Research Square

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Development of a prognostic prediction model for prostate cancer patients using the MIMIC-IV database

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Abstract

Purpose

To develop and validate a prognostic model for risk stratification in critically ill prostate cancer (PCa) patients admitted to the intensive care unit (ICU) using a large clinical database.

Methods

A retrospective cohort of PCa patients admitted to the ICU was derived from the Medical Information Mart for Intensive Care (MIMIC) database and randomly divided into training and validation sets at a 7:3 ratio. Prognostic variables were identified using univariate and multivariate Cox regression. Least Absolute Shrinkage and Selection Operator (LASSO) Cox regression was applied to construct a parsimonious model and calculate individual risk scores, which were incorporated into a nomogram. Model performance was assessed using Kaplan–Meier analysis, receiver operating characteristic curves, calibration plots, decision curve analysis, restricted cubic splines, and subgroup analyses.

Results

A total of 343 patients were included. Serum chloride, respiratory rate, and the Simplified Acute Physiology Score II (SAPS II) were identified as independent prognostic factors. Patients were stratified into high- and low-risk groups based on the model score, with the high-risk group showing significantly worse prognosis ($p < 0.05$). The model demonstrated predictive value for 28-day mortality (training AUC = 0.675; validation AUC > 0.6). The nomogram exhibited good calibration and positive net clinical benefit. Nonlinear relationships between predictors and mortality were observed, and a significant interaction was identified between chloride levels and atrial fibrillation.

Conclusion

A prognostic model incorporating serum chloride, respiratory rate, and SAPS II effectively stratifies critically ill PCa patients into distinct risk groups, facilitating early risk identification and individualized management in the ICU.

1. Background

Prostate cancer (Prostatic Carcinoma, PCa) is a malignant tumor originating from the glandular epithelial cells of the prostate. According to the latest GLOBOCAN 2022 statistics, PCa ranks fourth in global cancer incidence, accounting for 7.3% of all cancers worldwide[1]. In China, PCa incidence and mortality are rising rapidly due to population aging, Westernized lifestyles, and widespread PSA screening, placing a heavy burden on patients, families, and the healthcare system[2]. Its core clinical

feature lies in marked heterogeneity, with the disease spectrum ranging from slow-growing, indolent tumors requiring no immediate intervention to highly invasive, metastatic, lethal diseases[3, 4]. The development of PCa results from complex interactions between genetic susceptibility and environmental factors[5] .With the continuous advancement of cancer treatment strategies, the survival rate of cancer patients has been significantly improved. Concomitantly, the proportion of cancer patients requiring intensive care unit (ICU) admission has been on the rise, mainly due to disease progression, treatment-related complications, or concurrent critical illnesses. Among prostate cancer patients, those with advanced disease or severe systemic complications are also frequently confronted with the need for ICU admission, and their clinical outcomes are influenced by multiple factors, including tumor intrinsic characteristics, organ function status, and response to critical care interventions.

However, the applicability of existing prognostic assessment tools in this specific patient population remains notably limited. On the one hand, general ICU scoring systems (e.g., APACHE II and SAPS II) have been shown to systematically underestimate the mortality risk in cancer patients and lack adequate calibration [6]. On the other hand, existing cancer-specific ICU scoring systems (such as ICMM) have faced questions regarding their predictive performance, as the patient cohorts on which they were developed no longer adequately reflect current clinical characteristics [7].

Furthermore, existing prognostic models developed for a broad spectrum of ICU patients (e.g., CanICU) include an extremely low proportion of prostate cancer patients and thus lack specific analysis and validation for this tumor type [8]. Given these limitations, the development of a specialized prognostic assessment tool that integrates intensive care physiological parameters with the clinical characteristics of prostate cancer holds significant clinical value for improving risk stratification and personalized management of this patient population.

MIMIC-IV is a large, publicly available, single-center clinical database covering intensive care unit (ICU) patients admitted to Beth Israel Deaconess Medical Center in Boston, USA, between 2008 and 2019, with comprehensive, de-identified clinical data[9]. This database integrates multidimensional information, including vital signs, laboratory tests, medication records, diagnostic and therapeutic procedures, and clinical outcomes, providing high-quality real-world data resources for critical care medicine and disease-specific research[10]. Its strengths lie in its large scale, rich variables, and open access, having been widely applied in constructing clinical prediction models and evaluating healthcare quality for critical illnesses such as sepsis and acute respiratory distress syndrome[11] .

This study systematically extracted and analyzed clinical data from a retrospective cohort of ICU-admitted PCa patients using the MIMIC-IV large-scale critical care clinical database. By integrating survival analysis, multivariate regression analysis, and machine learning algorithms, we screened for independent prognostic factors across multiple dimensions, including demographic characteristics, vital signs, laboratory indicators, and disease severity scores, and constructed a prognostic assessment model specifically tailored to the ICU setting. The model's performance was further assessed via calibration, discrimination, and clinical utility analyses to ensure its reliability and applicability in clinical

practice. Based on routinely accessible clinical variables, this model provides clinicians with an immediate and objective risk stratification tool, facilitating the early identification of high-risk patients and supporting the optimization of monitoring and intervention strategies. Ultimately, this study aims to provide practical, evidence-based support for more refined and individualized management of critically ill PCa patients in real-world clinical scenarios.

2. Methods

This study leveraged the MIMIC-IV large-scale critical care clinical database to systematically extract and analyze clinical information from a retrospective cohort of PCa patients admitted to the ICU. By integrating survival analysis, multivariate regression, and machine learning algorithms, we screened independent prognostic factors across multiple dimensions—including demographic characteristics, vital signs, laboratory indicators, and disease severity scores—and constructed a prognostic assessment model tailored specifically to the ICU setting. The model's performance was further evaluated through calibration, discrimination, and clinical utility analyses to ensure its reliability and applicability. Based on routinely available clinical variables, this model offers clinicians an immediate and objective risk stratification tool to facilitate early identification of high-risk patients and support the optimization of monitoring and intervention strategies. Ultimately, this study aims to provide practical, evidence-based support for more refined individualized management of critically ill PCa patients in real-world clinical practice.

2.1 Data Preparation

Study data were obtained from the MIMIC-IV database, which contains clinical records of ICU patients at Beth Israel Deaconess Medical Center in Boston, USA. This study adheres to the Declaration of Helsinki (1975 edition), and informed consent was obtained from all participants.

First, patients diagnosed with PCa using ICD-9 code (185) and ICD-10 code (C61) were included (access date: October 29, 2025). Inclusion criteria were: (1) age ≥ 18 years; (2) first ICU admission; (3) ICU stay > 24 hours. Exclusion criteria were: (1) age < 18 years; (2) non-first ICU admission; (3) death within 24 hours of ICU admission; (4) severe missing key prognostic data or baseline information. Eligible patient data were then randomly split into training and validation sets at a 7:3 ratio. The recruitment process is illustrated in Fig. 1.

2.2 Baseline Feature Analysis

Baseline characteristics were extracted from MIMIC-IV using the first 24-hour values. Variables comprised five categories: (1) demographics (age, race, weight); (2) ICD-defined comorbidities (hypertension, atrial fibrillation, diabetes, chronic kidney disease, chronic obstructive pulmonary disease); (3) laboratory indicators (white blood cell count, hemoglobin, platelet count, serum sodium, serum potassium, serum chloride, bicarbonate, blood urea nitrogen, creatinine, blood glucose); (4) vital

signs (systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, body temperature, transcutaneous oxygen saturation); (5) severity scores: Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) (Table 1). Based on the training set from MIMIC-IV, enrolled PCa patients were divided into survival and death groups by survival status. Differences in baseline characteristics were analyzed using the R package "tableone" (v 0.13.2)[12] via ANOVA for continuous variables and chi-square tests for categorical variables ($p < 0.05$).

Table 1
Research Variable Information Table.

Covariate	English Name	Description
Race	race	Black, White, Other
Sex	gender	Male, Female
Age	age	≥ 18 years, continuous
Weight	weight	Continuous
White blood cell	wbc	Continuous
Hemoglobin	hemoglobin	Continuous
Platelet count	platelets	Continuous
Blood urea nitrogen	bun	Continuous
Creatinine	creatinine	Continuous
Potassium	potassium	Continuous
Sodium	sodium	Continuous
Bicarbonate	bicarbonate	Continuous
Chloride	chloride	Continuous
Glucose	glucose	Continuous
Diastolic blood pressure	dbp	Continuous
Systolic blood pressure	sbp	Continuous
Mean blood pressure	mbp	Continuous
Respiratory rate	resp_rate	Continuous
Temperature	temperature	Continuous
Peripheral oxygen saturation	spo2	Continuous
SAPS II score	sapsii	Continuous
SOFA score	sofa	Continuous
Atrial fibrillation	atrial_fibrillation	No, Yes
Chronic kidney disease	chronic_kidney_disease	No, Yes
Chronic obstructive pulmonary disease	copd	No, Yes
Hypertension	hypertension	No, Yes
Diabetes mellitus	diabetes	No, Yes

2.3 Screening of prognostic variables

To identify variables closely associated with prognosis in patients with severe PCa, this study performed stepwise regression analysis on the training set. First, for variables with significant intergroup differences ($p < 0.05$) in baseline analysis, univariate Cox proportional hazards regression was performed using the R package "survival" (v 3.7-0)[13]. (Hazard Ratio(HR) ≠ 1, $p < 0.05$) as the threshold. To ensure the regression model satisfied the proportional hazards (PH) assumption, PH tests were performed on all variables significant in univariate analysis. Variables with $P > 0.05$ were considered meeting the PH assumption and were listed as candidate variables.

Subsequently, using the R package "survival" (v 3.7-0), all candidate variables were simultaneously entered into a multivariate Cox proportional hazards regression model to assess their independent prognostic value and eliminate confounding effects. Variables in the model results that maintained statistical significance for HR (HR ≠ 1, $p < 0.05$) and again passed the PH assumption test were ultimately identified as independent prognostic variables influencing patients with severe PCa.

2.4 Construction, Evaluation, and Validation of Prognosis Models

To build a streamlined prognostic model, LASSO Cox regression was applied to the training set using the R package "glmnet" (v 4.1-8)[14] with 10-fold cross-validation to further screen the identified independent prognostic variables. The penalty coefficient λ (lambda.min) yielding the smallest cross-validation error was selected as optimal, with variables retaining non-zero coefficients retained as key variables for the final model.

Based on the selected key variables and their corresponding regression coefficients, a continuous risk score was calculated for each patient. The formula is as follows:

$$\text{Riskscore} = \sum_{i=1}^{n} \beta i * xi$$

β denotes the coefficient, and x represents the sample value. In the training set, the survival_cutpoint function from the R package "survival" (minprop = 0.2) determined the optimal risk score cutoff for prognostic stratification, dividing patients into high- and low-risk groups (HRG and LRG). Survival differences were assessed via Kaplan-Meier **(k-m)** curves using the "survminer" (0.4.9)[15]. Model accuracy was evaluated with ROC curves ("survivalROC" [v 1.0.3.1][16]) at 28 days, calculating the Area Under the Curve (AUC) value (AUC > 0.6).

2.5 Construction and evaluation of the nomogram

Using the training set, a nomogram model incorporating key variables was constructed with the "rms" (v 6.8-1)[17] to predict PCa risk. Multi-dimensional validation was performed: calibration curves ("rms") compared predicted vs. observed 28-day mortality; discrimination was evaluated with 28-day ROC curves (AUC > 0.7) using "survivalROC"; and Decision Curve Analysis (DCA) via the "rmda" (v 1.6)[18] assessed clinical net benefit across thresholds, benchmarking against individual key variables to quantify clinical application value.

2.6 RCS analysis and risk stratification analysis of key variables

To explore the potential nonlinear relationship between key continuous predictor variables and outcome risk, this study conducted an analysis based on the training set using the restricted cubic spline method. Using the R package "rms", on the basis of adjusting other variables, each key variable was respectively incorporated into the Cox proportional hazards model in the form of spline functions (with three nodes set), using the R package "ggplot2" (v 3.5.1)[19] visualize the results to assess whether there is a nonlinear association between them and the risk of death, and explore possible clinical effect inflection points.

To understand the possibility of key variables and the risk of severe death due to PCa occurring in different populations, based on the training set, all categorical variables and SOFA scores were included for risk stratification analysis (all continuous variables were divided into high and low groups according to the median value), and the R package "jstable" (v 1.3.8)[20] A MultiCox regression model was constructed. The hazard ratios and significance p values obtained were aggregated. An interaction p-value < 0.05 indicated a significant subgroup effect for the key variable. The forest plot was generated using the "forestploter" (v 1.1.1)[21] .

2.7 Statistical analysis

R software (v 4.3.3) was used for data analysis. Between-group comparisons used analysis of variance for continuous variables (mean ± standard deviation) and chi-square tests for categorical variables (frequencies [percentages]), with statistical significance set at $p < 0.05$.

3. Results

3.1 Baseline characteristics of patients in the training set

This study ultimately included 343 PCa patients, randomly allocated to training (n = 251) and validation (n = 92) sets in a 7:3 ratio (**Supplementary Tables 1 and 2**). Comparing baseline characteristics between survival and death groups in the training set identified seven variables with significant effects on survival in severe PCa patients ($p < 0.05$). Including white blood cells (wbc), platelet count (platelets), chloride ions (chloride), mean blood pressure (mbp), respiratory rate (resp_rate), SAPSII score, and SOFA score. Elevated white blood cell count, elevated platelet count, decreased chloride level, decreased blood

pressure, increased respiratory rate, and higher SAPS II and SOFA scores were significantly associated with poor prognosis in severe PCa patients (Table 2).

Table 2
Comparison of baseline Characteristics of Patients in the Training set.

n	level	Alive	Death	p
		220	**31**	
race (%)	BLACK	27 (12.3)	4 (12.9)	0.985
	OTHER	38 (17.3)	5 (16.1)	
	WHITE	155 (70.5)	22 (71.0)	
age (mean (SD))		76.61 (10.26)	78.20 (9.29)	0.415
fracture_type (%)	185	117 (53.2)	13 (41.9)	0.326
	C61	103 (46.8)	18 (58.1)	
weight (mean (SD))		84.42 (20.12)	84.35 (15.54)	0.985
wbc (mean (SD))		9.26 (4.36)	11.91 (8.52)	0.007
hemoglobin (mean (SD))		9.92 (2.24)	9.27 (2.94)	0.15
platelets (mean (SD))		169.64 (77.22)	218.35 (130.85)	0.003
sodium (mean (SD))		137.35 (5.17)	136.77 (4.16)	0.556
potassium (mean (SD))		3.90 (0.53)	4.05 (0.62)	0.142
chloride (mean (SD))		102.60 (6.05)	100.10 (5.69)	0.031
bicarbonate (mean (SD))		21.46 (4.20)	20.77 (5.95)	0.423
bun (mean (SD))		26.89 (19.51)	32.16 (14.31)	0.148
creatinine (mean (SD))		1.47 (1.38)	1.36 (0.88)	0.691
glucose (mean (SD))		116.46 (31.98)	112.71 (42.46)	0.559
sbp (mean (SD))		91.35 (17.89)	87.23 (15.79)	0.224
dbp (mean (SD))		46.68 (10.55)	44.94 (10.22)	0.388
mbp (mean (SD))		59.68 (13.24)	54.45 (14.63)	0.043
resp_rate (mean (SD))		12.20 (3.89)	15.08 (4.48)	< 0.001
spo2 (mean (SD))		91.51 (5.53)	89.68 (8.38)	0.109
temperature (mean (SD))		36.23 (0.72)	36.35 (0.47)	0.38

Note: The first column represents variables. Continuous variables are expressed as mean ± standard deviation (SD), and categorical variables are expressed as percentages (%). "Level" indicates the level of the categorical variable; "Alive" indicates the survival group, and "Death" indicates the death group. The P-value indicates significance.

n	level	Alive	Death	p
		220	**31**	
sapsii (mean (SD))		40.52 (11.08)	51.52 (14.69)	< 0.001
sofa (mean (SD))		4.55 (2.92)	6.03 (3.34)	0.01
hypertension (%)	NO	56 (25.5)	10 (32.3)	0.557
	YES	164 (74.5)	21 (67.7)	
atrial_fibrillation (%)	NO	175 (79.5)	26 (83.9)	0.746
	YES	45 (20.5)	5 (16.1)	
chronic_kidney_disease (%)	NO	164 (74.5)	25 (80.6)	0.607
	YES	56 (25.5)	6 (19.4)	
diabetes (%)	NO	162 (73.6)	24 (77.4)	0.817
	YES	58 (26.4)	7 (22.6)	
copd (%)	NO	190 (86.4)	26 (83.9)	0.922
	YES	30 (13.6)	5 (16.1)	

Note: The first column represents variables. Continuous variables are expressed as mean ± standard deviation (SD), and categorical variables are expressed as percentages (%). "Level" indicates the level of the categorical variable; "Alive" indicates the survival group, and "Death" indicates the death group. The P-value indicates significance.

3.2 Results of univariate and multivariate Cox regression analyses

From univariate analysis, four variables were significantly associated with prognosis in severe PCa patients ($p < 0.05$). Chloride acted as a protective factor (HR = 0.92), with increased levels reducing death risk, whereas platelet count (HR = 1.002), respiratory rate (HR = 1.12), and SAPS II score (HR = 1.05) were risk factors (Fig. 2a). All four satisfied the PH assumption ($p > 0.05$), indicating proportional hazards over time, and were therefore included as candidate variables (Fig. 2b). Multivariate Cox regression subsequently demonstrated that after adjusting for other variables, platelet count no longer remained significant, while chloride, respiratory rate, and SAPS II score continued to show independent prognostic effects ($HR \neq 1$, $p < 0.05$). Indicating that the influence of these key variables on critically ill patients with PCa is not disturbed by other variables, they are independent prognostic factors for PCa (Fig. 2c). In addition, the PH hypothesis test showed that the risk of these three variables (chloride ions, respiratory rate, and SAPSII score) for severe PCa patients did not change over time ($p > 0.05$) (Fig. 2d), and they were recorded as independent prognostic variables. These three independent prognostic factors—reflecting electrolyte balance, respiratory function, and overall disease severity—could be integrated into a clinical risk-stratification model to better identify high-risk patients and guide tailored management

strategies. Future validation in larger cohorts may further confirm their utility in optimizing prognostic assessment for critically ill PCa patients.

3.3 Construction and validation of prognostic risk models

LASSO Cox regression analysis was performed on the three identified independent prognostic variables. Under the optimal penalty coefficient (log(λ) = -6.2047), chloride ions, respiratory rate, and SAPS II score were all retained and recorded as key variables (Fig. 3a-b). Based on this, a risk scoring formula was constructed. In the training set, patients were divided into HRG (n = 85) and LRG (n = 166) using the optimal cutoff value (-2.684). K-M survival analysis showed that the in-hospital survival rate was significantly lower in the HRG than in the LRG (Log-rank $p < 0.05$) (Fig. 3c). The AUC of this model for predicting the 28-day mortality risk was 0.675, indicating that the prediction effect of each time node was of reference value (Fig. 3d). These three key variables effectively predicted patient survival, indicating good model performance. In the validation set, the same scoring formula and optimal cutoff value (-2.461) were applied, significantly dividing patients into HRG (n = 19) and LRG (n = 73) (Log-rank $p < 0.05$). The HRG showed lower survival, consistent with the training set trend (Fig. 3e). Meanwhile, the AUC value at 28 days was 0.627, indicating that the prognostic risk model of the 3-point validation set was relatively good(Fig. 3f).

3.4 Construction and performance evaluation of predictive nomogram

A nomogram was constructed for three key variables. The results showed that the SAPS II score had the longest line segment, indicating its greatest contribution to the risk of death, followed by the chloride ion level, and the contribution of respiratory rate was relatively the smallest (Fig. 4a). The calibration curve showed strong agreement between the model's predicted 28-day death probability and the actual observed probability, indicating good calibration (Fig. 4b). The nomogram achieved a 28-day AUC of 0.677, reflecting good predictive performance (Fig. 4c). DCA further confirmed that across a wide range of threshold probabilities, the net benefit of using this nomogram to guide clinical decision-making was consistently higher than that of any single key variable, indicating superior clinical utility (Fig. 4d).

3.5 The results of the interaction analysis between RCS and subgroups

The RCS analysis results showed that there were nonlinear associations between chloride ion levels, respiratory rate, and SAPS II scores and the risk of death. Specifically, when chloride ion levels exceed 103, respiratory rate is below 13 breaths per minute, and the SAPS II score is under 40, the hazard ratio (HR) is less than 1, indicating a relatively low risk of death (Fig. 5a-c). These values may provide potential reference thresholds for clinical risk assessment and intervention. Subgroup interaction analysis revealed a significant interaction between chloride ions and atrial fibrillation ($p < 0.05$). In the high

chloride level group, patients with atrial fibrillation had a significantly higher risk of death than those without atrial fibrillation (HR = 4.52) (Fig. 5d), suggesting that the prognostic impact of chloride ions may differ in patients with atrial fibrillation. However, in the subgroup analysis of respiratory rate and SAPS II score, no significant interaction was found with other demographic characteristics or comorbidities ($p > 0.05$) (Fig. 5e-f), suggesting that the effects of these two variables as risk prediction indicators were relatively stable in different populations.

4. Discussion

PCa is the second most common malignancy in men worldwide, characterized by highly heterogeneous clinical courses, with advanced patients facing a poor prognosis[1]. Currently, prognostic assessment tools for critically ill PCa patients are lacking. As a large public intensive care clinical database, MIMIC-IV provides real-world data support for such research[22]. Based on MIMIC-IV, this study systematically analyzed prognostic risk factors of critically ill PCa patients. Through multi-stage statistical modeling and machine learning, we identified chloride ion level, respiratory rate, and SAPS II score as independent key indicators for in-hospital mortality. Using these easily accessible variables, we constructed and validated a prognostic risk model and its visual nomogram, providing a potential quantitative basis for rapid identification of high-risk PCa patients and risk stratification management in the ICU.

Baseline analysis revealed significant differences between survival and death groups in critically ill PCa patients for white blood cell count, platelet count, chloride level, mean arterial pressure, respiratory rate, SAPS II, and SOFA scores. Subsequent univariate and multivariate Cox regression further identified chloride ion, respiratory rate, and SAPS II score as independent prognostic factors for in-hospital mortality, which has important clinical implications.

As a core extracellular anion, the chloride ion is closely related to acid-base balance, neuromuscular excitability, and renal function[23, 24]. In critically ill patients, hypochloremia is associated with poor prognosis, possibly due to renin-angiotensin system activation, aggravated inflammation, and altered vascular tone[25, 26]. This study identified lower chloride level as a mortality risk factor in critically ill PCa patients, suggesting that hypochloremia may serve as a potential biomarker for predicting mortality risk in advanced prostate cancer. Further prospective studies are warranted to investigate whether correction of hypochloremia could improve clinical outcomes in this patient population. As an easily monitorable vital sign, respiratory rate reflects physiological reserve and stress state, serving as an early signal of hypoxia, infection, and other pathological conditions[27, 28]. In tumor patients, it may also indicate cancer-related fatigue or pulmonary metastasis[29]. This study identified it as an independent risk factor, emphasizing the importance of continuous respiratory monitoring in ICU PCa patients; its abnormal increase can warn of disease deterioration. SAPS II score, a widely used ICU disease severity evaluation tool[30], integrates multi-dimensional information to quantify acute physiological disorders[31]. For critically ill PCa patients, an elevated respiratory rate in cancer patients may suggest the presence of lung metastasis, pleural effusion, or infectious complications, and may serve as an early indicator of impaired overall physiological reserve. This is consistent with the findings of our study, in

which an increased respiratory rate was predictive of mortality risk[27]. A prognostic model and nomogram were constructed and validated based on these three variables. Higher SAPS II scores denote more severe critical illness and exhibit moderate predictive utility for short-term mortality, which is consistent with the overall discriminative performance of the model developed in the present study.. ROC curve analysis revealed that our model demonstrated moderate discriminative performance in both the training and validation datasets, with corresponding AUC values of 0.675 and 0.627. Given the complexity of clinical conditions and the multitude of confounding variables in critically ill ICU patients, this predictive accuracy still provides certain reference value for clinical practice. However, these findings also highlight several limitations of the current model, which should be addressed and further validated in future prospective studies.

The three prognostic indicators identified in this study—serum chloride, respiratory rate, and SAPS II score—collectively constitute a rapid, bedside risk stratification tool for critically ill patients with PCa. A major strength of this model is that all three variables are routinely measured in the ICU, with no need for additional testing or specialized equipment, thus enabling straightforward clinical translation[32, 33]. In contrast to traditional single-score systems, the nomogram provides a visual representation of the relative contribution of each risk factor, allowing clinicians to better appreciate how these variables jointly affect prognosis and calculate individualized mortality probabilities at the bedside[34]. DCA further confirmed that the nomogram provides a higher net clinical benefit across a wider range of threshold probabilities than any single predictor alone, supporting its incremental value over existing risk-stratification tools[35] .

Subgroup interaction analysis identified a significant interaction between serum chloride levels and atrial fibrillation in predicting mortality. In the main analysis, higher chloride levels were associated with reduced mortality risk; however, this protective association was significantly attenuated or even abolished in patients with concomitant AF, suggesting that AF may mitigate or negate the beneficial effect of elevated chloride levels. These findings indicate that the prognostic value of chloride is not homogeneous across all patient subgroups. Accordingly, the presence of AF should be taken into account when performing chloride-based risk stratification in critically ill patients.

The biological mechanism underlying this interaction may be linked to the well-documented hemodynamic consequences of AF in critically ill populations. AF impairs synchronized atrial contraction, reduces cardiac output, and promotes systemic hypoperfusion, thereby compromising the maintenance of electrolyte homeostasis and amplifying the physiological impact of electrolyte disturbances[36]. In this setting, even with serum chloride within an ostensibly favorable range, concurrent AF independently contributes to progressive circulatory dysfunction and adverse clinical outcomes.

This interaction carries particular clinical relevance in patients with advanced PCa, in whom AF is not merely an incidental comorbidity. A network meta-analysis of 26 randomized controlled trials showed that androgen receptor pathway inhibitors (ARPIs) more than double the risk of atrial fibrillation (AF)

compared with standard treatments[37]. Pharmacovigilance data further indicate that abiraterone is associated with a significantly higher risk of atrial tachyarrhythmias compared with other androgen deprivation therapies, partly due to mineralocorticoid excess[38]. This effect may concurrently trigger electrolyte disorders, including hypokalemia and chloride imbalance. Thus, in patients with advanced PCa receiving ARPIs, AF and electrolyte disturbances may coexist and act synergistically to drive poor clinical outcomes. For these patients, we recommend integrated cardiac rhythm monitoring and dynamic electrolyte evaluation. The exact mechanistic basis of this interaction merits further exploration in prospective clinical studies.

The three prognostic indicators identified in this study—serum chloride, respiratory rate, and SAPS II score—collectively constitute a rapid, bedside risk stratification tool for patients with severe prostate cancer (PCa). A major strength of this model is that all three variables are routinely measured in the intensive care unit (ICU) without requiring additional laboratory tests or specialized equipment, thereby facilitating straightforward implementation in routine clinical practice [32, 33]. In contrast to traditional single-score prognostic systems, the decision tree model visually depicts the relative contribution of each risk factor, allowing clinicians to better comprehend the combined effects of variables on prognosis and compute individualized mortality probabilities at the bedside [34]. Furthermore, receiver operating characteristic (ROC) curve analysis in the present study confirmed that our integrated model yields a higher net clinical benefit across a broad spectrum of threshold probabilities compared with any individual predictor alone, supporting its incremental value over existing prognostic tools [35]. The results provide a direct quantitative basis for the rapid risk identification and stratified management of PCa patients with high heterogeneity in the complex ICU environment, and are expected to promote the interdisciplinary collaboration between oncology and intensive care medicine. However, this study has certain limitations. First, as a retrospective study, it inevitably involves selection bias and unmeasurable confounding factors. Second, the data are derived from the ICU of a single center, so caution should be exercised when extrapolating its conclusions to PCa patients in other medical institutions or general wards. Finally, this study primarily focuses on short-term in-hospital outcomes and does not evaluate the impact of these risk factors on long-term survival or quality of life. Future studies can adopt multi-center, prospective designs, integrate more tumor-specific variables (such as Gleason score, PSA dynamics, and treatment regimens), and long-term follow-up data to construct a more comprehensive and accurate prognostic prediction system, and promote the in-depth translation of research results into clinical practice.

5. Conclusions

A prognostic model incorporating serum chloride, respiratory rate, and SAPS II was developed and validated to stratify critically ill prostate cancer patients into distinct risk groups. The nomogram demonstrated good calibration and net clinical benefit. Nonlinear associations were observed between predictors and mortality, with a significant interaction identified between chloride levels and atrial fibrillation. This model provides a practical tool for early risk identification and individualized management in the ICU.

Abbreviations

Abbreviation	Full Term
AAG	human serum alpha-1-acid glycoprotein
AF	atrial fibrillation
AUC	area under the curve
DCA	decision curve analysis
HR	hazard ratio
ICU	intensive care unit
LASSO	least absolute shrinkage and selection operator
MIMIC	Medical Information Mart for Intensive Care
MIMIC-IV	Medical Information Mart for Intensive Care IV
PAF	platelet-activating factor
PH	proportional hazards
RCS	restricted cubic spline
SD	standard deviation
SOFA	sequential organ failure assessment

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data supporting the findings of this study are publicly available. Clinical data were obtained from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, which contains intensive care unit records from Beth Israel Deaconess Medical Center, Boston, USA. These data can be accessed upon approval by the institutional review board and completion of a data use agreement via the MIMIC-IV repository (https://physionet.org/content/mimiciv/). Patients diagnosed with prostate cancer were identified using ICD-9 code 185 and ICD-10 code C61. No new primary data were generated in this study.

Competing interests

The authors declare that they have no competing interests

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Author contributions

Zhengyonigqing□kuangmiao analyzed and interpreted the patient data regarding the hematological disease and the transplant. Xiaocui□Chengpeinan performed the histological examination of the kidney, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures

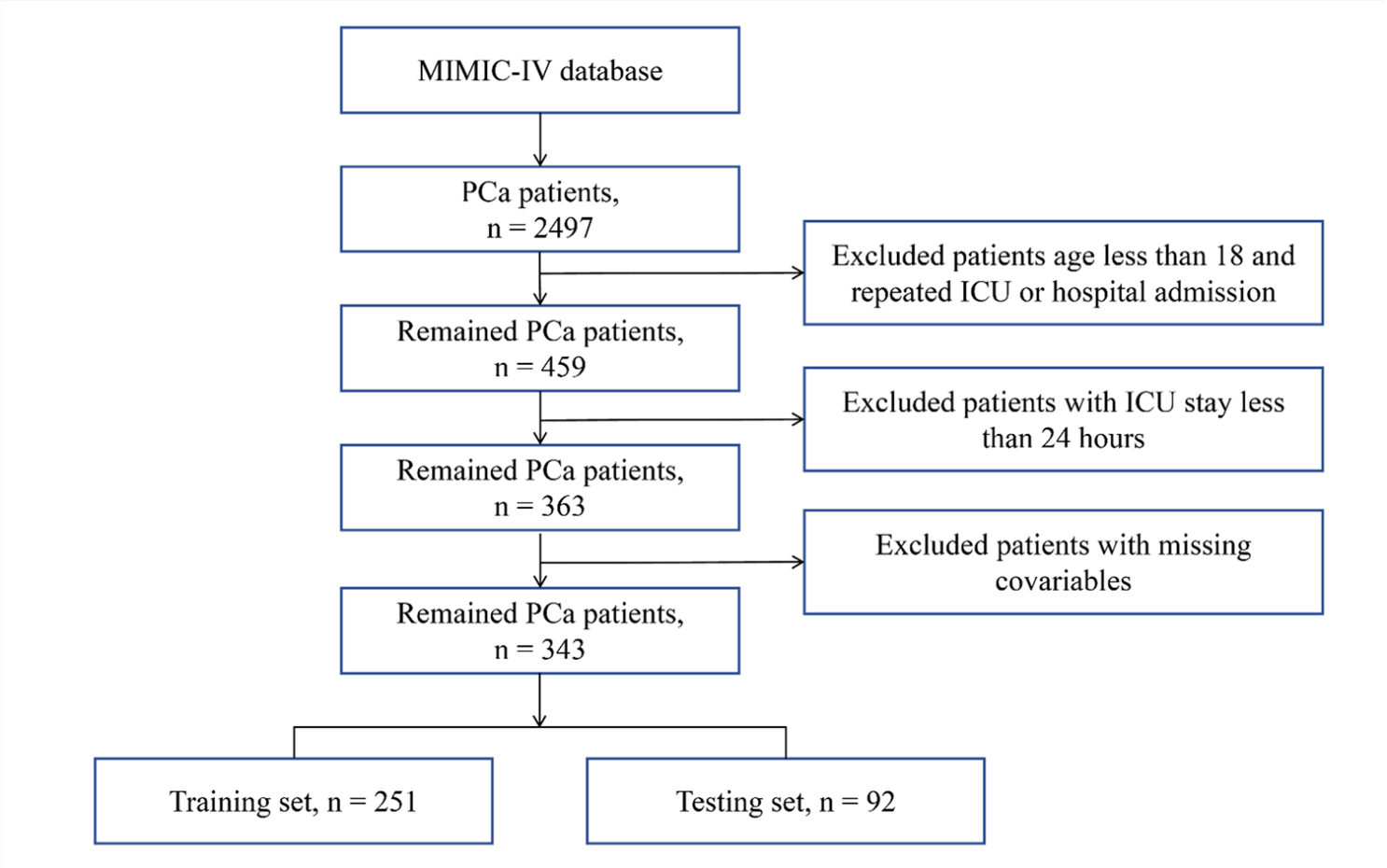


Figure 1

Flowchart of patient screening

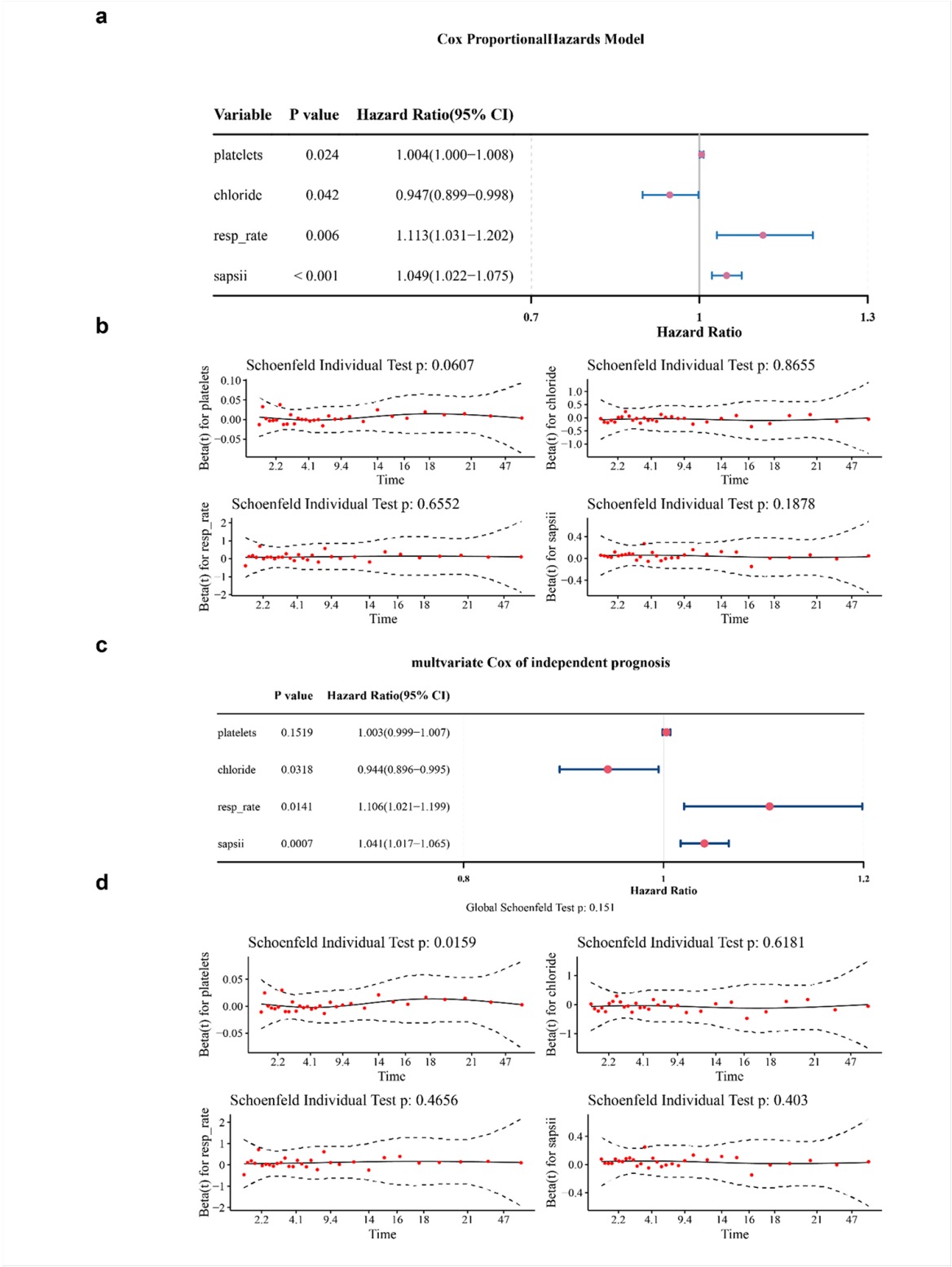


Figure 2

Univariate and multivariate Cox regression analyses.**(a)** Forest map of univariate Cox regression analysis.**(b)** Proportional hazard hypothesis test chart for significant variables in univariate analysis**(c)** Forest map of multivariate Cox regression analysis.**(d)** Proportional hazard hypothesis test chart of independent prognostic variables in multivariate analysis.Note: The solid line represents the smooth trend line of the residual value, which is used to observe the trend of the residual over time. The dotted

line of 95% represents the confidence interval. A p > 0.05 indicates that the hazard ratio of the variable is constant over time

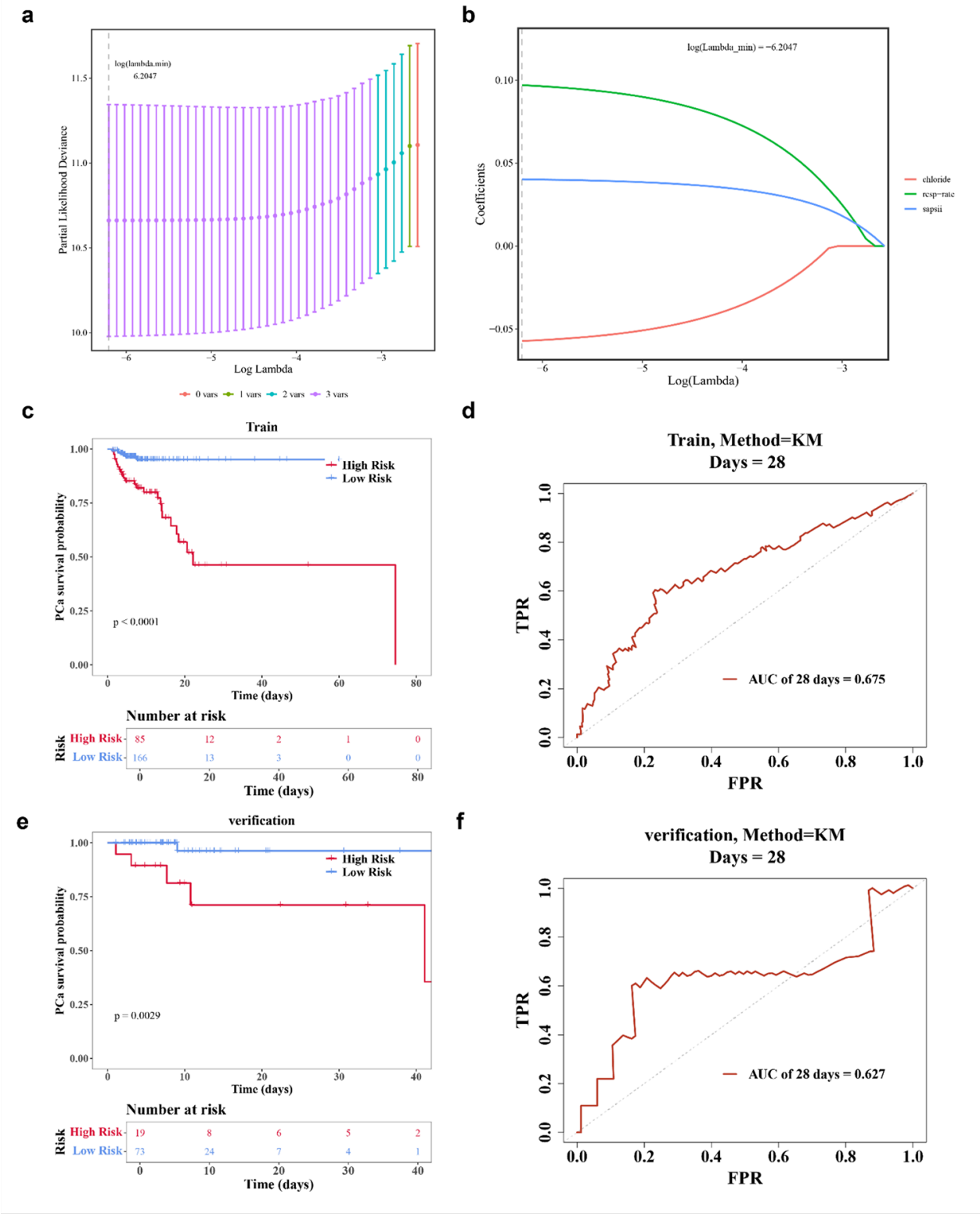


Figure 3

Screening, construction and validation of prognostic models**(a)** The contraction path diagram of variable coefficients in LASSO regression.**(b)**The 10-fold cross-validation error curve of LASSO regression.**(c)**

Kaplan-Meier survival curves of the high-risk group and the low-risk group in the training set**(d)** The ROC curve of the prognostic model for predicting the 28-day mortality risk in the training set.**(e)**Verify the Kaplan-Meier survival curves of the high-risk group and the low-risk group in the validation set.**(f)** The ROC curve of the prognostic model for predicting the 28-day mortality risk in the validation set

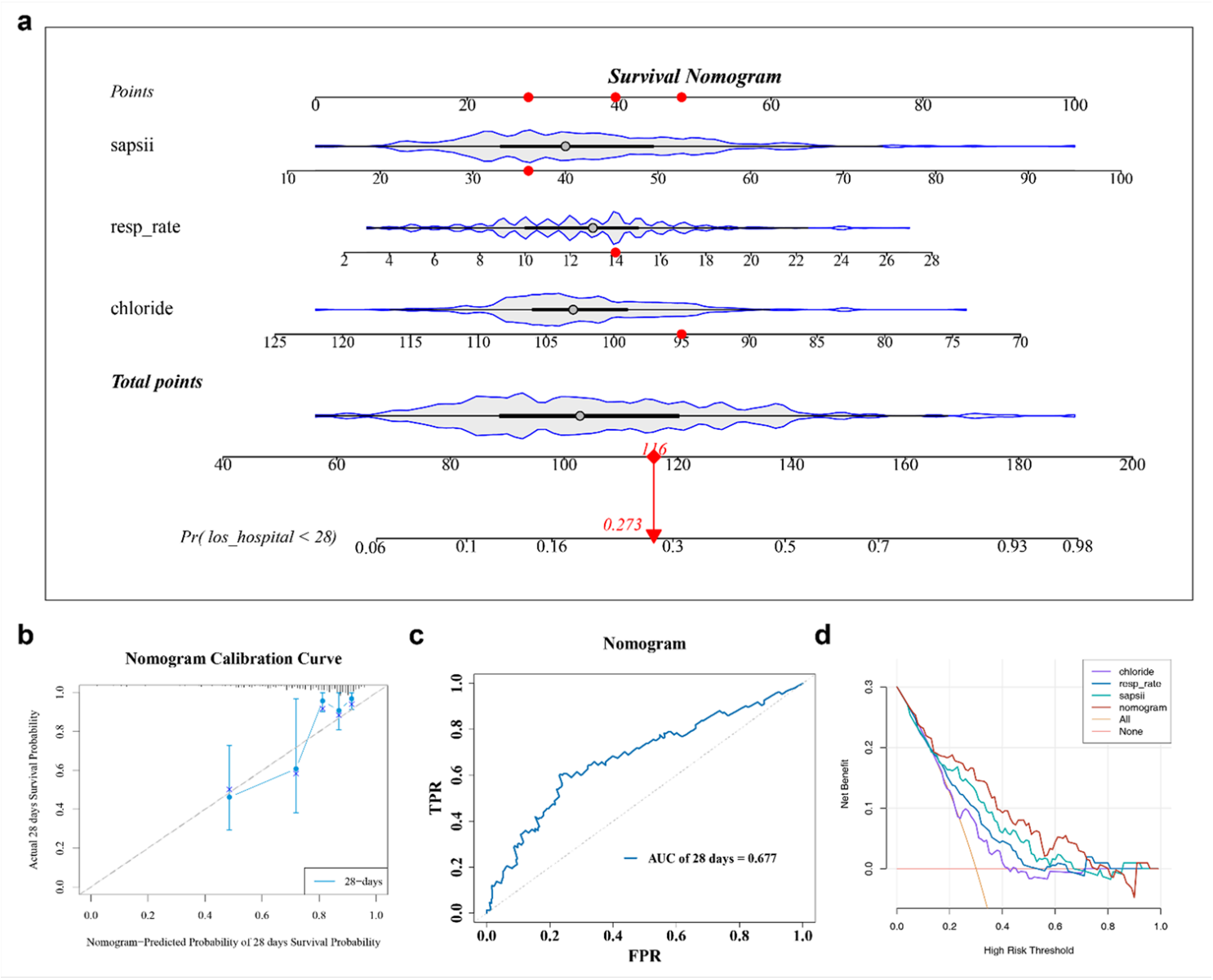


Figure 4

Nomogram and its performance evaluation**(a)** A nomogram for predicting the 28-day risk of death.**(b)** Calibration curve of the nomogram model.**(c)** The ROC curve of the nomogram for predicting the 28-day risk of death.**(d)** Analysis of the nomogram and decision curve of a single variable

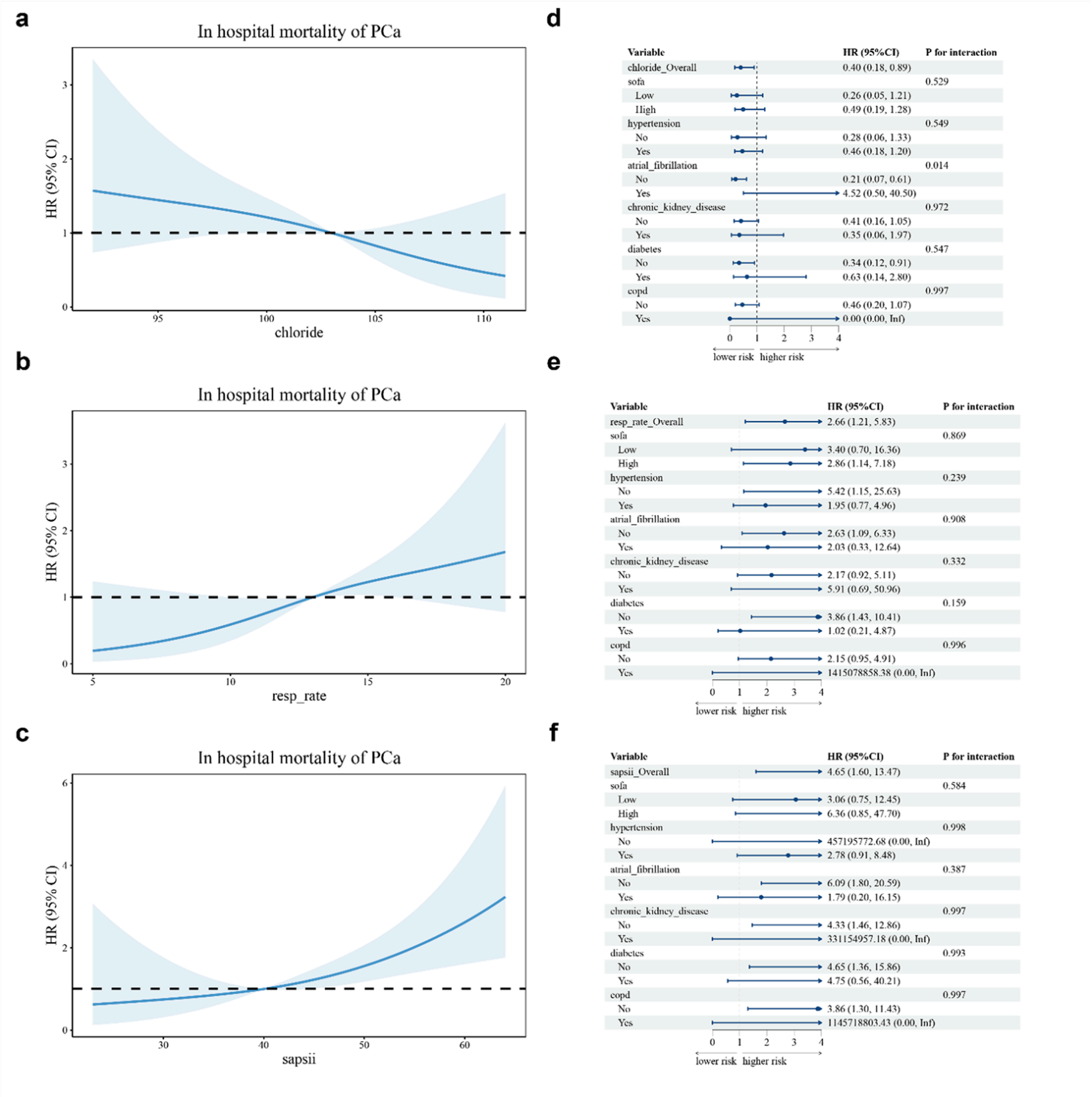


Figure 5

Nonlinear Relationship of Key Variables and Subgroup Analysis**(a)** The RCS curve of chloride ion levels versus the risk of death.**(b)** The RCS curve of respiratory rate versus risk of death.**(c)** The RCS curve of SAPS II score versus risk of death.**(d)** Subgroup analysis of the prognostic effect of chloride ions forest plot.**(e)** Subgroup analysis of the prognostic effect of respiratory rate forest plot.**(f)**Subgroup analysis of the prognostic effect of SAPS II score forest map.Note: The blue dots in the figure represent specific HR values. Those with HR>1 are risk factors, while those with HR<1 are protective factors. The p value is the

interaction p value between covariates and key variables. A p value <0.05 indicates a significant difference

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