

Prognosis assessment model based on low serum calcium in patients with acute pulmonary thromboembolism

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Abstract

Background and objective: The pulmonary embolism severity index (PESI) and simplified PESI (sPESI) are recommended to recognize patients with acute pulmonary thromboembolism (PTE) with low prognosis risk, which is of great significance for treatment. This study aims to verify the influence of hypocalcaemia on the prognosis of patients with PTE and to establish a new prognosis assessment model.

Methods: This is an observational, multicentre study enrolling patients with PTE from February 2010 to June 2020 across 12 Chinese hospitals. Variables in PESI, serum calcium levels and patient survival status as of 5 July 2020 were collected. The area under the curve of the receiver operating characteristic curve, sensitivity, specificity and Youden index were used to evaluate model performance.

Results: In the cohort of 4196 patients with PTE, independent associations existed between hypocalcaemia and mid- and long-term mortalities ($p < 0.05$). By including hypocalcaemia, the new 30-day death risk prediction rule, Peking Union Medical College Hospital rule (PUMCH rule), showed significantly higher specificity (0.622 [0.582, 0.661]; $p < 0.001$) than the PESI (0.514 [0.473, 0.554]) and sPESI (0.484 [0.444, 0.525]) and similar sensitivity (0.963 [0.810, 0.999]; $p = 0.161$) with PESI (0.889 [0.708, 0.976]) and sPESI

Yu-qing Yang and Xin Wang contributed equally to this work.

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(0.963 [0.810, 0.999]) in the internal validation cohort. Well-performing predictive validity was also verified on a constructed external validation cohort.

Conclusion: Hypocalcaemia is independently associated with mid- and long-term PTE mortalities. The PUMCH rule showed significantly higher specificity than the PESI and sPESI and similar sensitivity, which may be used as a prognostic assessment tool for patients with acute PTE.

KEYWORDS

acute pulmonary thromboembolism, hypocalcaemia, prognosis assessment model

INTRODUCTION

Acute pulmonary thromboembolism (PTE) is a common and fatal cardiovascular disease, which leads to $\leq 300,000$ deaths in the United States annually with a 14-day mortality of 11.4%.^{1,2} In a large population of 454.4 million in six European countries, 370,000 deaths were attributed to PTE, of which 34% died before effective treatment.³ Prognostic assessment for patients with PTE, especially the evaluation of early death risk, shows great significance for treatment. The European Cardiology Society and Respiratory Society recommended the pulmonary embolism severity index (PESI) or its simplified version, the simplified PESI (sPESI), to stratify PTE prognosis and identify patients at low risk.^{1,4,5}

Calcium is a routine test item and participates in the coagulation process as coagulation factor IV. Hypocalcaemia is a common electrolyte disorder in hospitalized patients related to the poor prognosis of several cardiopulmonary diseases.^{6–10} However, rare studies reported hypocalcaemia as a marker of prognosis following acute PTE.^{11,12} In our previous study, after receiving thrombolytic therapy, the serum calcium level was significantly lower in patients with acute PTE who died within 30 days than that of the surviving patients.¹³ Then, hypocalcaemia (serum calcium ≤ 2.13 mmol/L) at the time of admission was proven to be an independent predictor of the 30-day mortality following acute PTE.¹¹ On a small single-centre data set, we built a prediction rule based on hypocalcaemia to assess the prognosis risk following acute PTE. The prediction rule showed higher validity than PESI and sPESI.¹¹ To further verify the influence of hypocalcaemia on the prognosis in patients with acute PTE, this study aims to prove it in a multicentre Chinese patient data set and optimize the PESI model to establish a new PTE prognosis assessment model.

METHODS

Study design and objectives

We enrolled consecutive inpatients aged 18 or older who were diagnosed with PTE between February 2010 and June 2020 at 12 hospitals (Figures S1 and S2 in the Supporting Information). Patients were excluded if they were diagnosed and transferred from other healthcare facilities due to incomplete medical records. Only the first available medical record was included for patients with repeated hospitalizations due to

SUMMARY AT A GLANCE

Currently, pulmonary embolism severity index (PESI) and simplified PESI (sPESI) are recommended to recognize pulmonary thromboembolism (PTE) patients with low prognosis risk. In this multicentre research, a new prognosis assessment model including hypocalcaemia, which is confirmed to be independently associated with mid- and long-term PTE mortalities, showed significantly higher specificity with PESI and sPESI and similar sensitivity.

PTE. Patients who were confirmed by computed tomographic pulmonary angiography, enhanced computed tomography of the chest, scintigraphic ventilation–perfusion scan revealing the high probability of PTE or diagnosed by qualified specialist clinically based on typical PTE symptoms, detection of deep venous thrombosis in the extremities by venous ultrasound/phlebography and positive D-dimer were diagnosed with PTE.

Variables, outcomes and follow-ups

Patient demographic information, medical history, related risk factors and clinical outcomes were primarily collected by two qualified doctors and then reviewed by specialists from the pulmonary department. The variables in the PESI (age, sex, body temperature, pulse rate, respiratory rate, blood pressure [BP], cancer, chronic heart failure, chronic pulmonary disease, altered mental status and arterial oxygen saturation) and serum calcium level were collected. All patients completed at least a 1-month follow-up and confirmed their survival status as of 5 July 2020. Patients with unknown survival status were excluded from the relevant mortality analysis and model derivation.

Statistical analysis

The abnormally distributed variables were denoted as medians with quartiles, and categorical variables were formatted with counts and proportions. The association between a single variable and the 30-day PTE all-cause mortality was computed using univariate logistic regression

analysis. Following our previous study, patients with serum calcium level of ≤ 2.13 mmol/L were classified as hypocalcaemia (Figure S3 in the Supporting Information).¹¹ To verify the independent effect of hypocalcaemia on the 30-day PTE mortality and eliminate non-independently associated variables, multivariate logistic regression analysis was performed.

All 30-day dead and surviving patients from nine hospitals were randomly classified into a rule derivation cohort and an internal clinical validation cohort with a ratio of 4:1. An external clinical validation cohort was constructed by including all patients from three hospitals (Figure S2 in the Supporting Information). Patients with missing variables were excluded from the derivation cohort.

In the rule derivation cohort, categorical variables that significantly associated with the 30-day PTE mortality were included to build a prediction rule to predict the 30-day risk of death. A weighted linear rule was constructed by assigning every variable an integral point from 0 to 5. The points of the variables were adjusted randomly to generate different prediction rules, and the optimal rule with the maximum area under the curve (AUC) value of the receiver operating characteristic (ROC) curve was selected. When the sum of points of the variables exceeded a certain threshold, the patient was considered to be at high risk. Based on the ROC curve of the optimal rule, the best threshold was determined by comparing sensitivities and specificities related to different thresholds.

Finally, the optimal prediction rule was compared with the PESI and sPESI in both the internal and external validation cohorts. The sample size of the prediction rule was estimated via the website (<https://mvansmeden.shinyapps.io/BeyondEPV/>).¹⁴ The values and CIs of the AUC, sensitivity, specificity, Youden index, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were estimated. The threshold of the *p*-value was 0.05. Statistical analysis was conducted using IBM SPSS software (version 26.0, International Business Machines Corp., Chicago, IL, USA), Python 3.7.4 and RStudio 1.1.447. The optimal combination of the points of the variables was selected with the maximum AUC value using the 'Hyperopt' toolkit.¹⁵

RESULTS

Baseline information

A total of 4286 patients with acute PTE were enrolled in this study, and 90 patients were excluded because of incomplete medical records. Among 4196 patients, 246 (5.86%) patients lacked a final survival state as of 5 July 2020, and the follow-up time of 199 (4.74%) patients was less than 30 days. During hospitalization and follow-up, 911 patients died, with an overall mortality of 23.06% (911/3950) and a 30-day mortality of 4.40% (176/3997). The median follow-up time was 637 days

TABLE 1 Patients demographic and clinical characteristics and the univariate associations with 30-day PTE mortality on rule derivation cohort

Variable name	All patients (<i>n</i> = 2592)	30-day mortality β (95% CI) [<i>p</i> -value]
<i>N</i>	—	4.98% (129/2592)
Male sex	51.16% (1326/2592)	1.541 (1.072, 2.215) [0.020]
Age (years)	68 (59, 77)	1.012 (0.999, 1.025) [0.074]
Age > 80 years	16.17% (419/2592)	2.282 (1.539, 3.384) [<0.001]
Systolic BP (mm Hg)	126 (110, 140)	0.961 (0.951, 0.971) [<0.001]
Pulse rate (bpm)	81 (72, 96)	1.024 (1.015, 1.032) [<0.001]
Temperature ($^{\circ}$ C)	36.5 (36.3, 36.9)	1.076 (0.966, 1.199) [0.183]
Respiratory rate	19 (18, 20)	1.029 (0.996, 1.063) [0.089]
Serum calcium (mmol/L)	2.19 (2.09, 2.29)	0.064 (0.024, 0.172) [<0.001]
Arterial oxyhaemoglobin saturation	95 (92.3, 96.8)	0.955 (0.945, 0.966) [<0.001]
Altered mental status	10.11% (262/2592)	4.727 (3.183, 7.020) [<0.001]
Chronic heart failure	20.29% (526/2592)	2.934 (2.037, 4.226) [<0.001]
Chronic pulmonary disease	11.88% (308/2592)	2.270 (1.474, 3.496) [<0.001]
Cancer	17.28% (448/2592)	3.915 (2.717, 5.641) [<0.001]
Systolic BP < 100 mm Hg	12.50% (324/2592)	6.747 (4.663, 9.763) [<0.001]
Pulse rate \geq 110 bpm	12.27% (318/2592)	4.636 (3.170, 6.780) [<0.001]
Temperature < 36 $^{\circ}$ C	1.74% (45/2592)	0.886 (0.212, 3.700) [0.868]
Respiratory rate > 30 breaths per minute	2.39% (62/2592)	6.125 (3.282, 11.432) [<0.001]
Serum calcium \leq 2.13 mmol/L	32.75% (849/2592)	2.834 (1.980, 4.055) [<0.001]
Arterial oxyhaemoglobin saturation < 90%	12.89% (334/2592)	6.706 (4.640, 9.693) [<0.001]

Note: Missing data: 0.62% for systolic BP (mm Hg), 0.48% for pulse rate (bpm), 0.98% for temperature ($^{\circ}$ C), 1.38% for respiratory rate, 1.62% for serum calcium (mmol/L) and 16.68% for arterial oxyhaemoglobin saturation.

Abbreviations: BP, blood pressure; PTE, pulmonary thromboembolism.

(283.5, 1257). Overall, 2085 (49.69%) patients were men, with a median age of 68 (58, 77) years. The short- and long-term mortalities are shown in Tables S1 and S2 in the Supporting Information.

Associations between variables and PTE mortality

The univariate associations between the clinical variables and 30-day PTE mortality in the rule derivation cohort are shown in Table 1. For the variables included in the PESI or sPESI, except for 'age' and 'temperature < 36°C', the remaining 10 variables were all significantly associated with the 30-day PTE mortality ($p < 0.05$). Both the 'serum calcium' and related categorical variable, 'serum calcium ≤ 2.13 mmol/L', showed strong associations with the 30-day PTE mortality ($p < 0.001$). In addition, the

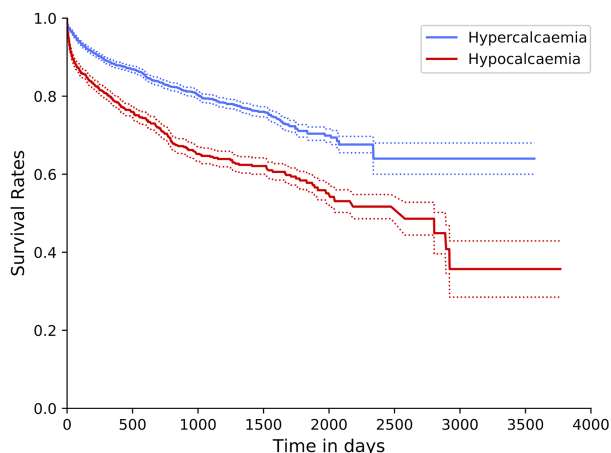


FIGURE 1 Comparison of survival curves between 'serum calcium > 2.13 mmol/L' and 'serum calcium ≤ 2.13 mmol/L'. The dotted lines represent the value of standard

results of the Kaplan–Meier analysis (Figure 1) demonstrated that patients with hypocalcaemia showed a lower probability of >30-day survival (log-rank test, $p < 0.001$). Multiple variables logistic regression analysis demonstrated that 'temperature < 36°C' and 'respiratory rate > 30 breaths per minute' did not have an independent effect on the 30-day mortality. The independent association of 'serum calcium ≤ 2.13 mmol/L' with a 30-day PTE mortality was verified ($p = 0.005$; β [95% CI] = 1.779 [1.185, 2.670]).

Furthermore, univariate and multivariable logistic associations between variables and other short- and long-term mortalities in all patients ($N = 4196$) are listed in Tables S1–S4 in the Supporting Information. 'Serum calcium ≤ 2.13 mmol/L' was not associated with 1- and 2-day mortalities ($p = 0.197$ and 0.056, respectively), but not independently associated ($p \geq 0.05$) with other short-term mortalities (3-, 7- and 14-day mortalities). Inversely, its independent associations with mid- and long-term mortalities (30-, 90-, 180- and 360-day mortalities) were verified ($p < 0.05$). Besides, 'age > 80 years', 'altered mental status', 'cancer', 'pulse rate ≥ 110 bpm', 'systolic BP ≤ 100 mm Hg' and 'arterial oxyhaemoglobin saturation < 90%' showed independent associations with all short- and long-term mortalities, while 'chronic pulmonary disease', 'chronic heart failure' and 'male sex' were independently associated with the mid- and long-term mortalities.

The prediction rule derivation and clinical validation

Based on the above-mentioned results, 'respiratory rate > 30 breaths per minute' and 'temperature < 36°C' were filtered out and the other 10 categorical variables were included to establish a new prediction rule for 30-day PTE deaths. By setting the event fraction (30-day mortality) to 0.04 and the mean squared prediction error to 0.02 (mean absolute prediction error = 0.01), the minimum required

TABLE 2 Variables and their points used in PESI, sPESI and the PUMCH rule

Variable	PESI	sPESI	PUMCH rule
Age	Age in years	1 point (if age > 80 years)	2 points (if age > 80 years)
Male sex	10 points		1 point
Cancer	30 points	1 point	5 points
Chronic heart failure	10 points	1 point	2 points
Chronic pulmonary disease	10 points		3 points
Pulse rate ≥ 110 bpm	20 points	1 point	3 points
Systolic blood pressure < 100 mm Hg	30 points	1 point	3 points
Respiratory rate > 30 breaths per minute	20 points		
Temperature < 36°C	20 points		
Altered mental status	60 points		2 points
Arterial oxyhaemoglobin saturation < 90%	20 points	1 point	1 point
Serum calcium ≤ 2.13 mmol/L			1 point

Note: For PUMCH rule, patients with ≥ 4 points are classified as high risk. For PESI, patients with ≥ 86 points are classified as high risk. Abbreviations: PESI, pulmonary embolism severity index; PUMCH, Peking Union Medical College Hospital; sPESI, simplified PESI.

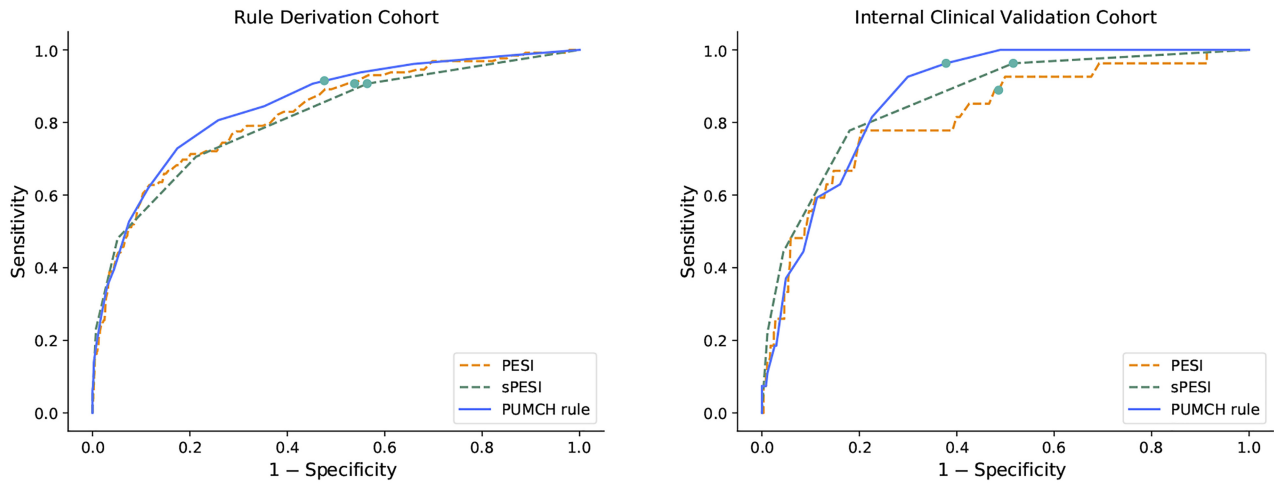


FIGURE 2 ROC curves of new prediction rule on derivation and internal validation cohorts. Thresholds of three prediction rules that are used to recognize high-risk patients are marked with green points in ROC curves. ROC, receiver operating characteristic

TABLE 3 Predictive validity of PESI, sPESI and PUMCH rule on clinical validation cohorts

Characteristic	PESI (95% CI)	sPESI (95% CI)	PUMCH rule (95% CI)
Internal validation cohort			
AUC	0.817 (0.730, 0.904)	0.863 (0.793, 0.932)	0.873 (0.827, 0.919)
Sensitivity	0.889 (0.708, 0.976)	0.963 (0.810, 0.999)	0.963 (0.810, 0.999)
Specificity	0.514 (0.473, 0.554)	0.484 (0.444, 0.525)	0.622 (0.582, 0.661)
Youden index	0.403 (0.182, 0.531)	0.447 (0.254, 0.524)	0.585 (0.392, 0.660)
PPV	0.074 (0.048, 0.109)	0.076 (0.050, 0.110)	0.101 (0.067, 0.145)
NPV	0.991 (0.973, 0.998)	0.997 (0.981, 0.999)	0.997 (0.985, 0.999)
PLHR	1.829 (1.564, 2.138)	1.868 (1.679, 2.078)	2.547 (2.246, 2.888)
NLHR	0.216 (0.074, 0.630)	0.076 (0.011, 0.524)	0.060 (0.009, 0.408)
External validation cohort			
AUC	0.749 (0.641, 0.857)	0.751 (0.645, 0.857)	0.835 (0.765, 0.905)
Sensitivity	0.900 (0.683, 0.988)	0.900 (0.683, 0.988)	1.000 (0.832, 1.000)
Specificity	0.396 (0.361, 0.432)	0.418 (0.382, 0.454)	0.511 (0.475, 0.548)
Youden index	0.296 (0.043, 0.420)	0.318 (0.065, 0.442)	0.511 (0.306, 0.548)
PPV	0.038 (0.023, 0.060)	0.040 (0.024, 0.062)	0.052 (0.032, 0.079)
NPV	0.993 (0.976, 0.999)	0.994 (0.977, 0.999)	1.000 (0.990, 1.000)
PLHR	1.491 (1.274, 1.744)	1.546 (1.319, 1.810)	2.047 (1.902, 2.202)
NLHR	0.252 (0.068, 0.943)	0.239 (0.064, 0.894)	0.000 (0.000, —)

Abbreviations: AUC, area under the curve; NLHR, negative likelihood ratio; PESI, pulmonary embolism severity index; PLHR, positive likelihood ratio; PPV, positive predictive value; PUMCH, Peking Union Medical College Hospital; sPESI, simplified PESI.

sample size was 2380 for 10 candidate predictors. In this study, 2592 patients were included in the rule derivation cohort, with the internal and external validation cohorts consisting of 638 and 767 patients, respectively (Tables S5 and S6 in the Supporting Information). Finally, 10 variables were included in the proposed prediction rule, called the Peking Union Medical College Hospital (PUMCH) rule, and the variable weights are summarized in Table 2. Patients with a sum of points ≥ 4 were classified as high-risk.

Then, the ROC curves of the PUMCH rule were compared with the PESI and sPESI for both the rule derivation

and validation cohorts. As shown in Figure 2, the curve of the PUMCH rule is higher than that of the PESI and sPESI in most cases. Table 3 lists the details of the predictive validity of the three rules on two validation cohorts.

In the internal validation cohort, the AUC scores of the PUMCH rule (0.873 [0.827, 0.919]) were similar with both the PESI ($p = 0.111$) and sPESI ($p = 0.662$). There were no significant differences in the sensitivities compared to the PUMCH rule (0.963 [0.810, 0.999]) with the PESI and sPESI ($p = 0.161$). However, the value of the PUMCH rule's specificity (0.622 [0.582, 0.661]) was obviously higher than those

TABLE 4 Sensitivities and specificities of PESI, sPESI and PUMCH rule for short- and long-term PTE mortalities

Mortality	PESI		sPESI		PUMCH rule	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
1 day	100% (57/57)	44.63% (1778/3984)	100% (57/57)	43.04% (1715/3984)	98.25% (56/57)	53.87% (2146/3984)
2 days	100% (67/67)	44.74% (1778/3974)	100% (16/16)	43.16% (1715/3974)	98.51% (66/67)	54.00% (2146/3974)
3 days	98.68% (75/76)	44.79% (1775/3963)	98.68% (75/76)	43.20% (1712/3963)	94.74% (72/76)	54.02% (2141/3963)
7 days	94.90% (93/98)	44.98% (1768/3931)	95.92% (94/98)	43.35% (1704/3931)	94.90% (93/98)	54.26% (2133/3931)
14 days	93.60% (117/125)	45.27% (1763/3894)	95.20% (119/125)	43.66% (1700/3894)	95.20% (119/125)	54.67% (2129/3894)
30 days	90.34% (159/176)	45.72% (1747/3821)	91.48% (161/176)	43.99% (1681/3821)	92.61% (163/176)	55.25% (2111/3821)
90 days	87.23% (246/282)	46.60% (1714/3678)	90.07% (254/282)	45.02% (1656/3678)	87.94% (248/282)	56.42% (2075/3678)
180 days	87.37% (332/380)	47.79% (1634/3419)	87.89% (334/380)	46.10% (1576/3419)	84.47% (321/380)	57.77% (1975/3419)
360 days	86.64% (441/509)	50.35% (1499/2977)	87.03% (443/509)	51.53% (1534/2977)	82.51% (420/509)	60.36% (1797/2977)

Abbreviations: PESI, pulmonary embolism severity index; PTE, pulmonary thromboembolism; PUMCH, Peking Union Medical College Hospital; sPESI, simplified PESI.

of PESI (0.514 [0.473, 0.554]; $p < 0.001$) and sPESI (0.484 [0.444, 0.525]; $p < 0.001$). In the external validation cohort, the same pattern was found, and the PUMCH rule had similar sensitivity ($p = 0.163$) and superior specificity ($p < 0.001$). In addition, the AUC scores of the proposed rule were greater than those of the PESI ($p = 0.018$) and sPESI ($p = 0.004$).

Furthermore, for all enrolled patients, the sensitivities and specificities of the three rules for other short- and long-term PTE mortalities were also calculated (Table 4). Compared with those of PESI and sPESI, the PUMCH rule showed good sensitivity and higher specificity for all short-term PTE mortalities (1-, 2-, 3-, 7- and 14-day mortalities) and two long-term PTE mortalities (30- and 90-day mortalities). For 180- and 360-day mortalities, the sensitivities of the PUMCH rule were lower than those of the PESI and sPESI, however, with the advantage of high specificity for long-term mortality.

DISCUSSION

In this study, the predictive value of hypocalcaemia (serum calcium ≤ 2.13 mmol/L) for acute PTE prognosis was validated in a large, multicentre data set, which was established based on data from 12 different hospitals and more representatives. As calcium is a routine test item, especially in the emergency room, the prognosis of acute PTE assessment based on hypocalcaemia can be inexpensive, easily available and practical.

Several studies reported that decreased serum calcium levels were related to higher short- and long-term mortalities of patients with PTE and two hypotheses may provide explanations.^{11–13,16} First, as calcium participates in platelet function and the coagulation cascade, hypocalcaemia may affect this process to increase the mortality of patients with PTE, a kind of haemorrhagic and coagulation disorder. It is reported that deaths caused by PTE mostly occur within a short period (within 7 days), and most of them are within 1–3 days.¹⁷ Our results of multivariable logistic regression

analysis revealed that ‘serum calcium ≤ 2.13 mmol/L’ is an independent risk factor for 30-, 90-, 180- and 360-day PTE mortalities but not for 1-, 2-, 3-, 7- and 14-day PTE mortalities. That is, hypocalcaemia is independently associated with mid- and long-term mortalities rather than short-term mortality. Therefore, it is speculated that hypocalcaemia might not directly increase mortality by affecting the coagulation status of patients with PTE, or at least does not serve as the main reason. Second, patients with hypocalcaemia were reported to be affected with more comorbid conditions, especially some severe complications, such as acute respiratory failure, acute kidney injury, cardiac arrhythmia and seizures.^{12,18} The higher mortality of PTE patients with hypocalcaemia may be the result of higher number of complications, more severe disease conditions and worse overall health status. Our data also showed that hypocalcaemia is independently associated with mid- and long-term mortalities of patients with PTE, not the short-term mortality, which means that hypocalcaemia may serve as a marker of overall health status and mainly affect mid- or long-term prognoses. Further research is still needed to verify these explanations.

Furthermore, patients with hypocalcaemia showed significantly higher short-, mid- and long-term mortalities than those without hypocalcaemia. Whether calcium supplementation can improve a patient’s prognosis requires further investigation. Other factors including male sex, older age, altered mental status, chronic heart failure, chronic pulmonary disease, cancer, higher pulse rate, lower systolic BP and lower arterial oxyhaemoglobin saturation were also proven to be independent risk factors of the 30-day mortality, which was consistent with previous literature reports and confirmed the rationality of our data.^{1,4,5,11}

The PESI and sPESI were recommended to stratify the patients with acute PTE with low prognosis risk and provide evidence of not administering thrombolytic therapy, which means that the model specificity is of great significance. By supplementing the hypocalcaemia to build a risk prediction rule, the PUMCH rule shows a dramatic advantage in specificity over the PESI and sPESI, without sacrificing the rules’ sensitivity, which verifies the prognostic value of hypocalcaemia on

a 30-day mortality following acute PTE. In particular, the PUMCH rule included 10 non-zero categorical variables, which shares more similarity with variable types with PESI. Furthermore, the PUMCH rule shows better sensitivities and higher specificities than the PESI and sPESI for short-term PTE mortality (1-, 2-, 3-, 7- and 14-day mortalities) and a certain predictive validity for long-term mortality, which proves its value in clinical trials. Although hypocalcaemia is not independently associated with short-term mortality, the PUMCH rule still shows favourable predictive ability owing to the well-optimized points of 10 variables.

This study had several limitations. First, the causal relationship between hypocalcaemia and the prognosis following acute PTE cannot be explained and needs further exploration. Second, our multicentre data were only based on a Chinese population. As PTE is a disease related to race, the role of hypocalcaemia and the performance of the PUMCH rule have yet to be verified on data sets from other races, such as Caucasians.

In conclusion, hypocalcaemia is an independent marker of 30-day and long-term PTE mortalities. The PUMCH rule based on hypocalcaemia was derived and validated on a multicentre data set, showing higher specificity than the PESI and sPESI and similar sensitivity for both 30-day and short-term PTE mortalities, which can be employed as a prognostic assessment tool for patients with acute PTE.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Yu-qing Yang: Data curation (equal); formal analysis (equal); methodology (equal); software (equal). **Xin Wang:** Data curation (equal); formal analysis (equal); methodology (equal); writing – original draft (equal). **Yun-jian Zhang:** Data curation (equal); formal analysis (equal); investigation (equal); writing – original draft (equal). **Yan-fan Chen:** Data curation (equal); resources (equal). **Ling Wang:** Data curation (equal); resources (equal). **Xiao-wen Hu:** Data curation (equal); resources (equal). **Ling Niu:** Data curation (equal); resources (equal). **Hong-mei Pu:** Data curation (equal); resources (equal). **Xin Zhang:** Data curation (equal); resources (equal). **Zhen Zhang:** Data curation (equal); resources (equal). **Lan Wang:** Data curation (equal); resources (equal). **Fang-wei Chen:** Data curation (equal); resources (equal). **Juhong Shi:** Conceptualization (equal); data curation (equal); funding acquisition (equal); investigation (equal); resources (equal); writing – review and editing (equal). **Ying-qun Ji:** Conceptualization (equal); data curation (equal); investigation (equal); resources (equal); writing – review and editing (equal).

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

HUMAN ETHICS APPROVAL DECLARATION

This multicentre observational study was approved by the Institutional Review Board of the Peking Union Medical College Hospital (PUMCH) (Ethical review number: B164) according to the Declaration of Helsinki. All patients enrolled in the study provided informed consent.

Clinical trial registration: NCT04411888 at [ClinicalTrials.gov](https://clinicaltrials.gov)

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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