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Impact of Procalcitonin Kinetics on Mortality in Intensive Care Patients with Sepsis

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Abstract

Background and Objectives: Procalcitonin (PCT) kinetics have emerged as a promising prognostic marker in sepsis; however, their interpretation is complicated by dynamic changes in renal function during acute illness. Most previous studies relied on a single baseline estimated glomerular filtration rate (eGFR), which may lead to misclassification in patients with evolving acute kidney injury. This study aimed to evaluate the prognostic value of procalcitonin kinetics (ΔPCT) for 30-day mortality in critically ill patients with sepsis or septic shock by incorporating serial kinetic eGFR measurements and renal function–adapted ΔPCT cut-off values based on the mean kinetic eGFR during the first 72 hours of intensive care unit (ICU) admission. Materials and Methods: This retrospective cohort study included 106 adult patients admitted to a general ICU with sepsis or septic shock. Procalcitonin levels were measured serially, and ΔPCT was calculated as the logarithmic ratio of follow-up to baseline values. Renal function was assessed using kinetic eGFR calculated at serial time points from ICU admission, and the mean kinetic eGFR over the first 72 hours was used for renal function stratification. Multivariable logistic regression models incorporating ΔPCT and severity scores (APACHE II and SOFA) were constructed, and discriminative performance was evaluated using receiver operating characteristic (ROC) curve analysis. Results: Thirty-day mortality was 43.4%. ΔPCT was a strong independent predictor of mortality across all models. When stratified according to mean kinetic eGFR, optimal ΔPCT cut-off values expressed as absolute proportional PCT decline differed markedly by renal function: an 81.2% decrease in PCT best discriminated mortality in the overall cohort, whereas renal function–specific thresholds were 63.7% for patients with mean kinetic eGFR <30 mL/min, 87.6% for those with kinetic eGFR 30–59 mL/min, and 92.6% for patients with kinetic eGFR ≥60 mL/min. The combination of APACHE II and ΔPCT demonstrated the highest discriminative performance (AUC 0.946). Conclusions: Procalcitonin kinetics provide robust prognostic information in sepsis when interpreted alongside dynamic renal function. Using serial kinetic eGFR measurements and the 72-hour mean renal function enables renal function–adapted ΔPCT cut-off determination and may improve mortality risk stratification in critically ill septic patients.

Keywords: sepsis; procalcitonin kinetics; delta procalcitonin; kinetic eGFR; acute kidney injury; mortality prediction

1. Introduction

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Procalcitonin (PCT) is a 116–amino acid precursor of the hormone calcitonin encoded by the CALC-1 gene. Under physiological conditions, PCT is primarily synthesized by the C cells of the thyroid gland and, to a lesser extent, by neuroendocrine cells, and is virtually undetectable in the systemic circulation. However, in response to systemic bacterial infections, transcription of the CALC-1 gene is upregulated in multiple extra-thyroidal tissues, including adipocytes and fibroblasts, under the influence of pro-inflammatory cytokines and bacterial endotoxins such as lipopolysaccharides. This leads to widespread PCT production and release into the bloodstream, resulting in markedly elevated plasma concentrations. Elevated PCT levels correlate with the severity of bacterial infection, while declining concentrations are generally associated with clinical improvement and effective antimicrobial therapy. In clinical practice, plasma PCT levels below 0.2 ng/mL are considered to make bacterial sepsis unlikely, whereas values exceeding 0.5 ng/mL warrant further evaluation for possible sepsis. Markedly elevated PCT levels are predominantly associated with bacterial infections and are less commonly observed in viral or fungal infections. [1–3]

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection and represents a major cause of morbidity and mortality worldwide. If not recognized and treated promptly, sepsis may progress to septic shock, multiple organ dysfunction syndrome, and death. Although a wide spectrum of pathogens can trigger sepsis, bacterial infections remain the most common etiology compared with viral or fungal causes.[4]

In this context, PCT has emerged as a valuable biomarker for the assessment and monitoring of critically ill patients with sepsis in the intensive care unit (ICU). Plasma PCT concentrations typically begin to rise within 2–6 hours following exposure to an inflammatory stimulus, peak at approximately 12–24 hours, and exhibit a biological half-life of about 24 hours, although reported ranges vary between 22 and 35 hours. Importantly, renal function plays a critical role in determining circulating PCT levels. Given its relatively small molecular weight (approximately 14.5 kDa), PCT is at least partially cleared by the kidneys, and impaired renal function may lead to delayed clearance and persistently elevated plasma levels. Both acute kidney injury (AKI) and chronic kidney disease (CKD) have been shown to influence baseline PCT concentrations and alter its kinetic profile, thereby complicating interpretation based on single measurements.[5–7]

Accordingly, serial measurements of PCT and assessment of its kinetic behavior may provide more reliable prognostic information than isolated values, particularly in patients with dynamic changes in renal function. Evaluating PCT kinetics rather than absolute concentrations may better reflect the biological response to infection and treatment, and may improve risk stratification in patients with sepsis or septic shock. [8–10]

In critically ill patients, particularly those with sepsis or septic shock, renal function often changes rapidly during the early phase of hospitalization, rendering a single baseline estimated glomerular filtration rate (eGFR) insufficient to accurately reflect true renal clearance capacity. To address this limitation, the concept of **kinetic estimated glomerular filtration rate (kinetic eGFR)** has been proposed, which incorporates the rate of change in serum creatinine over time and provides a dynamic assessment of renal function during non–steady-state conditions. [11] In the context of sepsis, where both inflammatory burden and renal clearance directly influence circulating biomarker levels, the use of kinetic eGFR may allow a more physiologically appropriate interpretation of procalcitonin kinetics. Accordingly, integrating serial kinetic eGFR measurements into the evaluation of procalcitonin dynamics may reduce misclassification related to fluctuating renal function and improve prognostic stratification in septic patients.

Therefore, this study aimed to investigate procalcitonin kinetics in critically ill patients with sepsis or septic shock and to evaluate the association between ΔPCT and mortality by incorporating serial kinetic eGFR measurements to account for dynamic changes in renal function.

2. Materials and Methods

This retrospective observational study was conducted in the 120-bed General Intensive Care Unit (ICU) of İzmir City Hospital, a tertiary-care center admitting both medical and surgical critically

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ill patients. The study population consisted of all consecutive patients hospitalized between January 1 and March 31, 2025, with a diagnosis of sepsis or septic shock according to contemporary Sepsis-3 definitions. Patients aged ≥18 years with an ICU length of stay of at least 72 hours, availability of serial biochemical analyses at 24-hour intervals including procalcitonin (PCT), and documented APACHE II and SOFA scores at ICU admission were eligible for inclusion. Patients with cardiopulmonary arrest on admission, major trauma, recent surgery, or malignancy-associated PCT elevation were excluded.

The investigation was conducted in two sequential phases. In the first phase, the association between 72-hour procalcitonin reduction and 30-day mortality was evaluated, and the incremental prognostic value of ΔPCT beyond established severity scores (APACHE II and SOFA) was assessed. ΔPCT was calculated as the logarithmic ratio of PCT values at 72 hours to baseline values obtained at ICU admission ($\Delta PCT = \log_{10}[PCT_{72}h / PCT_0h]$).

In the second phase, renal function was quantified using kinetic estimated glomerular filtration rate (kinetic GFR), calculated for each patient using serial serum creatinine measurements obtained during the first 72 hours of ICU admission. Kinetic GFR was calculated according to the validated kinetic GFR formula:

$$\mathbf{kGFR} = \frac{(\mathbf{SCr_{baseline}} \times \mathbf{SCr_0})}{(\frac{\mathbf{SCr_{72h}} + \mathbf{SCr_0}}{\mathbf{2}})} \times (\mathbf{1} - \frac{\mathbf{24} \times (\mathbf{SCr_{72h}} - \mathbf{SCr_0})}{\mathbf{72} \times \mathbf{1.5}})$$

where SCr_0 represents the serum creatinine concentration at ICU admission, $SCr_{72}h$ the creatinine concentration at 72 hours, and 1.5 mg/dL/day denotes the maximal theoretical rate of creatinine increase. This formula estimates real-time glomerular filtration by incorporating both baseline creatinine concentration and its rate of change over time, thereby providing a dynamic assessment of renal function that is more responsive to acute fluctuations than conventional static creatinine-based equations.

Patients were subsequently stratified into renal function groups according to kinetic GFR values, and renal function–specific ΔPCT thresholds for discriminating survivors from non-survivors were determined using receiver operating characteristic (ROC) curve analysis with the Youden index.

All statistical analyses were performed using SPSS version 26.0 for Windows (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation, and categorical variables as counts and percentages. Between-group comparisons were conducted using the Student's t-test or Mann–Whitney U test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate. Variables associated with 30-day mortality at a significance level of $p < 0.05$ in univariate analyses were entered into a binary logistic regression model. Predictive performance was evaluated using ROC curve analysis and supported by graphical representations, including scatter plots, boxplots, and ROC visualizations.

The study protocol was approved by the İzmir City Hospital Non-Interventional Clinical Research Ethics Committee (approval number: 2025/1847). Due to the retrospective design of the study, the requirement for informed consent was waived.

Generative artificial intelligence tools were used solely for language editing and improvement of manuscript clarity. No AI tools were used for study design, data collection, data analysis, interpretation of results, or figure generation. All scientific content was reviewed and approved by the authors.

3. Results

A total of 106 patients were included in the study. Of these, 64.2% were male; 71.7% were admitted with sepsis and 28.3% with septic shock. The prevalence of diabetes mellitus was 49.1%, hypertension 61.3%, chronic kidney disease 38.7%, and chronic obstructive pulmonary disease 31.1%. Infections were hospital-acquired in 60.4% of cases, and blood cultures were positive in 39.6%, with gram-negative bacteria accounting for 21.7% of isolates. Acute kidney injury (AKI) occurred in 72.6%

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of patients, and 39.6% were classified as AKI stage 3. The 30-day mortality rate was 43.4%. Baseline demographic and clinical characteristics of the study cohort are summarized in Table 1.

Table 1. Distribution of categorical variables in the study cohort (n = 106).

Variable	Categories	n (%)
Sex	Female	38 (35.8)
	Male	68 (64.2)
Sepsis category	Sepsis	76 (71.7)
	Septic shock	30 (28.3)
Diabetes mellitus	Present	52 (49.1)
	Absent	54 (50.9)
Hypertension	Present	65 (61.3)
	Absent	41 (38.7)
COPD	Present	33 (31.1)
	Absent	73 (68.9)
Chronic kidney disease	Present	41 (38.7)
	Absent	65 (61.3)
Coronary artery disease	Present	34 (32.1)
	Absent	72 (67.9)
Source of infection	Community-acquired	42 (39.6)
	Hospital-acquired	64 (60.4)
Blood culture result	No growth	57 (53.8)
	Growth present	42 (39.6)
	Culture not obtained	7 (6.6)
Pathogen type	No pathogen detected	62 (58.5)
	Gram-negative	23 (21.7)
	Gram-positive	12 (11.3)
	Fungal	8 (7.5)
	Viral	1 (0.9)
Empiric antibiotic adequacy	Adequate	34 (32.1)
	Inadequate	9 (8.5)
	Unknown	62 (58.5)
RRT modality	None	75 (70.8)
	IHD	13 (12.3)
	CRRT	7 (6.6)
	Chronic HD patient	11 (10.4)
AKI stage	No AKI	29 (27.4)

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Variable	Categories	n (%)
	Stage 1	13 (12.3)
	Stage 2	10 (9.4)
	Stage 3	42 (39.6)
	Chronic HD	12 (11.3)
AKI outcome	No AKI	31 (29.2)
	Complete recovery	27 (25.5)
	Partial recovery	7 (6.6)
	ESRD	9 (8.5)
	AKI-related death	32 (30.2)
30-day mortality	Survived	60 (56.6)
	Died	46 (43.4)

Data are presented as number (%). AKI: acute kidney injury; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease.

When continuous variables were compared according to mortality status, APACHE II scores were higher in non-survivors than in survivors (37.54 ± 11.58 vs. 21.15 ± 7.22; $p < 0.001$). SOFA scores were also higher in the non-survivor group (8.71 ± 3.50 vs. 6.60 ± 2.94; $p = 0.001$). Baseline procalcitonin values differed significantly between groups ($p = 0.027$). Baseline creatinine ($p = 0.086$) and baseline estimated GFR ($p = 0.086$) did not differ significantly; however, mean kinetic GFR was lower in non-survivors (38.30 ± 27.04 vs. 56.71 ± 32.43; $p = 0.007$). Survivors exhibited a greater proportional decrease in procalcitonin levels over 72 hours ($p < 0.001$). Descriptive statistics and group comparisons for continuous variables are presented in Table 2.

Table 2. Continuous variables compared between survivors and non-survivors.

Variable	Survivors Mean ± SD	Non-survivors Mean ± SD	p-value
Age (years)	68.92 ± 16.82	73.17 ± 12.87	0.431
APACHE II	21.15 ± 7.22	37.54 ± 11.58	<0.001
SOFA	6.60 ± 2.94	8.71 ± 3.50	0.001
Procalcitonin (baseline)	24.00 ± 32.24	18.56 ± 32.83	0.027
Creatinine (baseline)	2.18 ± 1.86	2.61 ± 1.89	0.086
Estimated GFR (baseline)	52.33 ± 33.79	37.33 ± 29.66	0.086
MeanGFR (kinetic)	56.71 ± 32.43	38.30 ± 27.04	0.007
DeltaPCT (log10)	–0.7684 ± 0.4349	0.0943 ± 0.7413	<0.001

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Variable	Survivors Mean ± SD	Non-survivors Mean ± SD	p-value
Albumin (baseline)	30.38 ± 6.21	28.36 ± 5.54	0.092
Days until death	2.37 ± 10.33	9.41 ± 6.58	0.608

Values are expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test or Mann–Whitney U test, as appropriate. ΔPCT was calculated as $\log10(PCT_{72}h/PCT_0h)$.

In multivariable logistic regression analyses, the model including APACHE II and ΔPCT showed the strongest association with 30-day mortality ($\chi^2 = 83.582$; $p < 0.001$; Nagelkerke $R^2 = 0.740$; overall accuracy = 84.6%). In this model, both APACHE II (OR = 1.202; $p < 0.001$) and ΔPCT (OR = 68.750; $p < 0.001$) were independent predictors of mortality. In the model including SOFA and ΔPCT, the model was significant ($\chi^2 = 56.565$; $p < 0.001$), and ΔPCT remained an independent predictor ($p < 0.001$). In the model including ΔPCT alone, ΔPCT remained significant (OR = 47.063; $p < 0.001$), with an overall classification accuracy of 81.7%. Multivariable regression results are summarized in Table 3.

Table 3. Multivariable logistic regression models predicting 30-day mortality.

Model	p-value	OR (Exp B)	95% CI
Model 1 (APACHE II + ΔPCT)	<0.001	1.202	1.10 – 1.32
Model 2 (SOFA + ΔPCT)	<0.001	42.718	9.04 – 201.89
Model 3 (ΔPCT alone)	<0.001	47.063	9.77 – 225.60

OR: odds ratio; CI: confidence interval. Nagelkerke R^2 and overall classification accuracy are reported for each model. ΔPCT represents $\log10(PCT_{72}h/PCT_0h)$.

Receiver operating characteristic (ROC) curve analysis demonstrated the highest area under the curve (AUC) for the combined APACHE II + ΔPCT model (AUC = 0.946; 95% CI: 0.909–0.983; $p < 0.001$). The AUC values were 0.876 for ΔPCT, 0.877 for APACHE II, and 0.676 for SOFA. ROC analysis results are shown in Table 4.

Table 4. Area under the ROC curve for mortality prediction.

Predictor	AUC	Std Error	p-value	95% CI
APACHE II + ΔPCT	0.946	0.019	<0.001	0.909 – 0.983
SOFA + ΔPCT	0.883	0.033	<0.001	0.819 – 0.947
DeltaPCT	0.876	0.035	<0.001	0.807 – 0.945
APACHE II	0.877	0.037	<0.001	0.804 – 0.950
SOFA	0.676	0.054	0.002	0.569 – 0.782

AUC: area under the curve; CI: confidence interval. ROC comparisons were performed using the DeLong method.

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To evaluate the impact of renal function on mortality discrimination, patients were stratified according to mean kinetic GFR. In patients with kinetic GFR < 30 mL/min, both ΔPCT (OR = 95.415; p = 0.018) and APACHE II (OR = 1.169; p = 0.012) were independently associated with mortality, with an AUC of 0.921. In the kinetic GFR 30–59 mL/min group, APACHE II was associated with mortality (AUC = 0.983; p < 0.001). In patients with kinetic GFR ≥ 60 mL/min, ΔPCT was associated with mortality (AUC = 0.928; p < 0.001), and the combined APACHE II + ΔPCT model yielded an AUC of 0.941. Logistic regression results stratified by kinetic GFR are presented in Table 5, and corresponding ROC analyses are shown in Table 6.

Table 5. Logistic regression models stratified by kinetic GFR.

GFR Group	Variable	B	SE	Wald	p-value	OR (ExpB)
<30 mL/min	DeltaPCT	4.558	1.932	5.567	0.018	95.415
	APACHE II	0.156	0.062	6.274	0.012	1.169
	Constant	–2.990	1.597	3.506	0.061	0.050
30–59 mL/min	DeltaPCT	146.206	9977.346	0.000	0.987	3.1×10^{63}
	APACHE II	23.069	1407.520	0.000	0.987	1.04×10^{10}
	Constant	–629.381	38506.102	0.000	0.987	0.000
≥60 mL/min	DeltaPCT	6.436	2.561	6.316	0.012	624.148
	APACHE II	0.147	0.077	3.630	0.057	1.159
	Constant	–1.588	1.946	0.666	0.415	0.204

Table 6. Area under the ROC Curve (AUC) for each GFR group.

GFR Group	Predictor	AUC	SE	p-value	95% CI
<30 mL/min	APACHE II + DeltaPCT	0.921	0.041	<0.001	0.841–1.000
	SOFA + DeltaPCT	0.853	0.061	<0.001	0.733–0.973
	DeltaPCT	0.815	0.069	0.001	0.681–0.950
	APACHE II	0.819	0.074	0.001	0.674–0.964
	SOFA	0.743	0.080	0.011	0.586–0.900
30–59 mL/min	APACHE II + DeltaPCT	0.967	0.033	<0.001	0.902–1.000
	SOFA + DeltaPCT	0.867	0.076	0.004	0.717–1.000
	DeltaPCT	0.825	0.091	0.010	0.646–1.000
	APACHE II	0.983	0.022	<0.001	0.941–1.000
	SOFA	0.538	0.134	0.767	0.274–0.801
≥60 mL/min	APACHE II + DeltaPCT	0.941	0.035	<0.001	0.872–1.000
	SOFA + DeltaPCT	0.919	0.046	<0.001	0.829–1.000
	DeltaPCT	0.928	0.043	<0.001	0.845–1.000

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GFR Group	Predictor	AUC	SE	p-value	95% CI
	APACHE II	0.841	0.066	0.001	0.711–0.970
	SOFA	0.564	0.115	0.545	0.339–0.789

When ΔPCT logarithmic ratios were converted into proportional percentage reductions, the overall optimal threshold for mortality discrimination (−0.7255) corresponded to an 81.2% decrease in procalcitonin. The optimal thresholds differed by renal function: 63.7% for kinetic GFR < 30 mL/min, 87.6% for kinetic GFR 30–59 mL/min, and 92.6% for kinetic GFR ≥ 60 mL/min. These ΔPCT thresholds and corresponding percentage reductions are presented in Table 7. Percentage reductions were calculated using the formula (1 − 10^ΔPCT) × 100.

Table 7. Optimal ΔPCT thresholds expressed as logarithmic ratios and absolute percentage decline in procalcitonin.

Group	ΔPCT Cut-off (log10)	Ratio (10^ΔPCT)	Required PCT Decline (%)
All patients	–0.7255	0.1879	81.2% decrease
GFR <30 mL/min	–0.4408	0.3631	63.7% decrease
GFR 30–59 mL/min	–0.9048	0.1241	87.6% decrease
GFR ≥60 mL/min	–1.1330	0.0737	92.6% decrease

Percentage reduction was calculated using the formula (1 − 10^ΔPCT) × 100. ΔPCT represents $\log10(PCT_{72}h/PCT_0h)$.

4. Discussion

In this study, conducted among critically ill patients with sepsis or septic shock defined according to Sepsis-3 criteria, we demonstrated that ΔPCT, reflecting procalcitonin kinetics over the first 72 hours of ICU admission, carries substantial prognostic value for predicting 30-day mortality. The finding that ΔPCT alone provides meaningful discrimination, and that its predictive performance improves further when combined with clinical severity scores—particularly APACHE II—supports the concept that sepsis risk assessment should not rely solely on baseline severity, but should also incorporate the dynamic biological response over time. This approach is consistent with the contemporary conceptualization of sepsis as a syndrome driven by dysregulated host response and evolving organ dysfunction rather than a static disease state. [4,12,13]

Previous literature has consistently highlighted the heterogeneous prognostic performance of single-time-point PCT measurements, whereas non-clearance or kinetic PCT parameters have demonstrated more robust and reproducible associations with mortality. Failure of PCT to decline in the early course of sepsis may reflect persistent infectious burden, inadequate source control, inappropriate antimicrobial therapy, or sustained systemic inflammation. In this context, evaluating PCT as a temporal dynamic rather than an absolute value offers a biologically more plausible assessment aligned with clinical trajectory. The strong prognostic performance of ΔPCT observed in our cohort reinforces this body of evidence.[9,14,15]

The observation that the combination of ΔPCT and APACHE II yielded the strongest model performance suggests a clinically meaningful complementarity between these parameters. APACHE II captures the initial physiological derangement, age, and chronic health burden at ICU admission, whereas ΔPCT reflects the biological response to treatment and the evolution of inflammatory burden over time. Integrating baseline severity with dynamic biomarker response therefore allows a more comprehensive estimation of mortality risk than either dimension alone. The limited incremental contribution of SOFA in certain models may be attributable to its single-time-point assessment, which may inadequately capture the dynamic evolution of organ dysfunction, as well as partial informational overlap between organ failure scores and inflammatory biomarkers. Importantly, these

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findings should not be interpreted as diminishing the relevance of clinical scoring systems, but rather as highlighting the additional and dominant prognostic information provided by ΔPCT in this cohort.[12,13,16]

One of the most distinctive methodological strengths of this study is the evaluation of procalcitonin kinetics in the context of renal function using serially calculated kinetic eGFR rather than a single baseline eGFR value. Renal function was assessed using kinetic eGFR calculated from serial creatinine measurements obtained from ICU admission through the first 72 hours, and the mean kinetic eGFR over this period was used as the reference for stratification. This approach was chosen based on the premise that dynamic renal function changes, which are common in sepsis, cannot be adequately represented by a single static eGFR measurement at admission.

In septic patients, particularly those who develop acute kidney injury, reliance on baseline eGFR may result in misclassification of renal clearance capacity and consequently misinterpretation of procalcitonin kinetics. By incorporating serial kinetic eGFR measurements and using the early 72-hour mean renal clearance as a reference, our approach aims to more accurately reflect the true biological and eliminative dynamics of procalcitonin. The finding that optimal ΔPCT cut-off values differed significantly across kinetic eGFR strata supports the physiological plausibility of this methodology.

Notably, a more pronounced decline in procalcitonin was required to discriminate mortality among patients with preserved renal function, suggesting that effective renal clearance necessitates larger proportional biomarker reductions to reflect true biological improvement. Conversely, in patients with impaired renal function, smaller ΔPCT reductions retained prognostic relevance, underscoring the importance of interpreting procalcitonin kinetics in relation to renal clearance capacity. These findings challenge the notion of a single universal PCT cut-off in sepsis and support the use of renal function–adjusted, time-sensitive thresholds for clinical risk stratification.[7,17,18]

From a clinical perspective, ΔPCT may serve not only as a prognostic marker but also as a decision-support tool for monitoring treatment response. Randomized controlled trials have demonstrated that PCT-guided algorithms can safely reduce antibiotic exposure, and some studies have reported favorable mortality signals. More recent meta-analyses suggest that PCT-guided strategies shorten antibiotic duration without adversely affecting clinical outcomes and may confer benefit in selected contexts. Nevertheless, international guidelines emphasize that PCT should not replace clinical judgment and should be interpreted within the broader clinical and microbiological context. Accordingly, our findings position ΔPCT not as a standalone decision-making tool, but as an integrated risk indicator used alongside severity scores, clinical assessment, and microbiological data.[19,20]

Finally, compared with emerging prognostic models that combine multiple serial biomarkers, the ability of ΔPCT alone to generate a strong prognostic signal may represent a cost-effective and readily implementable advantage in routine clinical practice. Studies evaluating combined serial biomarkers—such as lactate and procalcitonin clearance—have similarly demonstrated that clearance-based metrics are closely associated with mortality, placing ΔPCT within a broader paradigm of dynamic biomarker-based risk assessment. Nonetheless, given potential variability across centers in measurement timing, laboratory platforms, and treatment protocols, external validation remains essential.[21,22]

The main strengths of this study include the use of procalcitonin kinetics rather than static measurements, the integration of ΔPCT with established severity scores, and the novel application of serial kinetic eGFR to contextualize biomarker interpretation under dynamically changing renal function.

Several limitations should be acknowledged. The single-center, retrospective design limits causal inference and generalizability. Procalcitonin measurement timing was determined by clinical practice rather than a fully standardized protocol, potentially introducing variability in ΔPCT calculation. Subgroup analyses stratified by renal function—particularly in the intermediate kinetic eGFR range—were limited by sample size, which may have contributed to coefficient instability and

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wider confidence intervals in regression models. Finally, not all potential confounders, such as timing of source control, antimicrobial appropriateness, and infection focus, could be fully accounted for, leaving the possibility of residual confounding.

5. Conclusions

ΔPCT provides significant prognostic information for 30-day mortality in critically ill patients with sepsis or septic shock, and its predictive performance is enhanced when interpreted in conjunction with clinical severity scores and renal function assessed by kinetic eGFR.

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Informed Consent Statement: Due to the retrospective design of the study, the requirement for informed consent was waived.

Data Availability Statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request. Due to ethical and institutional restrictions related to patient privacy and data protection regulations, the data are not publicly available.

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Abbreviations

The following abbreviations are used in this manuscript:

Abbreviation	Definition
AKI	Acute kidney injury
APACHE II	Acute Physiology and Chronic Health Evaluation II
AUC	Area under the curve
CI	Confidence interval
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CRRT	Continuous renal replacement therapy
ΔPCT	Delta procalcitonin ($\log_{10}[PCT_{72}h/PCT_{0}h]$)
eGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
ICU	Intensive care unit
IHD	Intermittent hemodialysis
kGFR	Kinetic estimated glomerular filtration rate
OR	Odds ratio
PCT	Procalcitonin
ROC	Receiver operating characteristic

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Abbreviation	Definition
SD	Standard deviation
SOFA	Sequential Organ Failure Assessment

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