Critical Care

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The procalcitonin trajectory as an effective tool for identifying sepsis patients at high risk of mortality

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Sepsis is a critical condition that significantly burdens healthcare systems globally. Given the heterogeneity among sepsis patients, identifying high-risk mortality groups is crucial [1]. Procalcitonin (PCT) is a well-established biomarker for evaluating sepsis severity and guiding antibiotic therapy [2]. In practice, PCT is usually measured repeatedly during the hospital stay. While single PCT values are helpful, dynamic trends through repeated measurements offer deeper insights into patient prognosis. Traditional analysis methods often fail to fully capture the complexity of these data [3]. By employing a hierarchical linear mixed-effects (HLME) model [4], this study aims to explore distinct PCT trajectories in sepsis patients and their association with mortality, providing a refined approach to risk stratification.

We here report our main findings in this study. The medical ethics committee of Zhongshan Hospital Fudan University reviewed and approved this study (B2021-501R). Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data. Between Jan 2019 and March 2024, 537 patients (167 females, 370 males; median age 69 years old [IQR 59–77]) were included. The proportion of patients with septic shock is 47.5%. Abdomen (274/51.0%) and respiratory (202/37.6%) were the two main sites of infection. The median length of stay (LOS) was 10 days [IQR 4–20] in ICU and 15 days [IQR 10–25] in hospital. One hundred sixty-five in-hospital deaths were observed.

A total of 2492 PCT measurements were available for trajectory modeling analyses. Three classes were identified using the HLME model (Fig. 1A). Class 1, also known as the "high-value-slow-decrease" class, included 43 patients (8%) and was characterized by initially high PCT values that remained stable for the first three days before gradually declining. Class 2, the "consistent-low" class, included 354 patients (66%) and displayed low initial PCT values that remained consistently low over the first 7 days in the ICU. Class 3, the "high-value-fast-decrease" class, included 140 patients (26%) and was marked by high initial PCT values that declined rapidly over time. Baseline characteristics differed significantly between the three PCT classes (Table 1). Patients in Class 1 and Class 3 had higher baseline SOFA scores and required more norepinephrine to maintain blood pressure compared to Class 2. In-hospital mortality was highest in Class 1 (42%) compared to Class 2 (32%) and Class 3 (24%) ($P=0.044$). Baseline variables (age, sex, baseline SOFA, baseline lactate, presence of septic shock, surgical intervention, infection sites) and PCT classes were included in the Cox proportional hazards model for in-hospital mortality. With Class 1 as the reference level, Class 2 (HR: 0.507 [95% CI 0.287–0.895], $P=0.020$) and Class 3 (HR 0.449 [95% CI 0.244–0.827], $P=0.011$) were independent protective factors for in-hospital mortality. Kaplan–Meier survival curves were used to illustrate the in-hospital mortality of the 3 classes (Fig. 1B).

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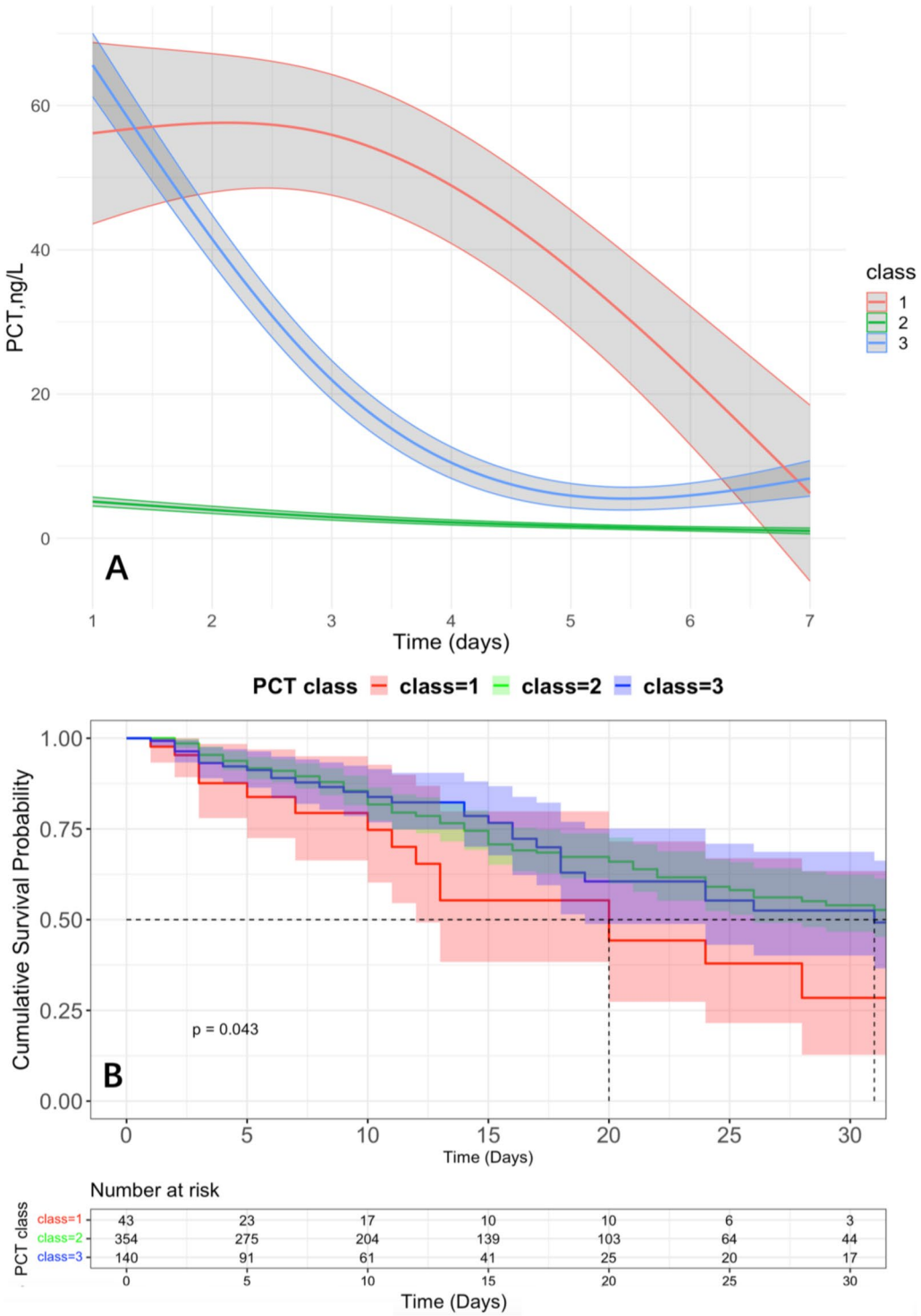

Fig. 1 **A** Shows the 3 distinct procalcitonin classes. **B** Contains Kaplan–Meier curves for patients in the 3 classes. Class 1: "high-value-slow-decrease" class; Class 2: "consistent-low" class; Class 3: "high-value-fast-decrease" class

Three distinct PCT trajectories were identified in this study. Despite notable baseline differences across the classes, the "high-value-slow-decrease" PCT trajectory is an independent risk factor for higher in-hospital mortality. Given the strong link between PCT trajectories and mortality, continuous monitoring of PCT levels is

Table 1 Comparison of baseline characteristics among the three PCT classes

	Class 1 N = 43	Class 2 N = 354	Class 3 N = 140	*P*-value
Age, years	68 (55, 78)	70 (59, 77)	67 (59.75, 75)	0.205
Sex: female, n(%)	7 (16)	110 (31)	50 (36)	0.055
Surgery, n (%)	35 (81)	151 (43)	97 (69)	< 0.001
Infection sites, n (%)				
- Abdomen	33 (77)	143 (40)	95 (68)	< 0.001
- Respiratory	5 (12)	178 (50)	19 (14)	< 0.001
- Others	6 (14)	51 (14)	37 (26)	0.005
Septic shock, n (%)	29 (67)	128 (36)	98 (70)	< 0.001
SOFA, baseline	7 (5, 10)	6 (4, 8)	8 (6, 10)	< 0.001
Lactate, baseline, mmol/L	3.20 (2.30, 4.60)	1.7 0(1.26, 2.30)	2.50 (1.57, 4.70)	< 0.001
NE, baseline, n (%)	34 (79)	169 (48)	102 (73)	< 0.001
LOS ICU, days	5 (3, 13)	11 (5, 21)	7 (3, 15.25)	0.002
LOS hospital, days	17 (9.5, 25)	15 (10, 25)	13 (7, 20)	0.014
In-hospital death, n (%)	18 (42)	114 (32)	33 (24)	0.044

SOFA, Sequential organ failure assessment; NE, Norepinephrine; LOS, Length of stay

essential for clinicians to detect potential high-risk sepsis patients. The insights from this study provide clinicians with information to optimize clinical decision-making and may support the development of more personalized and effective sepsis management strategies, ultimately benefiting patient outcomes.

Author contributions

XW was responsible for the methodological design, coordination, data preparation, and statistical analysis. SL contributed to data collection and statistical analysis. XW drafted and revised the manuscript. JS and MZ conceived and designed the study and assisted in drafting the paper. XW, SL, MZ, and JS contributed to the preparation and critical review of the manuscript. All authors approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to containing information that could compromise the privacy of research participants, but are available from the corresponding authors, JS and MZ, on reasonable request.

Declarations

Competing interests

The authors declare no competing interests.

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