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### Effects of dynamic monitoring of plasma procalcitonin levels in sepsis patients in guiding antibiotic treatment on course of treatment, drug resistance and prognosis

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Abstract: Objective To explore the effects of dynamic monitoring of plasma procalcitonin (PCT)levels in patients with sepsis in guiding antibiotic treatment on course of treatment and drug resistance, and to evaluate its significance in predicting patient prognosis. Methods A retrospective analysis was performed on the clinical data of 200 patients with sepsis in ICU of Xingtai Central Hospital from December 2020 to October 2024. Among all patients, there were 100 cases in control group (routine empirical antibiotics treatment, December 2020 to November 2022) and 100 cases in quidance group (antibiotics treatment under the guidance of dynamic PCT monitoring, December 2022 to October 2024). The dynamic changes of PCT levels, as well as antibiotics course, drug-resistance and prognosis were compared between the two groups. According to prognosis, patients in control group were divided into survival group(n=85) and death group(n=15). The predictive value of dynamic PCT for death of sepsis patients in ICU was analyzed by receiver operating characteristic (ROC)curves. Results After 3 d, 5 d and 7 d of treatment, PCT levels in guidance group were(1.20±0.24)ng/mL, (0.24±0.14)ng/mL and(0.15±0.07)ng/mL, lower than those in control group  $[(1.44\pm0.25) \text{ng/mL}, (0.85\pm0.20) \text{ng/mL}, (0.25\pm0.18) \text{ng/mL}]$ , the differences were statistically significant (P < 0.05). After 5 d of treatment, control rate of antibiotics use in guidance group was higher than that in control group (75.00% vs 55.00%,  $\chi$ 2=8.791, P=0.003). ICU treatment time and cumulative mortality rates after 7 d, 21 d and 28 d of treatment in guidance group were  $(12.22 \pm 2.35)$ d, 2.00%, 4.00% and 6.00%, significantly lower than those in control group [(14.55 ± 2.56)d, 9.00%, 12.00%, 15.00%] (P<0.05). After 1 d, 3 d, 5 d and 7 d of treatment, PCT levels in survival group were lower than those in death group, with statistical significance (P<0.05). ROC curves analysis showed that areas under the curve (AUC) values of PCT after 1 d, 3 d, 5 d and 7d of treatment for predicting death of sepsis patients were 0.714, 0.768, 0.770 and 0.775, respectively. Conclusion Dynamic monitoring of PCT levels in ICU patients with sepsis to guide antibiotic treatment can significantly shorten course of antibiotics and reduce incidence of multi-drug resistance, and enable patients to achieve better prognosis.

**Keywords**: Dynamic monitoring; Procalcitonin; Sepsis; Course of antibiotic; Prognosis; Multi-drug resistance **Fund program**: Key Research and Development Plan Project of Xingtai City(2020ZC294)

Sepsis, a life-threatening organ dysfunction caused by a dysregulated host response to infection, is associated with high morbidity and mortality [1-2]. Although the 2021 Surviving Sepsis Campaign (SSC) Guidelines [3] recommend initiating broad-spectrum antibiotic therapy within 1 hour as a core intervention, the overreliance on empirical treatment has led to a worsening crisis of antibiotic abuse, exacerbating the prevalence of various multidrugresistant organisms. In traditional sepsis management, antibiotic courses are mostly based on empirical judgment or fixed durations, lacking guidance from objective biomarkers. Despite the widespread use of inflammatory indicators such as C-reactive protein (CRP) and white blood cell (WBC) count, they are severely interfered by noninfectious factors (e.g., trauma, surgical stress), making it difficult to accurately distinguish between infection control and persistent inflammatory states. Additionally, clinical signs are confounded by sedative therapy and organ support measures, further reducing the reliability of assessments [4]. Against this backdrop, procalcitonin (PCT), a highly specific biomarker for bacterial infections, whose dynamic changes are closely associated with infection severity and treatment efficacy, has provided a new direction for personalized antibiotic management [5]. Although previous studies have confirmed that a single PCT test can assist in the diagnosis of sepsis, the clinical utility of its dynamic monitoring in treatment remains unclear. This study aimed to explore the impact of dynamic PCT monitoring-guided antibiotic therapy on treatment duration and antimicrobial resistance in sepsis, as well as its prognostic value.

### 1 Materials and Methods

### 1.1 General Information

A retrospective study was conducted on 200 sepsis patients admitted to the Intensive Care Unit (ICU) of Xingtai Central Hospital from December 2020 to October 2024. Among them, 100 patients admitted from December 2020 to November 2022 were assigned to the control group, and 100 patients admitted from December 2022 to October 2024 were included in the guidance group (Table 1). All patients underwent microbiological culture or etiological examination during hospitalization and required long-course antibiotic therapy. This study was approved by the Ethics Committee of Affiliated Hospital of Xingtai Medical

College (Approval No.: 2020-KY-07).

### 1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Diagnosed with sepsis according to the Expert Consensus on Early Prevention and Blockade of Sepsis in Emergency Medicine of China [6], characterized by inflammatory changes in body tissues or local organs caused by pathogenic microorganisms within a short period, with a Sequential Organ Failure Assessment (SOFA) score  $[7] \ge 2$  points, and meeting the indications for antibiotic therapy; (2) Aged > 18 years; (3) Disease duration ≤ 5 days at admission; (4) Informed consent obtained from patients or their family members with signed documentation. Exclusion criteria: (1) Chronic infection, special bacterial infection, or history of MDRO colonization; (2) History of glucocorticoid, immunosuppressant, or antibiotic use within 7 days; (3) Immunocompromised status or concurrent malignant tumors with an expected survival time of less than 3 months.

### 1.3 Study Methods

### 1.3.1 Dynamic PCT Detection

Venous blood (3 mL) was collected from patients in both groups within 24 hours of admission, centrifuged at 2000 r/min (centrifugal radius: 15 cm) for 10 minutes, and the supernatant was separated. PCT levels were measured using quantitative immunochromatography with a colloidal gold immunochromatographic analyzer (Haigede Biotechnology Co., Ltd., Model: HG-300GM5). Dynamic monitoring was further performed on days 1, 3, 5, and 7 after admission.

### 1.3.2 Control Group

Routine antibiotic therapy was administered in accordance with the Guidelines for the Treatment of Severe Sepsis and Septic Shock in China (2014) [8]. Empirical broad-spectrum antibiotic therapy was initiated within 1 hour of admission. For non-resistant patients with Gramnegative bacterial infections confirmed by etiological testing, intravenous piperacillin/tazobactam Pharmaceutical Preparation Co., Ltd., National Medical Product Administration (NMPA) Approval No.: H20203746; Specification: 2.0 g; Dosage: 4.5 g every 6 hours) or ceftazidime (Jiangxi Dongfeng Pharmaceutical Co., Ltd., NMPA Approval No.: H20073140; Specification: 1.5 g; Dosage: 2 g every 8 hours) was preferred. For patients with abdominal or pelvic infections requiring coverage of Bacteroides fragilis, metronidazole (Jilin Pharmaceutical Co., Ltd., NMPA Approval No.: H22023068; Specification: 0.5 g; Dosage: 500 mg every 8 hours) was added. Meanwhile, fluid resuscitation and infection source control were performed: an initial 30 mL/kg crystalloid infusion was administered to maintain a mean arterial pressure (MAP) target ≥ 65 mmHg, and abscess drainage and debridement of necrotic tissue were completed within 6-12 hours.

### 1.3.3 Guidance Group

Antibiotic therapy was guided by dynamic PCT monitoring in accordance with the Expert Consensus on the Rational Clinical Application of Antibacterial Agents Guided by Procalcitonin [9]. The principles for antibiotic use based on dynamic PCT results were as follows: (1) Discontinue antibiotics if PCT < 0.1 ng/mL; (2) Determine antibiotic use based on comprehensive clinical indicators (e.g., fever, neutrophil count, WBC count) if PCT is 0.1-0.25 ng/mL; (3) Mandate antibiotic use if PCT is 0.26-10 ng/mL; (4) Recommend immediate antibiotic use if PCT > 10 ng/mL; reduce antibiotic dosage based on clinical indicators if PCT decreases by  $\geq$  80% in subsequent tests; consider discontinuing antibiotics if PCT  $\leq$  0.25 ng/mL after 48 hours of continuous antibiotic therapy.

#### 1.4 Outcome Measures

(1) Dynamic changes in PCT levels: Comparison of PCT levels between the two groups on days 1, 3, 5, and 7 after treatment. (2) Antibiotic course shortening and antimicrobial resistance: Comparison of antibiotic-related outcomes (compliance rate of antibiotic use at day 5, time to compliance, antibiotic costs) and resistance-related outcomes (resistance types, treatment costs of drug-resistant infections) between the two groups. Compliance with antibiotic use was defined as PCT  $\leq 0.25$  ng/mL based on dynamic monitoring results. The monitored drug-resistant carbapenem-resistant included hypervirulent Klebsiella pneumoniae (CR-hvKP), multidrug-resistant Acinetobacter baumannii (MDRO), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), and carbapenem-resistant Acinetobacter baumannii (CR-PA). (3) Prognostic outcomes: Duration of ICU stay and 28-day survival rate, with comparison of survival differences between the two groups. (4) PCT level analysis in patients with different prognoses: Patients in the control group were divided into the survival subgroup (n=85) and the non-survival subgroup (n=15) based on survival status. Dynamic PCT levels on days 1, 3, 5, and 7 after treatment were compared between the two subgroups, and receiver operating characteristic (ROC) curve analysis was used to evaluate the value of dynamic PCT in predicting mortality in ICU sepsis patients.

### 1.5 Statistical Methods

SPSS 25.0 software was used for data analysis. Measurement data conforming to a normal distribution were expressed as  $\overline{x}\pm s$  and compared using the t-test. Multi-time point comparisons were performed using repeated-measures analysis of variance (ANOVA), with pairwise comparisons using the SNK-q test. Categorical data were expressed as n (%) and compared using the  $\chi^2$  test. Survival curves were plotted using the Kaplan-Meier method, and differences were compared using the Log-rank test. ROC curve analysis was used to assess the prognostic value of dynamic PCT for mortality in sepsis patients. P<0.05 was considered statistically significant.

#### 2 Posulte

### 2.1 Comparison of Baseline Data Between the Two Groups

No statistically significant differences were observed in gender, age, infection site, disease duration, initial SOFA score, or initial PCT level between the two groups (P > 0.05) (Table 1).

### 2.2 Dynamic Changes in PCT Levels Between the Two Groups

PCT levels in both groups showed a decreasing trend with prolonged treatment duration, and the PCT levels in the guidance group were significantly lower than those in the control group on days 3, 5, and 7 after treatment (P < 0.05) (Table 2).

### 2.3 Analysis of Antibiotic Course and Antimicrobial

Resistance Between the Two Groups

The compliance rate of antibiotic use at day 5 in the guidance group (75.00%) was significantly higher than that in the control group (55.00%) (P < 0.05). The time to compliance, antibiotic costs, treatment costs of drugresistant infections, and the incidence of MDRO, VRE, and CR-PA in the guidance group were significantly lower than those in the control group (P < 0.05) (Table 3).

### 2.4 Comparison of Prognostic Outcomes Between the Two Groups

The duration of ICU stay and the cumulative mortality rates at days 7, 21, and 28 in the guidance group were significantly lower than those in the control group (P < 0.05) (Table 4). Survival curve analysis showed that the 28-day mortality rate in the guidance group (6.00%) was significantly lower than that in the control group (15.00%) (Log-rank  $\chi^2$ =4.390, P < 0.05) (Figure 1).

**Tab.1** Comparison of baseline data between the two groups  $(n=100, \bar{x}\pm s)$ 

	Gender [ca		Infection site [case (%)]				Initial SOFA	Initial PCT	
Group	Male	Female	Age (years)	Pulmonary infection	Abdominal infection	Urinary system infection	Disease course (d)	score (points)	(ng/mL)
Guidance group	67(67.00)	33(33.00)	44.58±3.27	44(44.00)	28(28.00)	28(28.00)	2.49±0.40	5.11±0.22	1.85±0.35
Control group	59(59.00)	41(41.00)	45.16±2.89	51(51.00)	24(24.00)	25(25.00)	2.52±0.42	5.16±0.24	$1.82\pm0.33$
χ²/t value	1.373	3	1.329		0.993		0.517	1.536	0.624
P value	0.24	1	0.185		0.609		0.606	0.126	0.534

# 2.5 Analysis of PCT Changes Within 7 Days in Patients with Different Prognoses

PCT levels in both subgroups decreased with prolonged treatment duration, and the PCT levels in the survival subgroup were significantly lower than those in the non-survival subgroup on all days of treatment (P < 0.05) (Table 5).

## 2.6 ROC Curve Analysis of Dynamic PCT Levels in Predicting Mortality in Sepsis Patients

The area under the curve (AUC) of PCT levels on days

1, 3, 5, and 7 after treatment for predicting mortality in sepsis patients was 0.714, 0.768, 0.770, and 0.775, respectively, with optimal cut-off values of 1.71 ng/mL, 1.38 ng/mL, 0.85 ng/mL, and 0.30 ng/mL (Table 6, Figure 2).

**Tab.2** Comparison of dynamic levels of PCT between the two groups  $(ng/mL, \bar{x}\pm s)$ 

	groups	(IIg/IIIL)	34-57					
Group	Day 1 of treatment	Day 3 of treatment	Day 5 of treatment	Day 7 of treatment				
Guidance group	1.64±0.35	1.20±0.24a	$0.24\pm0.14^{ab}$	0.15±0.07 <sup>abc</sup>				
Control group	1.70±0.33	1.44±0.25a	$0.85\pm0.20^{ab}$	$0.25\pm0.18^{abc}$				
F/P group	227.500/<0.001							
$F/P_{\text{time}}$	1642.000/<0.001							
F/P interaction		55.98	30/<0.001					

Note: Compared with day 1 of treatment,  ${}^{o}P<0.05$ ; compared with day 3 of treatment,  ${}^{b}P<0.05$ ; compared with day 5 of treatment,  ${}^{c}P<0.05$ .

**Tab.3** Analysis of antibiotic treatment duration and resistance between the two groups  $(n=100, \bar{x}\pm s)$ 

	Antibiotic compliance	Time to antibiotic	Antibiotic cost		Drug-re	sistant specie	es [case(%)]		Treatment cost of drug-
Group	rate at day 5 of treatment (%)	compliance (d)	(10,000 yuan)	CR-hvKP	MDRO	MRSA	VRE	CRPA	resistant infection (10,000 yuan)
Guidance group	75 (75.00)	7.15±1.25	1.75±0.46	5 (5.00)	7 (7.00)	4 (4.00)	4 (4.00)	2 (2.00)	0.78±0.15
Control group	55 (55.00)	8.94±1.35	2.11±0.62	7 (7.00)	18 (18.00)	7 (7.00)	12 (12.00)	10 (10.00)	$0.84 \pm 0.14$
χ²/t value	8.791	9.729	4.663	0.355	5.531	0.866	4.348	5.674	2.924
P value	0.003	0.000	0.000	0.552	0.019	0.352	0.037	0.017	0.004

**Tab.4** Comparison of ICU treatment time and 28-day mortality between two groups (n=100)

Group	ICU treatment time	Cumulative death [case(%)]						
	$(\mathbf{d}, \overline{x} \pm s)$	Day 1 of treatment	Day 7 of treatment	Day 21 of treatment	Day 28 of treatment			
Guidance group	12.22±2.35	1 (1.00)	2 (2.00)	4 (4.00)	6 (6.00)			
Control group	14.55±2.56	1 (1.00)	9 (9.00)	12 (12.00)	15 (15.00)			
χ²/t value	6.705	0.000	4.714	3.348	4.310			
P value	0.000	1.000	0.030	0.037	0.038			

<b>Tab.5</b> Analysis of PCT changes within	7 days in control grou	ip patients with different prognoses	$(ng/mL, \bar{x}\pm s)$

	-								
Group	case	Day 1 of treatment	Day 3 of treatment	Day 5 of treatment	Day 7 of treatment				
Survival group	85	1.68±0.24	$1.35\pm0.20^{a}$	$0.80\pm0.20^{ab}$	$0.26\pm0.08^{abc}$				
Death group	15	1.75±0.20	$1.43\pm0.28^{a}$	$0.86\pm0.16^{ab}$	$0.32\pm0.10^{abc}$				
F/P group		24.460/<0.001							
$F/P_{\text{time}}$		2118.000/<0.001							
F/P interaction			0.123	/0.947					

Tab.6 ROC analysis of dynamic PCT levels to predict mortality in sepsis patients

Indecx	AUC	SE	P	95%CI	Cut-off	Sensitivity	Specificity
PCT after 1 day treatment	0.714	0.052	0.001	0.612~0.816	1.71	0.684	0.619
PCT after 3 days treatment	0.768	0.052	< 0.001	0.666~0.869	1.38	0.645	0.742
PCT after 5 days treatment	0.770	0.055	< 0.001	$0.661 \sim 0.878$	0.85	0.671	0.710
PCT after 7 days treatment	0.775	0.045	< 0.001	0.687~0.863	0.30	0.711	0.645

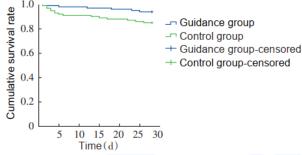


Fig.1 Survival curve

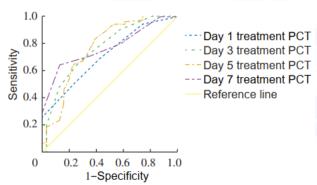


Fig.2 ROC curve of dynamic PCT levels to predict death in sepsis patients

#### 3 Discussion

Studies have shown that approximately 35% of broadspectrum antibiotic prescriptions in ICU patients lack clear evidence of infection, directly exacerbating the prevalence of various MDROs [10]. The World Health Organization (WHO) has listed antimicrobial resistance as one of the top ten global public health threats, highlighting the urgent need to establish precise treatment strategies to balance antiinfective efficacy and resistance prevention and control [11].

The results of this study showed that PCT levels decreased in both groups with prolonged treatment, and the decrease was more significant in the guidance group, indicating that dynamic PCT monitoring can effectively reduce PCT levels in sepsis patients. PCT levels reflect the degree of inflammatory response to infection, and dynamic PCT monitoring can real-time reflect changes in the patient's inflammatory status, thereby providing accurate basis for adjusting antibiotic therapy [12]. In the guidance group,

antibiotic dosage was appropriately adjusted based on dynamic PCT changes, which alleviated the inflammatory response, controlled infection, and further promoted the decrease in PCT levels. A study by Ding et al. [13] also found in clinical practice that adjusting antibacterial agents guided by dynamic PCT monitoring is more conducive to reducing the body's inflammatory response and improving prognosis, which is consistent with the results of this study.

The guidance group had a higher compliance rate of antibiotic use, shorter time to compliance, lower antibiotic costs and treatment costs of drug-resistant infections, and a lower incidence of MDRO, VRE, and CR-PA resistance, indicating that dynamic PCT monitoring is beneficial for shortening the antibiotic course and reducing the incidence of multidrug resistance. As a specific biomarker for bacterial infections, PCT has a half-life of only 25-30 hours, and its pharmacokinetics is highly synchronized with the progress of infection control. After dynamic monitoring, the state of host-pathogen interaction can be accurately identified. When the PCT decrease rate is  $\geq$  80% or the absolute value is  $\leq 0.25$  ng/mL, it indicates that the inflammatory response is effectively controlled. Discontinuing antibiotics at this time can avoid excessive exposure, reduce antibiotic dosage and costs, and effectively lower the incidence of multidrug resistance caused by overuse of antibiotics [14]. However, a study by Wang et al. [15] pointed out that the clinical benefits of PCT monitoring are highly dependent on protocol compliance: when the compliance rate is > 80%, the effects of resistance prevention and control and cost savings are maximized; conversely, if the compliance rate is < 60%, the clinical benefits may be offset by increased testing costs. Therefore, it is necessary to improve the standardization of implementation through multidisciplinary collaboration the implementation of dynamic monitoring strategies.

The duration of ICU stay and mortality in the guidance group were significantly lower than those in the control group, indicating that antibiotic use guided by dynamic PCT monitoring is more conducive to improving patient prognosis. Through dynamic PCT monitoring, the endpoint of antibiotic therapy can be more accurately judged, ensuring the precision of the course and the effectiveness of treatment, reducing drug-related adverse reactions and complications, and thus may shortening the duration of ICU stay. Effective treatment helps reduce the occurrence of multiple organ dysfunction syndrome, resulting in a significant decrease in patient mortality [16]. In addition,

reducing antibiotic exposure also lowers the risk of healthcare-associated infections in patients, further improving their prognosis.

PCT levels in the survival subgroup were lower than those in the non-survival subgroup on days 1, 3, 5, and 7 after treatment, indicating that dynamic PCT changes have significant prognostic value for patients. This study found that PCT levels in the two subgroups showed a differentiation trend in the early stage, but the difference was greater at 5-7 days, suggesting that the dynamic decrease amplitude is more predictive. Persistently high PCT levels reflect the dual pathological processes of host-pathogen imbalance and immune disorders: on the one hand, pathogens continuously release toxic products such as lipopolysaccharide, which activate myeloid cells through Toll-like receptor 4 (TLR4) to promote PCT synthesis; on the other hand, uncontrolled inflammatory response leads to delayed polarization of macrophage M1 phenotype, forming a vicious cycle of "cytokine storm-persistent elevation of PCT", which promotes the occurrence of multiple organ failure in patients, thus more obviously reflecting the prognosis [17-19]. In addition, ROC analysis in this study found that the AUC of PCT levels on days 5 and 7 after treatment for predicting prognosis (0.770, 0.775) was significantly higher than that in previous time periods, which also highlights this point. Therefore, in clinical practice, the single-test mode should be abandoned, and multiple dynamic monitoring standards should be adopted to achieve the synergistic optimization of precise treatment and resistance prevention and control [20].

In conclusion, dynamic monitoring of PCT levels in ICU sepsis patients can better assist clinicians in adjusting antibiotic use, shortening the antibiotic course, reducing the incidence of multidrug resistance and associated medical costs, and improving patient prognosis, thus having high clinical application value.

#### Conflict of interest None

#### Reference

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· 论 著·

# 动态监测脓毒症患者血浆降钙素原水平指导抗生素治疗对疗程及耐药性和预后的影响

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摘要:目的 探讨动态监测脓毒症患者血浆降钙素原(PCT)水平指导抗生素治疗对疗程及耐药性的影响,评价其对患者预后预测的意义。方法 回顾性分析邢台市中心医院 2020年12月至2024年10月入住重症监护室(ICU)的200例脓毒症患者临床信息,将2020年12月至2022年11月接受常规经验性抗生素治疗的100例患者纳入对照组,将2022年12月至2024年10月以动态检测PCT结果作为抗生素用药指导的100例患者纳入指导组,比较两组PCT水平动态变化、抗生素疗程及耐药、预后情况;根据预后情况将对照组患者分为生存组(n=85)和死亡组(n=15),采用受试者工作特征(ROC)曲线分析动态PCT预测ICU脓毒症患者死亡的价值。结果 指导组治疗 3 d、5 d、7 d 时的 PCT 值[ $(1.20\pm0.24)$  ng/mL、 $(0.24\pm0.14)$  ng/mL、 $(0.15\pm0.07)$  ng/mL]均低于对照组[ $(1.44\pm0.25)$  ng/mL、 $(0.85\pm0.20)$  ng/mL、 $(0.25\pm0.18)$  ng/mL],差异有统计学意义(P<0.05)。指导组治疗 5 d 时抗生素使用达标率(75.00%)高于对照组(55.00%, $\chi^2=8.791$ ,P=0.003)。指导组ICU治疗时间及治疗 7 d、21 d、28 d 累积死亡率[ $(12.22\pm2.35)$ d、2.00%、4.00%、6.00%]低于对照组[ $(14.55\pm2.56)$ d、9.00%、12.00%、15.00%],差异有统计学意义(P<0.05)。 生存组治疗 1 d、3 d、5 d、7 d 时的 PCT 值 均低于死亡组,差异有统计学意义(P<0.05)。 ROC 曲线分析显示,治疗 1 d、3 d、5 d、7 d 时的 PCT 值 预测脓毒症患者死亡的曲线下面积分别为 0.714、0.768、0.770 和 0.775。结论 动态监测ICU脓毒症患者 PCT水平指导抗生素治疗,可以明显缩短抗生素疗程、降低多重耐药发生率,且能让患者获得更好的预后。

关键词: 动态监测; 降钙素原; 脓毒症; 抗生素疗程; 预后; 多重耐药

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### Effects of dynamic monitoring of plasma procalcitonin levels in sepsis patients in guiding antibiotic treatment on course of treatment, drug resistance and prognosis

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Abstract: Objective To explore the effects of dynamic monitoring of plasma procalcitonin (PCT) levels in patients with sepsis in guiding antibiotic treatment on course of treatment and drug resistance, and to evaluate its significance in predicting patient prognosis. Methods A retrospective analysis was performed on the clinical data of 200 patients with sepsis in ICU of Xingtai Central Hospital from December 2020 to October 2024. Among all patients, there were 100 cases in control group (routine empirical antibiotics treatment, December 2020 to November 2022) and 100 cases in guidance group (antibiotics treatment under the guidance of dynamic PCT monitoring, December 2022 to October 2024). The dynamic changes of PCT levels, as well as antibiotics course, drug-resistance and prognosis were compared between the two groups. According to prognosis, patients in control group were divided into survival group (n=85) and death group (n=15). The predictive value of dynamic PCT for death of sepsis patients in ICU was analyzed by receiver operating characteristic (ROC) curves. Results After 3 d, 5 d and 7 d of treatment, PCT levels in guidance group

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were  $(1.20\pm0.24)$  ng/mL,  $(0.24\pm0.14)$  ng/mL and  $(0.15\pm0.07)$  ng/mL, lower than those in control group [  $(1.44\pm0.25)$  ng/mL,  $(0.85\pm0.20)$  ng/mL,  $(0.25\pm0.18)$  ng/mL], the differences were statistically significant (P<0.05). After 5 d of treatment, control rate of antibiotics use in guidance group was higher than that in control group  $(75.00\% \ vs 55.00\%, \chi^2=8.791, P=0.003)$ . ICU treatment time and cumulative mortality rates after 7 d, 21 d and 28 d of treatment in guidance group were  $(12.22\pm2.35)$  d, 2.00%, 4.00% and 6.00%, significantly lower than those in control group [  $(14.55\pm2.56)$  d, 9.00%, 12.00%, 15.00%] (P<0.05). After 1 d, 3 d, 5 d and 7 d of treatment, PCT levels in survival group were lower than those in death group, with statistical significance (P<0.05). ROC curves analysis showed that areas under the curve (AUC) values of PCT after 1 d, 3 d, 5 d and 7d of treatment for predicting death of sepsis patients were 0.714, 0.768, 0.770 and 0.775, respectively. **Conclusion** Dynamic monitoring of PCT levels in ICU patients with sepsis to guide antibiotic treatment can significantly shorten course of antibiotics and reduce incidence of multi-drug resistance, and enable patients to achieve better prognosis.

**Keywords**: Dynamic monitoring; Procalcitonin; Sepsis; Course of antibiotic; Prognosis; Multi-drug resistance **Fund program**; Key Research and Development Plan Project of Xingtai City (2020ZC294)

脓毒症作为宿主对感染反应失调引发的危及生 命的器官功能障碍,具有较高的发病率和死亡率[1-2]。 尽管《拯救脓毒症运动(SSC)指南2021》[3]推荐1h内 启动广谱抗生素治疗作为核心干预措施,但过度依 赖经验性治疗导致的抗生素滥用问题日益严峻,加 剧了各类多重耐药菌的流行。传统脓毒症管理中, 抗生素疗程多基于经验性判断或固定周期,缺乏客 观生物标志物指导,尽管C反应蛋白(CRP)和白细 胞计数(WBC)等炎症指标被广泛使用,但其受非感 染因素(如创伤、手术应激)干扰严重,难以准确区 分感染控制与持续炎症状态。此外,临床体征受镇 静治疗及器官支持手段干扰,进一步降低评估的可 靠性[4]。在此背景下,降钙素原(procalcitonin,PCT) 作为一种具有高特异性的细菌感染生物标志物,其 动态变化与感染严重程度及治疗效果密切关联,为 个体化抗生素管理提供了新方向[5]。既往研究虽证 实PCT单次检测可辅助脓毒症诊断,但其动态监测 在治疗中的应用效果并不明确,本研究探讨动态监 测PCT指导脓毒症抗生素治疗对疗程和耐药性的 影响及对预测预后的意义。

### 1 资料与方法

1.1 一般资料 回顾性选择2020年12月至2024年10月在邢台市中心医院ICU接受治疗的脓毒症患者200例作为研究对象,2020年12月至2022年11月收入的100例患者纳入对照组,2022年12月至2024年10月收入的100例患者纳入指导组,见表1。所有患者在院期间均接受微生物学培养或病原学检查,且需要接受长程抗生素治疗。本研究经邢台市中心医院伦理委员会审批通过(2020-KY-07)。

1.2 纳入和排除标准 纳入标准:(1)参照《中国脓毒

症早期预防与阻断急诊专家共识》<sup>[6]</sup>,患者短时间内因病原微生物导致机体组织或局部器官出现炎性改变,且序贯器官衰竭评估(SOFA)评分□≥2分,可被诊断为脓毒症,且符合抗生素治疗适应证;(2)年龄>18岁;(3)就诊时病程均≤5d;(4)患者或家属知情,并签字同意参与研究。排除标准:(1)慢性感染或特殊细菌感染或有多重耐药菌定植史;(2)7d内有糖皮质激素、免疫抑制剂及抗生素治疗史;(3)免疫功能抑制或合并恶性肿瘤,且预计生存期不足3个月。

### 1.3 研究方法

1.3.1 PCT 动态检测 两组患者入院后 24 h 内抽取静脉血 3 mL,以 2 000 r/min 速率(离心半径为 15 cm) 离心,10 min 后取上层清液,利用定量免疫色谱法进行检测,仪器为胶体金免疫层析分析仪(海格德生物科技有限公司,HG-300GM5);并在此基础上分别于入院 1、3、5、7 d开展动态检测。

1.3.2 对照组 采用常规抗生素治疗,依据《中国严重脓毒症/脓毒性休克治疗指南(2014)》<sup>[8]</sup>提出的治疗方案,于入院1h内启动经验性广谱抗生素治疗,病原学检测结果为革兰阴性菌覆盖的非耐药患者首选静脉滴注哌拉西林/他唑巴坦(四川制药制剂,国药准字H20203746,规格:2.0g,用法用量:4.5g,6h/次)或头孢他啶(江西东风药业,国药准字H20073140,规格:1.5g,用法用量:2g,8h/次);而腹腔或盆腔感染患者需覆盖脆弱拟杆菌,加用甲硝唑(吉林省都邦药业,国药准字H22023068,规格:0.5g,用法用量:500 mg,8h/次);同时开展液体复苏和感染源控制,初始30 mL/kg晶体液输注,平均动脉压(mean arterial pressure, MAP)目标≥65 mmHg,并于6~12h内完成脓肿引流及坏死组织清创。

1.3.3 指导组 参照《降钙素原指导抗菌药物临床

合理应用专家共识》<sup>[9]</sup>标准,采取动态检测PCT指导的抗生素治疗,以PCT动态检测结果为依据综合考虑抗生素应用,其应用原则如下:(1)PCT<0.1 ng/mL建议停用抗生素;(2)PCT为0.1~0.25 ng/mL时,综合患者临床指标(发热情况、中性粒细胞水平、白细胞水平等)情况决定是否使用抗生素;(3)PCT>0.25~10 ng/mL时必须使用抗生素;(4)PCT>10 ng/mL时建议直接使用抗生素,如再次检测后下降80%则根据患者临床指标减量使用抗生素,如中途持续使用抗生素48 h后PCT≤0.25 ng/mL则考虑停用抗生素。

1.4 观察指标 (1) PCT 动态变化比较:对比两组治 疗1、3、5、7dPCT水平动态变化情况。(2) 抗生素疗 程缩短及耐药情况:对比两组抗生素使用相关情况 (治疗5 d时抗生素使用达标率、达标时间、抗生素费 用)及耐药情况(耐药类型、耐药菌感染处理费用); 根据动态PCT监测结果进行判断,当PCT≤0.25 ng/mL 时则可认为抗生素使用达标。本研究共监测耐药 类型包括碳青霉烯类耐药的高毒力肺炎克雷伯菌 (CR-hvKP)、多重耐药鲍曼不动杆菌(MDRO)、耐甲 氧西林金黄色葡萄球菌(MRSA)、耐万古霉素肠球 菌(VRE)、碳青霉烯类耐药的鲍曼不动杆菌(CRPA)。 (3) 预后情况:包括ICU治疗时间及28 d内存活情 况,比较两组间的生存差异。(4)不同预后患者的 PCT水平分析:根据对照组生存情况将其分为生存 组(n=85)和死亡组(n=15),比较两组治疗1d、3d、 5 d、7 d 动态 PCT 水平, 并利用受试者工作特征 (ROC)曲线分析动态 PCT 预测 ICU 脓毒症患者死亡 的价值。

1.5 统计学方法 采用 SPSS 25.0 进行数据分析。符合正态分布的计量资料以 $\bar{x}\pm s$ 表示,比较采用t检验。多时点比较采用重复测量方差分析,两两比较采用 SNK-q检验。计数资料以例(%)表示,比较采用 $\chi^2$ 检验。采用 Kaplan-Meier 法绘制生存曲线,并用 Log-rank 检验比较其差异。绘制 ROC 曲线分析动态 PCT 对脓毒症患者死亡的预测价值。检验标准取 $\alpha$ = 0.05,双侧检验。

### 2 结 果

- 2.1 两组基线资料比较 两组性别、年龄、感染部位、病程、初始 SOFA 评分及初始 PCT 经比较差异无统计学意义(*P*>0.05),见表1。
- 2.2 两组 PCT 值动态水平比较 两组 PCT 值均随着治疗时间增加而呈现下降趋势,且指导组治疗 3 d、5 d、7 d时的 PCT 值均低于对照组(P<0.05)。见表 2。
- 2.3 两组抗生素疗程及耐药情况分析 指导组治疗 5 d时抗生素使用达标率为 75.00%, 高于对照组的 55.00%(*P*<0.05); 指导组抗生素使用达标时间、抗生素费用、耐药菌感染处理费用及 MDRO、VRE、CRPA 发生率均低于对照组(*P*<0.05)。 见表 3。
- 2.4 两组预后情况比较 指导组ICU治疗时间及治疗7 d、21 d、28 d累积死亡率明显低于对照组(P<0.05),见表4。生存曲线分析显示,治疗28 d指导组死亡率为6.00%,低于对照组的15.00%(Log-rank  $\chi^2$ =4.390,P<0.05)。见图1。

表 1 两组基线资料比较  $(n=100, \bar{x}\pm s)$  Tab.1 Comparison of baseline data between the two groups  $(n=100, \bar{x}\pm s)$ 

组别	性别[6	列(%)]	- 年龄(岁)	!	感染部位[例(9	%)]	· 病程(d)	初始SOFA	初始 PCT
组別	男	女	十段(夕)	肺部感染	腹腔感染	泌尿系统感染	' 烟性(a)	评分(分)	(ng/mL)
指导组	67(67.00)	33(33.00)	44.58±3.27	44(44.00)	28(28.00)	28(28.00)	2.49±0.40	5.11±0.22	1.85±0.35
对照组	59(59.00)	41(41.00)	45.16±2.89	51(51.00)	24(24.00)	25(25.00)	2.52±0.42	5.16±0.24	1.82±0.33
χ²/t值	1.3	373	1.329		0.993		0.517	1.536	0.624
P值	0.2	241	0.185		0.609		0.606	0.126	0.534

表2 两组PCT值动态水平比较  $(ng/mL, \bar{x}\pm s)$ 

**Tab.2** Comparison of dynamic levels of PCT between the two groups  $(ng/mL, \bar{x}\pm s)$ 

		groups	(118/11112)	N±3/					
组别	例数	治疗 1 d	治疗3d	治疗5d	治疗7 d				
指导组	100	1.64±0.35	1.20±0.24ª	$0.24\pm0.14^{ab}$	0.15±0.07 <sup>abc</sup>				
对照组	100	$1.70\pm0.33$	1.44±0.25°	$0.85 \pm 0.20^{ab}$	$0.25{\pm}0.18^{\mathrm{abc}}$				
F <sub>组间</sub> /P <sub>组间</sub> 值			227.50	00/<0.001					
F时间/ $P$ 时间值		1 642.000/<0.001							
$F_{\phi\pi}/P_{\phi\pi}$ 值			55.98	0/<0.001					

注:与治疗1 d比较,\*P<0.05;与治疗3 d比较,\*P<0.05;与治疗5 d比较,\*P<0.05。

- 2.5 不同预后患者7 d 内 PCT 变化情况分析 两组 PCT 值均随治疗时间增加而递降,且生存组治疗各天的 PCT 值均低于死亡组(*P*<0.05)。见表5。
- 2.6 动态 PCT 水平预测脓毒症患者死亡的 ROC 分析 治疗 1 d、3 d、5 d、7 d时的 PCT 值预测脓毒症患者死亡的曲线下面积(AUC)分别为 0.714、0.768、0.770 和 0.775,最佳截断值分别为 1.71 ng/mL、1.38 ng/mL、0.85 ng/mL和 0.30 ng/mL,见表6、图 2。

表 3 两 约	₹抗生素疗程	及耐药情况	分析	$(n=100, \overline{x}\pm s)$
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<b>Tab.3</b> Analysis of antibiotic treatment duration and resistance between the two groups (n=
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组别	治疗5 d时抗生素	抗生素使用达标	抗生素费用			耐药菌感染处			
组加	使用达标率(%)	时间(d)	(万元)	CR-hvKP	MDRO	MRSA	VRE	CRPA	理费用(万元)
指导组	75(75.00)	7.15±1.25	1.75±0.46	5(5.00)	7(7.00)	4(4.00)	4(4.00)	2(2.00)	0.78±0.15
对照组	55(55.00)	8.94±1.35	2.11±0.62	7(7.00)	18(18.00)	7(7.00)	12(12.00)	10(10.00)	0.84±0.14
t/χ²值	8.791	9.729	4.663	0.355	5.531	0.866	4.348	5.674	2.924
P值	0.003	< 0.001	< 0.001	0.552	0.019	0.352	0.037	0.017	0.004

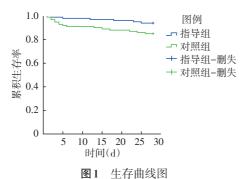


Fig.1 Survival curve

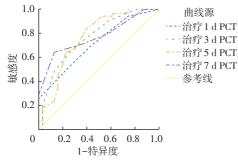


图 2 动态 PCT 水平预测脓毒症患者死亡的 ROC 曲线图 Fig. 2 ROC curve of dynamic PCT levels to predict death in sepsis patients

### 表 4 两组 ICU 治疗时间和 28 d 内死亡情况比较 (n=100)

**Tab.4** Comparison of ICU treatment time and 28-day mortality between two groups (n=100)

	•	0 1				
组别	ICU治疗	累积死亡情况[例(%)]				
	时间 $(d, \bar{x}\pm s)$	治疗1d 治疗7d 治疗21d 治疗2	8 d			
指导组	12.22±2.35	1(1.00) 2(2.00) 4(4.00) 6(6.0	0)			
对照组	14.55±2.56	1(1.00) 9(9.00) 12(12.00) 15(15.	00)			
t/χ²值	6.705	0 4.714 3.348 4.31	0			
P值	< 0.001	1.000 0.030 0.037 0.03	8			

### 3 讨论

研究显示,ICU患者中约35%的广谱抗生素处方缺乏明确感染证据,直接加剧了不同多重耐药菌的流行[10]。世界卫生组织(WHO)已将抗生素耐药性列为全球十大公共卫生威胁之一,迫切需要建立精准

表5 对照组不同预后患者7 d内PCT变化情况 (ng/mL,x±s)

Tab.5 Analysis of PCT changes within 7 days in control group patients with different prognoses (ng/mL,x±s)

			1 0				
组别	例数	治疗1d	治疗3d	治疗5 d	治疗7 d		
生存组	85	1.68±0.24	1.35±0.20ª	0.80±0.20 <sup>ab</sup>	0.26±0.08 <sup>abc</sup>		
死亡组	15	1.75±0.20	1.43±0.28 <sup>a</sup>	$0.86{\pm}0.16^{\mathrm{ab}}$	$0.32{\pm}0.10^{\mathrm{abc}}$		
$F_{\text{dis}}/P_{\text{dis}}$ (fig. 24.460/<0.001							
F时间/ $P$ 时间值	直 2 118.000/<0.001						
$F$ $_{\% \Xi}/P$ $_{\% \Xi}$ वि	Ĺ	0.123/0.947					

注:与治疗1 d比较,\*P<0.05;与治疗3 d比较,\*P<0.05;与治疗5 d 比较,\*P<0.05。

表6 动态 PCT 水平预测脓毒症患者死亡的 ROC 分析 Tab.6 ROC analysis of dynamic PCT levels to predict mortality in sepsis patients

指标	AUC	95%CI	P值	最佳 截断值	敏感度	特异度
1 d PCT	0.714	0.612~0.816	0.001	1.71 ng/mL	0.684	0.619
3 d PCT	0.768	0.666~0.869	< 0.001	1.38 ng/mL	0.645	0.742
5 d PCT	0.770	0.661~0.878	< 0.001	0.85 ng/mL	0.671	0.710
7 d PCT	0.775	0.687~0.863	< 0.001	0.30 ng/mL	0.711	0.645

注:1 d、3 d、5 d、7 d PCT表示治疗1 d、3 d、5 d、7 d的PCT。

化治疗策略以平衡抗感染疗效与耐药防控需求[11]。

本研究结果显示,两组PCT值均随着治疗时间增加而递降,且指导组下降更明显,提示动态PCT监测可以有效降低脓毒症患者PCT水平。PCT水平反映了机体对感染的炎症反应程度,动态PCT监测能够实时反映患者炎症状态的改变,从而为抗生素治疗提供精确的调整依据[12]。指导组基于PCT动态变化对抗生素用量进行适量调整,减轻炎症反应,控制感染,进一步促进PCT水平的下降。丁玲等[13]的研究也通过在临床实践中发现,以动态PCT监测为指导的抗菌药物调整更有利于患者减轻机体炎症反应,促进预后改善,本研究结果与之相符。

指导组抗生素使用达标率更高,达标时间缩短, 抗生素费用和耐药菌感染处理费用更低,及MDRO、 VRE、CRPA 耐药发生率更低,提示动态 PCT 监测有 利于缩短抗生素疗程,降低多重耐药发生率。PCT 作 为细菌感染特异性生物标志物,其半衰期仅为25~30 h,且代谢动力学与感染控制进程高度同步,在完成动态监测后能精准对宿主-病原体相互作用状态进行识别,当PCT下降速率>80%或绝对值<0.25 ng/mL时,提示炎症反应得到有效控制,此时停用抗生素可避免过度暴露,在减少抗生素用量、费用的同时可有效降低因过度使用抗生素引发的多重耐药发生率[14]。当然也有王学敏等[15]的研究指出PCT监测的临床获益高度依赖方案依从性,依从率>80%时,耐药防控及成本节约效应最大化;反之,若依从率<60%,则可能因检测费用增加抵消临床获益,因此需通过多学科协作提升执行规范性,确保动态监测策略的落实。

指导组ICU治疗时间及死亡率明显低于对照组,提示PCT动态监测指导下抗生素用药更有利于患者预后的改善。通过动态PCT监测,可以更准确地判断抗生素治疗的终点,确保疗程的精准和治疗的有效性,减少了药物相关的不良反应和并发症,进而可能缩短了患者在ICU的治疗时间,而有效的治疗有助于减少多器官功能障碍综合征的发生,使得患者死亡率明显降低[16]。此外,减少抗生素暴露也降低了患者发生医院获得性感染的风险,进一步改善了患者的预后。

生存组治疗1d、3d、5d、7d时的PCT值均低于 死亡组,提示动态PCT变化对于患者预后有明显预 测价值。本研究发现两组患者在早期PCT值即出现 分化趋势,但5~7 d差异更大,这表明动态降幅更具 预测意义,PCT的持续高水平反映宿主-病原体失衡 及免疫紊乱的双重病理过程,一方面病原体持续释 放脂多糖等毒性产物,通过Toll样受体4(TLR4)激活 髓系细胞,促进PCT合成;另一方面,失控的炎症反 应导致巨噬细胞 M1 表型极化延迟,形成"细胞因子 风暴-PCT持续升高"恶性循环,促使患者多器官衰竭 的产生,因此对于患者预后的反映也更为明显[17-19]。 此外本研究ROC分析发现治疗5d、7d时的PCT值预 测预后的 AUC(0.770、0.775)较之前时间段明显更 高,也突出了这一点,因此临床实践中应摒弃单次检 测模式,转而采用多次动态监测标准,以实现治疗精 准化和耐药防控的协同优化[20]。

综上所述,基于ICU脓毒症患者PCT水平的动态 监测可以更好地帮助临床医师调整抗生素用药,缩 短抗生素疗程,降低多重耐药发生率并降低其带来 的医疗成本,改善患者预后,具有较高的应用价值。 **利益冲突** 无

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