.6)	212 (95.1)

<sup>1</sup>expressed as n (%); <sup>2</sup>expressed as median [Q1, Q3]; \*Non-SIRS group vs. SIRS group in the development cohort,  $p < 0.001$ . WBC count, White blood cell count; ALT, Alanine aminotransferase; hs-CRP, high-sensitivity c-reaction protein; SIRS, systemic inflammatory response syndrome;

Variables	Development Cohort <sup>1</sup>		Validation Cohort <sup>1</sup>	
	Non-SIRS	SIRS	Non-SIRS	SIRS
	<b>4453 (75.4)</b>	<b>1451 (24.6)</b>	<b>882(79.8)</b>	<b>223(20.2)</b>
Yes	482 (10.8)	384 (26.5)	12 (1.36)	11 (4.93)
ICU admission <sup>1*</sup>				
No	4326 (97.1)	1005 (69.3)	863 (97.8)	132 (59.2)
Yes	127 (2.85)	446 (30.7)	19 (2.15)	91 (40.8)
Operation grade <sup>1*</sup>				
I/II	311 (6.98)	55 (3.79)	57 (6.46)	10 (4.48)
III	1672 (37.5)	309 (21.3)	311 (35.3)	33 (14.8)
IV	2470 (55.5)	1087 (74.9)	514 (58.3)	180 (80.7)
WBC <sup>2*</sup> , x10 <sup>9</sup> /L	6.34 [5.17,7.91]	7.04 [5.47,9.32]	6.46 [5.16,8.08]	7.66 [5.95,11.4]
Total volume of infusion <sup>2</sup> , mL	1500 [1000,2200]	2200 [1500,3200]	1500 [1000,2200]	2112 [1512,3050]
ALT <sup>2*</sup> , U/L	17.0 [13.0,25.0]	19.0 [13.0,30.0]	17.0 [13.0,25.0]	17.0 [12.8,28.0]
hs-CRP <sup>2*</sup> , mg/L	6.34 [5.11,7.97]	7.10 [5.47,9.60]	6.50 [5.10,8.31]	7.80 [6.01,11.8]
Albumin <sup>2*</sup> , g/L	40.3 [37.2,43.2]	38.2 [34.6,41.5]	39.9 [36.3,42.9]	37.8 [33.0,41.5]
Creatinine <sup>2*</sup> , μmol/L	74.0 [61.0,89.0]	78.0 [63.0,96.0]	71.0 [60.0,86.0]	74.0 [56.0,98.5]
Duration of surgery <sup>2*</sup> , min	125 [75.0,200]	192 [120,295]	131 [77.0,215]	193 [120,302]
Total volume of fluid, loss <sup>2*</sup> , mL	350 [110,700]	680 [350,1200]	400 [100,750]	800 [350,1125]
Blood loss <sup>2*</sup> , mL	50.0 [10.0,100]	100 [50.0,200]	40.0 [10.0,100]	100 [50.0,200]
Hemoglobin <sup>2*</sup> , g/L	128 [116,139]	124 [108,137]	126 [115,139]	116 [100,134]

<sup>1</sup>expressed as n (%); <sup>2</sup>expressed as median [Q1, Q3]; \*Non-SIRS group vs. SIRS group in the development cohort, *p* < 0.001. WBC count, White blood cell count; ALT, Alanine aminotransferase; hs-CRP, high-sensitivity c-reaction protein; SIRS, systemic inflammatory response syndrome;

## Variable selection

For univariate selection, we used a resampling technique with 10-fold cross-validation, to consider two logistic regression models for each variable: a null model containing only the intercept term, and a complex model with a single individual predictor in the risk set. We calculated the area under the receiver operating characteristic (ROC) curve in the two different models and performed a one-sided t-test to determine the difference between the two area under the receiver operating characteristics (AUC) values(16). The AUC value was calculated to determine the importance of each predictor.

## **Development of risk prediction model and external validation**

In reference to the univariate selection results, we used a combination of Brute Force algorithms (which considered the predictive effect of each combination of candidate variables for outcomes) and clinical guidance, and finally chose 6 variables to comprise our final model. The Hosmer-Lemeshow test was used to assess the model's goodness of fit. Using the lrm function of the RMS package, we constructed a nomogram to facilitate clinical decision-making. In this plot, each patient's score for each variable axis can be determined by plotting a line upward. The sum of these individual scores is plotted as a line down the total score axis to the risk axis, which predicts the likelihood of SIRS occurring in that patient. To perform external validation, we calibrated the intercept term  $\beta$  of the logistic with probabilities and recalculated the probabilities of the external validation set after calibration. All statistical analyses were performed by using R version 3.6.2 software (Institute for Statistics and Mathematics, Vienna, Austria; <http://www.r-project.org>)(17).

## **Results**

A total of 16141 patients aged  $\geq 65$  years spanning the period from January 2015 to September 2020 were included. As shown in Fig. 1, 533 patients with preoperative SIRS, 7835 patients receiving regional anesthesia or general anesthesia without intubation, 76 patients with missing anesthesia data, 650 patients whose total volumes of infusion or fluid loss were 0, and 35 patients with missing ASA classifications were excluded. Ultimately, 5904 patients receiving general anesthesia with endotracheal intubation and spanning from January 2015 to December 2019 were enrolled in the training cohort, whereas 1105 patients from January 2020 to September 2020 comprised the validation cohort. The incidence rates of postoperative SIRS in the two cohorts were 24.6% and 20.2%, respectively.

## **Characteristics of development and validation cohorts**

The demographic data and clinical characteristics of 7009 cases are displayed in Table S1. Three thousand twenty-one (43.1%) patients were women, and the average age was 70 (67.0–75.0) years. The numbers of SIRS patients in the development and validation cohorts were 1451 and 882, respectively. The prevalence rates of hypertension, diabetes mellitus, and smoking history were 58.7% (4113), 30.4% (2131), and 11.4% (802) respectively. Eight hundred eighty-nine (12.7%) patients had preoperative fever

and 9.74% (573) were transferred to the ICU. Most (65%) patients were categorized in ASA classification I/II. There were no significant differences in characteristics between the two patient cohorts (Table S1).

## Differences in characteristics between Non-SIRS and SIRS groups.

A total of 20 features were collected from each patient in the training cohort (Table 1). After comparing the characteristics of patients with or without postoperative SIRS, we found that patients who developed postoperative SIRS were older (71.0 [67.0,76.0] vs. 70.0 [67.0,75.0],  $p < 0.001$ , Table 1); more likely to have been assessed at ASA III/IV/V (54.3% vs. 28.0%,  $p < 0.001$ ); and more likely to have diabetes mellitus, a history of smoking, preoperative fever, and to have undergone preoperative intubation (all  $p < 0.001$ , Table 1). Grade IV surgeries were more frequent in the SIRS group (74.9% vs. 55.5%,  $p < 0.001$ ). Meanwhile, preoperative leukocyte counts and alanine aminotransferase, hs-CRP, and creatinine levels were higher in SIRS patients than in non-SIRS patients; while levels of hemoglobin and albumin were lower in SIRS patients (all  $p < 0.001$ ). Moreover, SIRS patients had larger intraoperative infusion, fluid loss, and blood loss volumes; and longer surgical durations than those of non-SIRS patients (all  $p < 0.001$ ).

## Prognosis of Non-SIRS and SIRS groups

As shown in Figure 2, compared with the Non-SIRS group, patients in the SIRS group were significantly more likely to experience postoperative complications that included agitation and delirium, hemorrhage, pneumonia, acute kidney injury, hypotension, coma, and cardiac arrest. Patients with SIRS had a significantly worse in-hospital survival rate than patients without SIRS (all  $p \leq 0.001$ , Table 2). SIRS patients also had higher hospitalization and surgical costs, and longer postoperative and total hospital stays than those without SIRS (all  $p < 0.001$ , Table 2).

Table 2  
Patients' postoperative prognosis between the two groups.

<b>Variables</b>	<b>Total (N = 7009)</b>	<b>Non-SIRS 5335 (76.1)</b>	<b>SIRS 1674 (23.9)</b>	<b>P value</b>
Hemorrhage <sup>1</sup>	2140 (30.5)	1394 (26.1)	746 (44.6)	< 0.001
ARDS <sup>1</sup>	26 (0.37)	9 (0.17)	17 (1.02)	< 0.001
Pneumonia <sup>1</sup>	550 (7.85)	169 (3.17)	381 (22.8)	< 0.001
Acute pulmonary embolism <sup>1</sup>	15 (0.21)	5 (0.09)	10 (0.60)	0.001
Cardiac arrest <sup>1</sup>	91 (1.30)	19 (0.36)	72 (4.30)	< 0.001
Hypotension <sup>1</sup>	187 (2.67)	73 (1.37)	114 (6.81)	< 0.001
Agitation and delirium <sup>1</sup>	187 (2.67)	51 (0.96)	136 (8.13)	< 0.001
Coma <sup>1</sup>	188 (2.68)	18 (0.34)	170 (10.2)	< 0.001
Mortality during hospitalization <sup>1</sup>	70 (1.00)	16 (0.30)	54 (3.23)	< 0.001
ICU Admission <sup>1</sup>	683 (9.74)	146 (2.74)	537 (32.1)	< 0.001
Acute kidney injury <sup>1</sup>	223 (3.18)	93 (1.74)	130 (7.77)	< 0.001
Postoperative hospital stay <sup>2</sup>	7.00 [5.00,12.0]	7.00 [4.00,10.0]	12.0 [8.00,20.0]	< 0.001
Total hospital stay <sup>2</sup>	15.0 [10.0,22.0]	13.0 [9.00,19.0]	21.0 [14.0,31.0]	< 0.001
Total cost <sup>2</sup>	55499 [29795,83605]	47077 [25392,71091]	89500 [59959,136333]	< 0.001
Costs of surgery <sup>2</sup>	5780 [3679,8389]	5300 [3340,7902]	7230 [4877,9816]	< 0.001

<sup>1</sup>expressed as n (%); <sup>2</sup>expressed as median [Q1, Q3];

## Variable selection

Univariate analysis of patient risk factors for perioperative SIRS was performed by using a resampling technique with 10-fold cross-validation. Results are shown in Table S2. The univariate association between each predictor and SIRS is represented by box chart, and percentages are shown in the stacked bar chart in Figure S1. Based on the results of resampling methods, previous literature reports, and clinical experience, we selected 6 feature variables that had strong independent discriminatory power for SIRS with maximal AUC to construct the logistic regression model. These included preoperative fever, preoperative albumin level, ASA classification, total intraoperative infusion volume, surgical duration, and postoperative ICU admission.

## **Model construction and external validation**

In the training cohort, the logistic regression model established by using the 6 selected predictors had a high AUC (0.800 [95% CI, 0.787–0.813]) to discriminate individuals with SIRS from those with non-SIRS, with a sensitivity of 71.8% and specificity of 71.8% (Fig. 2A, Table S3).

To better confirm the results of the logistic regression model, we then used the developed training model for external validation of another cohort of 1105 patients. The result of external validation showed that the AUC of the model was 0.823 (95% CI, 0.791, 0.855), with a sensitivity of 74.0% and specificity of 74.0% (Fig. 2B, Table S3). The calibration curve used to predict the presence or absence of SIRS is shown in Fig. 2C (Calibrated Hosmer-Lemeshow test,  $p = 0.01$ ).

In addition, we also used the six-variable model to analyze the validation cohort hierarchically based on the potential confounding factors of SIRS. We found no significant differences between subgroups of age, gender, diabetes mellitus, hypertension, blood loss and operation grade (Table 3), indicating that the predictive performance of the developed model in each subgroup was relatively stable, and illustrating its high-accuracy and generalizability in each subgroup.

Table 3  
Model effects of stratification analysis in the validation set

Characteristics	N(%)	AUC	95% CI
Total set	1105	0.823	0.791–0.855
Age (years)			
65–75	833 (75.4)	0.830	0.792–0.868
≥ 75	272 (24.6)	0.787	0.725–0.849
Gender			
Female	445 (40.27)	0.851	0.803–0.899
Male	660 (59.73)	0.804	0.762–0.847
Diabetes mellitus			
No	1021 (92.40)	0.825	0.791–0.859
Yes	84 (7.60)	0.781	0.671–0.891
Operation grade			
I/II	67 (6.06)	0.905	0.830–0.981
III	344 (31.13)	0.803	0.725–0.881
IV	694 (62.81)	0.802	0.762–0.842
Hypertension			
No	550 (49.77)	0.828	0.784–0.873
Yes	555 (50.23)	0.817	0.771–0.862
Blood loss (mL)			
< 100	724 (65.5)	0.816	0.769–0.863
≥ 100	379 (34.3)	0.772	0.719–0.825

## Predictive Nomogram

Based on the final regression analysis, a nomogram was constructed that incorporated the 6 significant risk factors for predicting postoperative SIRS (Fig. 3). As reported previously (18), each variable corresponding to the nomogram was scored on a point scale axis based on its contribution to our logistic regression model. The total points that corresponded to the risk of postoperative SIRS could be calculated easily that corresponded to the risk of postoperative SIRS could be calculated easily by adding each single score. An online risk calculator to further facilitate external validation can be visited at <http://wb.aidcloud.cn/zssy/SIRS.html>(19).

## Discussion

Because of the continuum between different stages of the inflammatory response from SIRS to sepsis and septic shock (20), early diagnosis of postoperative SIRS is critical to initiate timely interventions to prevent septic shock and improve clinical outcomes in elderly patients. Heretofore, the early prediction of postoperative SIRS has been challenging, and there have been no reliable and accurate methods to predict SIRS in the elderly. In this study, we identified 6 feature variables that have strong independent discriminatory power for SIRS with maximal AUC values. Furthermore, we constructed a nomogram composed of the 6 features that had high sensitivity and specificity to distinguish elderly patients at high risk for postoperative SIRS and to alert clinicians to provide early interventions.

Our novel nomogram has important implications for public health policy, clinical practice, and the informed consent process. Firstly, the early identification of elderly patients at risk of progression to postoperative SIRS and the generation of an individualized probability for each patient can be achieved by using our validated prediction tools. Implementation will potentially lead to better management and optimal use of medical resources, and will be critical to improve the survival rates of high-risk patients, especially those in surgical ICUs. Secondly, all of the variables integrated in the predictive model are measured routinely during the perioperative management for elderly surgical patients in China where both the elective patients and emergency patients admitted to the hospital have value of preoperative Albumin. To further facilitate its external validation and application, we have established an online risk calculator (<http://wb.aidcloud.cn/zssy/SIRS.html>)(19) and it has been accessible for all the peers in daily clinical practice. Moreover, the model can also be easily incorporated into EHR and HIS systems, thus having straightforward applicability, and thus enabling the integration of a risk prediction tool as a clinical decision support aid in perioperative elderly patient care(21). Additionally, our nomogram can be used as a decision support tool in the informed consent process by providing adequate information regarding risks and benefits defined by using a personalized medicine approach to estimate the individualized probability of postoperative SIRS.(22).

To our knowledge, this was the first study to develop a model and construct a quantitative nomogram to predict the probability of postoperative SIRS in aged patients. Because of the critical significance of the early prediction of postoperative SIRS, the identification of predisposing factors is of crucial importance. Several risk factors have been associated with postoperative SIRS including mannose-binding lectin deficiency(23), high levels of circulating GM-CSF + CD4 + T cells(24), bacteriuria and renal stone size (25), diabetes mellitus, and the intraoperative use of an intra-aortic balloon pump(26). However, their predictive values are limited because measurements of most of these parameters are generally not available or easily obtainable in routine testing, or only pertain to particular surgical operations. These limitations preclude their general application to the geriatric population. Fernando et al. developed a model using a Bayesian network approach to predict SIRS in patients admitted to ICU with acute infections (27). In comparison, a nomogram could present a quantitative and practical prediction tool for risk stratification for patients at risk for postoperative SIRS, with the ability to generate a patient-specific numerical probability of a clinical event by integrating diverse prognostic and determinant variables(28, 29).

Wang et al. developed a nomogram to predict SIRS after transrectal ultrasound-guided prostate biopsy (11). However, it was evaluated in a single-center study with a small sample size and without external validation. In the current study, we enrolled 16141 patients aged  $\geq 65$  years from two medical centers and divided the patients into training and validation cohorts. We trained the logistic regression model on 19 statistically significant features and incorporated 6 comprehensive and easily accessible variables to form our nomogram, which performed well as evidenced by the AUCs of 0.800 and 0.823 in the training and validation cohorts, respectively. Furthermore, the calibration curves of our nomogram demonstrated an agreement between predictions and actual observations.

The 6 easily-accessible features incorporated into our novel predictive model included preoperative fever, preoperative albumin level, ASA classification, intraoperative total infusion volume, surgical duration, and postoperative ICU admission; most of which have been associated with SIRS (30–35). All of the variables were chosen based on the results of resampling methods, previous literature, and clinical experience. Although some of the factors may be very practice dependent, for instance, the total volume of infusion and postoperative ICU admission are strong predictors that heavily weighted in the nomogram, we have tried to validate the utility of this nomogram in another 1105 patients in 2020 and found it performed well in predicting postoperative SIRS and provide clinicians with practical guidelines to facilitate early diagnosis and proactive interventions in elderly patients to avoid worsen complications, especially for the clinicians in surgical ICU and for the aged patient with preoperative fever, a preoperative albumin level  $< 30$  g/L, an ASA classification of III/IV/V, an intraoperative total infusion volume  $> 2000$  ml, a surgical duration of  $> 200$  min, and who is admitted to ICU after surgery (Fig. 3).

Several limitations in this study should be addressed. Firstly, the retrospective study design may be prone to collection and entry bias, as well as residual confounding. Secondly, we did not report the incidence of sepsis in the study since that the key data needed for sepsis-3 criteria to diagnose sepsis is missing due to the retrospective design. Thirdly, as the elderly patients receiving regional anesthesia in our hospital are generally in relatively good conditions and often require a short and minor operation that might have lower risk of postoperative SIRS, we only enrolled the patients with general anesthesia and endotracheal intubation in the study. Fourthly, despite having high sensitivity and specificity to identify elderly patients at high risk for postoperative SIRS, the model may potentially miss important factors that could not be accounted for in the retrospective analysis such as genetic or clinical factors that might be even more important to predict postoperative SIRS(26). Future prospective studies are needed to collect more clinical and genomic information to predict an individual patient's predisposition to SIRS more precisely.

## Conclusions

In conclusion, we have developed and externally validated an effective model for predicting the risk of postoperative SIRS in elderly patients. Based on the model, we constructed a practical nomogram that is highly accurate, and that exhibits excellent calibration. This nomogram might enable clinicians to make individualized predictions of each patient's probability of postoperative SIRS and to improve treatment recommendations for elderly patients.

# List Of Abbreviations

SIRS: systemic inflammatory response syndrome; AUC: area under the receiver operating characteristics curve; ICU: intensive care unit; MODS: multiple organ dysfunction syndrome; HER: Electronic Health Record; HIS: hospital information system; ROC: receiver operating characteristic.

## Declarations

### Funding

This study was supported partly by the National Natural Science Foundation of China (Grant No. 81974296 for Prof. Ziqing Hei), Postdoctoral Science Foundation of China (Grant No. 2019M663260; 2020T130148ZX for Dr. Chaojin Chen) and Basic and Applied Basic Research Foundation of Guangdong Province (Grant No. 2019A1515110020 for Dr. Chaojin Chen)

### Conflicts of interest

The authors declare that they have no conflicts of interest.

### Availability of data and material

The raw data supporting the conclusions of this article will be made available by the corresponding authors via email.

### Authors' contributions

Manuscript writing: CC, XL, QZ; Data analysis: ZL, YL, JC; Cases and supplementary search: TL, CC; Project guidance: ZH, SZ, ZL.

### Ethics approval

This study was approved by the Institutional Ethics Committee from the two hospitals and was censored on 18 May 2019 (No.[2019]02-609-01). The requirement for informed consent and clinical trial registration were waived by the committee.

### Consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Acknowledgments

The authors thank all of the patients who kindly participated in this study.

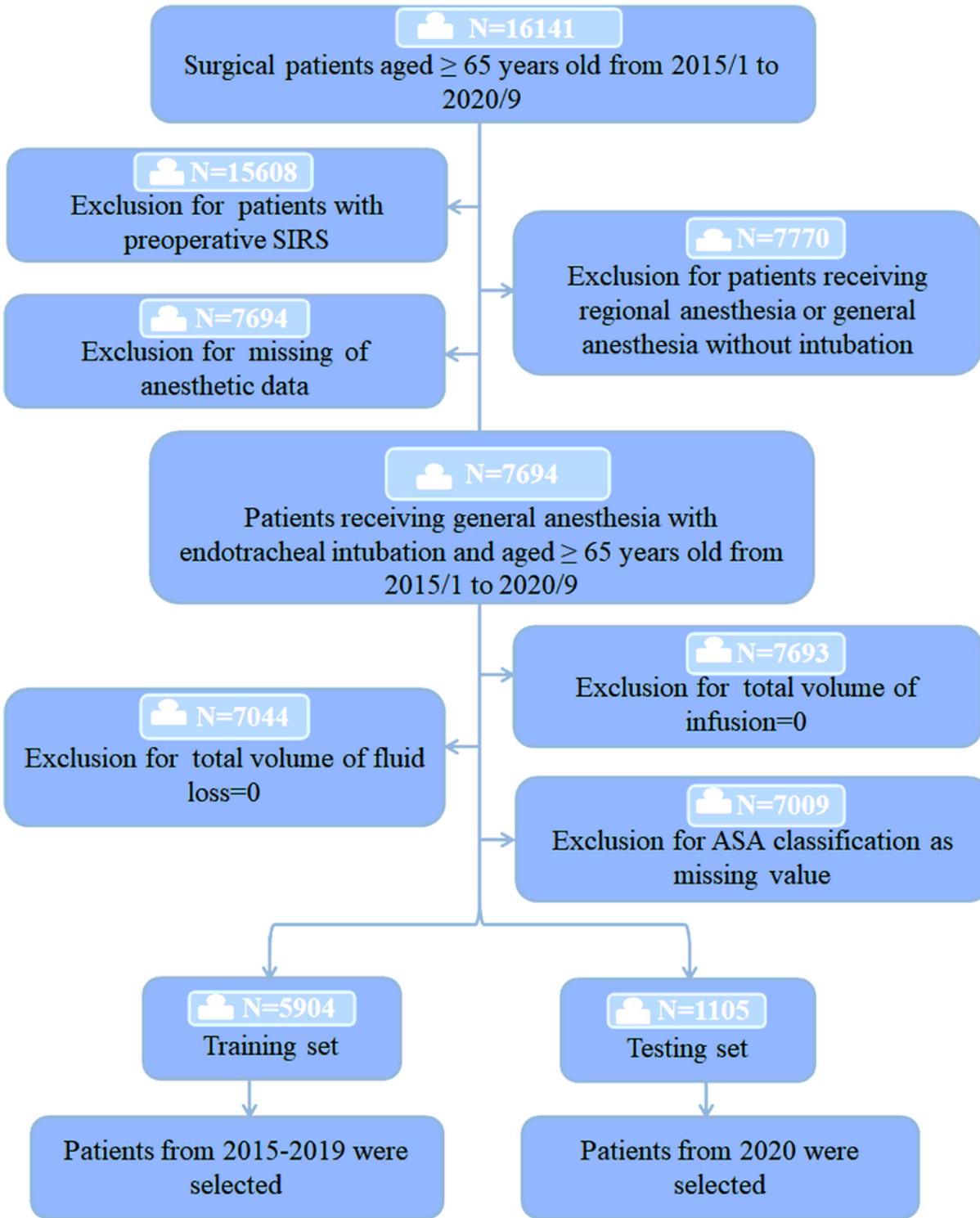
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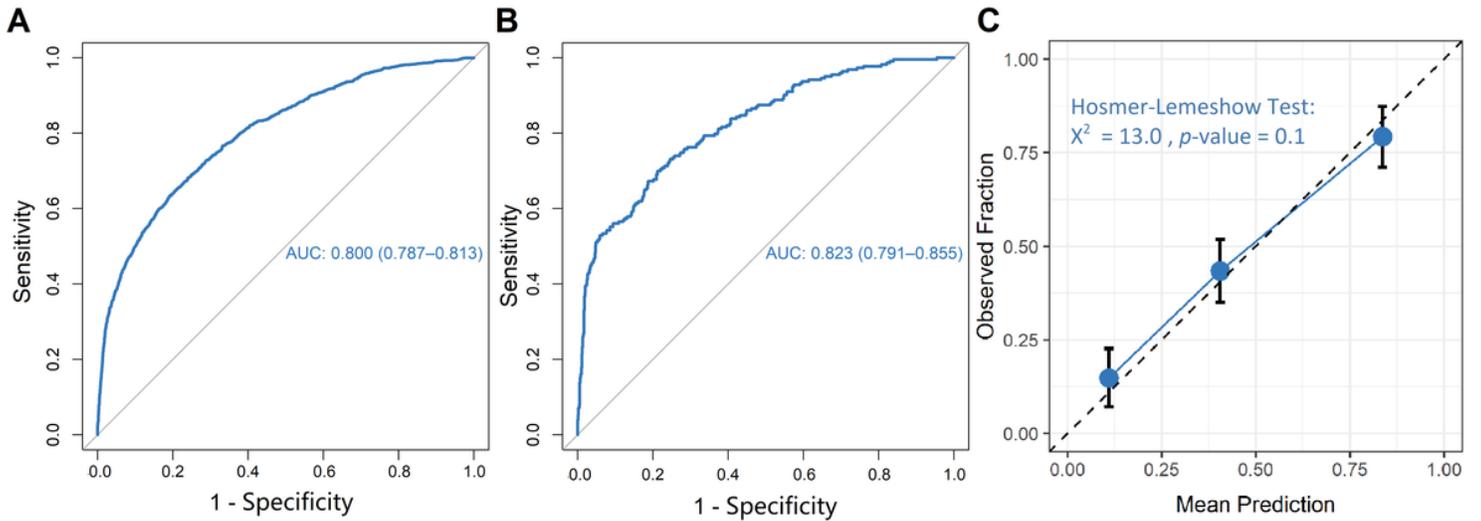
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## Figures



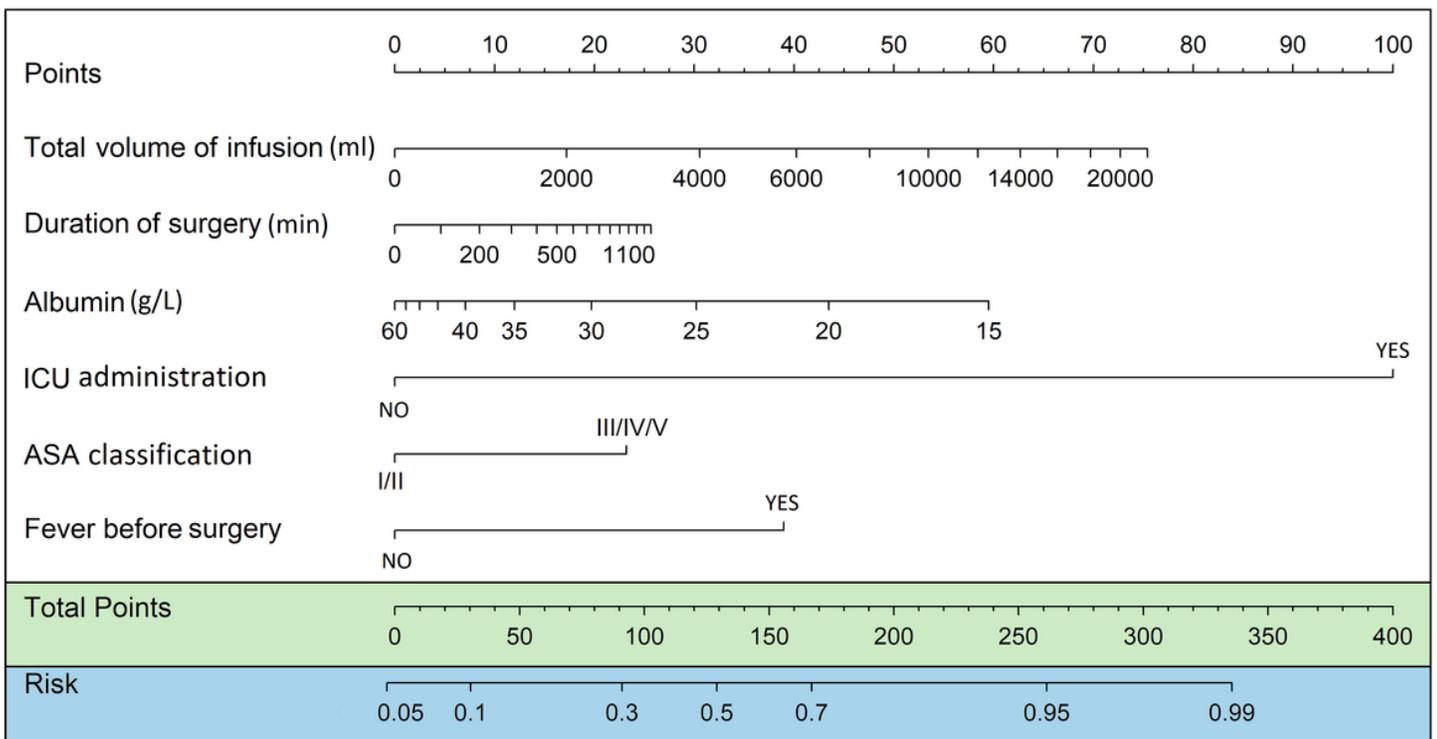
**Figure 1**

Flow chart demonstrating the patient selection process



**Figure 2**

ROC plot and calibration of the logistic regression model ROC plot for development (A) and validation (B) set; (C) The calibration curve for predicting patient SIRS.



**Figure 3**

Nomogram to predict postoperative SIRS in elderly patients

## Supplementary Files

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