·临床研究·

血清降钙素原、C-反应蛋白及乳酸对老年脓毒症患者的预后评估

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【摘 要】 **目的** 探讨老年脓毒症患者血清降钙素原(PCT)、C-反应蛋白(CRP)及乳酸水平与急性生理学与慢性健康状况评分系统Ⅱ(APACHEⅡ)评分及序贯性器官功能衰竭评估(SOFA)评分的相关性,分析其对脓毒症患者的预后评估价值。**方法** 选取我院收治的老年脓毒症患者 186 例,根据其 28 d 生存情况的随访结果分为存活组(110 例)和死亡组(76 例)。检测两组患者血清 PCT、CRP 及乳酸水平变化,并记录入院时 APACHEⅡ、SOFA 评分情况。采用 t 检验、重复测量的方差分析、χ^2 检验或 Fisher 精确检验对两组数据进行分析。应用受试者工作特征(ROC)曲线分析血清 PCT、CRP 及乳酸对老年脓毒症患者预后的评估价值。采用 Pearson 相关分析法分析死亡组血清 PCT、CRP 及乳酸水平与 APACHEⅡ、SOFA 评分的相关性。**结果** 死亡组第 1、3、7 天血清 PCT、CRP 及乳酸水平均明显高于存活组($P<0.05$),且死亡组第 7 天血清 PCT、CRP 及乳酸水平明显高于第 1、3 天($P<0.05$)。存活组第 7 天血清 PCT、CRP 及乳酸水平均明显低于第 1、3 天($P<0.05$)。Logistic 回归分析发现,PCT、CRP、乳酸及 SOFA 评分是老年脓毒症患者预后不良的独立影响因素。ROC 曲线显示,PCT_{d3}、CRP_{d3}及乳酸$_{d3}$评估老年脓毒症患者预后的最佳截值分别为 9.83 μg/L、86.42 mg/L 和 3.72 mmol/L,其敏感度和特异度较好,分别为 81.7% 和 85.3%,77.5% 和 79.8%,86.3% 和 76.2%。相关分析显示,死亡组血清 PCT_{d3} 与 APACHEⅡ评分、SOFA评分的相关性较好($r=0.703$,$P<0.001$;$r=0.802$,$P<0.001$)。**结论** 血清 PCT、CRP 及乳酸水平与老年脓毒症患者的病情严重程度及预后密切相关,第3 天血清 PCT 水平预测患者预后的价值最大。

【关键词】 老年人;脓毒症;降钙素原;C-反应蛋白;乳酸;预后评估
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Prognostic values of serum procalcitonin, C-reactive protein and lactate in elderly patients with sepsis

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【**Abstract**】 **Objective** To investigate the correlation of serum levels of lactate, procalcitonin (PCT), and C-reactive protein (CRP) with the score of acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) and sequential organ failure assessment (SOFA) score in the elderly patients with sepsis, and to analyze the prognostic values of these levels. **Methods** A total of 186 cases of senile sepsis in our hospital from January 2012 to December 2016 were selected and followed up for 28 d. According to their survival outcomes, they were divided into survival group ($n=110$) and death group ($n=76$). The serum levels of PCT, CRP and lactate in the 2 groups were detected, and the scores of APACHE Ⅱ and SOFA were recorded. Student's t test, repeated measures analysis of variance, and Chi-square test or Fisher exact test were adopted for the data. Receiver-operating characteristic (ROC) curve analysis was employed to evaluate the prognostic values of the serum PCT, CRP and lactate levels in the septic elderly. Correlations of serum PCT, CRP and lactate levels with APACHE Ⅱ and SOFA scores were analyzed in the death group by Pearson linear correlation analysis. **Results** The serum levels of PCT, CRP and lactate in the first, third and seventh days were significantly higher in the death group than in the survival group ($P<0.05$). What's more, the serum levels in the seventh day of the death group were obviously higher than those of the first and third days ($P<0.05$), but the levels in the seventh day of the survival group were notably lower than those of the first and third days ($P<0.05$). Logistic regression analysis found that serum levels of PCT, CRP and lactate, and SOFA score were independent factors for poor prognosis in the elderly patients with sepsis. The ROC curve showed that the best cut-off values of PCT_{d3}, CRP_{d3} and lactate$_{d3}$ were 9.83 μg/L, 86.42 mg/L and 3.72 mmol/L in the evaluation of prognosis, with the sensitivity and specificity of 81.7% and 85.3%, 77.5% and 79.8%, and 86.3% and 76.2%, respectively. Correlation analysis indicated that the serum PCT_{d3} level was positively correlated with APACHE Ⅱ and SOFA scores in the death group ($r=0.703$, $P<0.001$; $r=0.802$, $P<0.001$). **Conclusion** Serum PCT, CRP and lactate levels are closely related to the severity and prognosis of sepsis in elderly patients,

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and serum PCT level in the third day shows the greatest predictive value in the prognosis.

【Key words】 aged; sepsis; procalcitonin; C-reactive protein; lactate; prognosis evaluation

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脓毒症是由感染引起的全身炎症反应综合征，而老年患者由于基础状态差而病情进展迅速、病情凶险、病死率较高[1]。近年来的研究表明，降钙素原(procalcitonin，PCT)对脓毒症的诊断有较好的敏感度、特异度和准确度[2]；C－反应蛋白(C-reactive protein，CRP)是反映机体组织损伤和感染的有效指标[3]；动脉血乳酸水平是预测炎症感染和感染性休克的重要指标[4]。尽管对脓毒症的发病机制和诊断方法有了进一步的认识，但目前对于老年脓毒症预后评估的生物学标志物尚未明确。本研究通过检测老年脓毒症患者血清PCT、CRP及乳酸水平变化，分析其与APACHEⅡ、SOFA评分的相关性，并比较各指标对老年脓毒症患者的预后评估价值，旨在为老年脓毒症的诊疗提供依据。

1 对象与方法

1.1 研究对象

纳入2012年1月至2016年12月海南省人民医院急诊科和重症监护室(intensive care unit，ICU)收治的老年脓毒症患者186例，其中男107例，女79例，年龄65～87(74.9±9.8)岁。脓毒血症的诊断参照2012国际严重脓毒症及脓毒性休克诊疗指南[5]的诊断标准。排除标准：年龄<65岁；长期应用激素、免疫抑制剂；存在血液系统疾病或接受抗凝治疗；伴有严重肝脏、肾脏、肺部疾病及恶性肿瘤；病历资料不完整、不能配合本次研究。本研究经医院伦理委员会批准，并获得患者或家属知情同意。

1.2 方法

1.2.1 分组方法 将186例脓毒血症患者根据随访28 d的生存情况分为存活组和死亡组。其中存活组110例，男62例，女48例，年龄(74.6±9.7)岁；死亡组76例，男45例，女31例，年龄(75.3±9.8)岁。记录所有患者入院时的体质量指数(body mass index，BMI)、基础疾病(高血压、糖尿病、高脂血症等)、急性生理学与慢性健康状况评分系统Ⅱ(acute physiology and chronic health scoring system Ⅱ，APACHE Ⅱ)、序贯性器官功能衰竭评估(sequential organ failure assessment，SOFA)评分、感染部位等基本资料。

1.2.2 血液检测 分别于确诊第1、3、7天检测患者血清PCT、CRP及动脉血乳酸水平变化。使用全自动多功能酶标仪(美国Thermo公司)酶联免疫吸附法检测PCT水平，试剂盒为美国Rapidbio公司产品；罗氏全自动生化分析仪及配套试剂检测血清CRP；使用ABL90FLEX全自动血气分析仪检测动脉血乳酸、氧分压(partial pressure of oxygen，PO_2)、二氧化碳分压(partial pressure of carbon dioxide，PCO_2)，并计算氧合指数。操作过程均严格按照SOP文件进行。

1.3 统计学处理

应用SPSS 19.0统计软件分析，计量资料以均数±标准差($\bar{x}\pm s$)表示，组间比较采用成组t检验，组内比较采用重复测量的方差分析。计数资料以率表示，率的比较采用χ^2检验或Fisher精确检验。绘制受试者工作特征(receiver operating characteristic，ROC)曲线评价PCT、CRP及乳酸对脓毒症患者的预后评估价值，曲线下面积(area under cure，AUC)比较采用Z检验。采用logistic回归分析脓毒症存活组和死亡组的独立预测因素，相关性分析采用Pearson相关分析。$P<0.05$为差异有统计学意义。

2 结 果

2.1 两组患者一般资料比较

死亡组的APACHEⅡ、SOFA评分均明显高于存活组，差异有统计学意义($P<0.05$)；而两组的性别、年龄、BMI、糖尿病、高血压、高脂血症、感染部位、收缩压、PO_2、PCO_2及氧合指数比较，差异无统计学意义($P>0.05$；表1)。

2.2 两组患者血清PCT、CRP及乳酸水平比较

死亡组第1、3、7天血清PCT、CRP及乳酸水平均明显高于存活组，差异有统计学意义($P<0.05$)。死亡组第3、7天血清PCT、CRP及乳酸水平均明显高于第1天($P<0.05$)，且死亡组第7天血清PCT、CRP及乳酸水平明显高于第3天，差异有统计学意义($P<0.05$)。存活组第7天血清PCT、CRP及乳酸水平均明显低于第1、3天，差异有统计学意义($P<0.05$；表2)。

2.3 脓毒症患者死亡因素Logistic回归分析

对存活组和死亡组的PCT、CRP、乳酸、APACHEⅡ及SOFA评分进行logistic回归分析，发现PCT、CRP、乳酸及SOFA评分是老年脓毒症患者预后不良的独立影响因素，其OR(95% CI)值分别为1.824(1.419～2.386)、1.215(1.054～1.527)、1.503(1.208～2.106)、2.058(1.605～3.027)。详见表3。

表1 两组患者一般资料比较

Table 1 Comparison of general data between the two groups

Item	Survival group (n=110)	Death group (n=76)	χ^2/t	P value
Sex(Male/Female)	62/48	45/31	0.149	0.699
Age(years,$\bar{x}\pm s$)	74.63±9.72	75.26±9.83	0.206	0.673
BMI(kg/m^2,$\bar{x}\pm s$)	23.24±4.51	23.85±4.76	0.245	0.668
Diabetes[n(%)]	25(22.7)	21(27.6)	0.581	0.446
Hypertension[n(%)]	39(35.5)	30(39.5)	0.311	0.577
Hyperlipidemia[n(%)]	45(40.9)	33(43.4)	0.116	0.733
Infective site[n(%)]			0.327	0.631
Respiratory system	46(41.8)	34(44.7)		
Urinary system	23(20.9)	18(23.7)		
Digestive system	28(25.5)	17(22.4)		
Other	13(11.8)	7(9.2)		
Systolic pressure(mmHg,$\bar{x}\pm s$)	133.85±21.78	136.47±23.16	0.568	0.536
PO_2(mmHg,$\bar{x}\pm s$)	81.63±16.82	77.64±17.05	0.706	0.341
PCO_2(mmHg,$\bar{x}\pm s$)	38.25±7.42	36.27±6.91	0.395	0.787
Oxygenation index($\bar{x}\pm s$)	193.56±74.13	185.28±63.26	1.527	0.106
APACHEⅡ(score,$\bar{x}\pm s$)	18.24±6.57	25.38±7.91	8.739	<0.001
SOFA(score,$\bar{x}\pm s$)	5.93±2.64	9.14±3.57	7.863	<0.001

BMI: body mass index; PO_2: partial pressure of oxygen; PCO_2: partial pressure of carbon dioxide; APACHEⅡ: acute physiology and chronic health scoring system Ⅱ; SOFA: sequential organ failure assessment

表2 两组患者血清PCT、CRP及乳酸水平比较

Table 2 Comparison of serum PCT, CRP and lactate levels between the two groups ($\bar{x}\pm s$)

Item	Survival group (n=110)	Death group (n=76)	t	P value
PCT (μg/L)				
Day 1	4.81±1.36	9.35±3.64	4.316	0.017
Day 3	3.05±1.04	18.27±7.05*	15.814	<0.001
Day 7	0.72±0.24*#	30.66±15.28*#	31.827	<0.001
CRP(mg/L)				
Day 1	83.64±22.36	91.52±26.18	3.907	0.031
Day 3	79.82±20.57	128.62±41.36*	13.652	<0.001
Day 7	65.13±14.26*#	160.42±45.73*#	21.674	<0.001
Lactate(mmol/L)				
Day 1	2.03±0.84	4.16±1.37	9.638	<0.001
Day 3	2.08±0.92	6.27±2.25*	15.146	<0.001
Day 7	1.25±0.46*#	8.63±3.65*#	30.647	<0.001

PCT: procalcitonin; CRP: C-reactive protein. Compared with day 1, *P<0.05; compared with day 3, #P<0.05

表3 脓毒症患者死亡因素logistic回归分析

Table 3 Logistic regression analysis of death factors in patients with sepsis

Factor	β	*SE*	*Wald* value	*OR* value	95% *CI*	P value
PCT	0.617	0.186	10.218	1.824	1.419-2.386	<0.001
CRP	0.116	0.042	3.524	1.215	1.054-1.527	0.042
lactate	0.308	0.091	5.037	1.503	1.208-2.106	0.013
APACHEⅡscore	0.057	0.015	2.812	0.962	0.893-1.166	0.068
SOFA score	0.763	0.197	7.526	2.058	1.605-3.027	<0.001

PCT: procalcitonin; CRP: C-reactive protein; APACHEⅡ: acute physiology and chronic health scoring system Ⅱ; SOFA: sequential organ failure assessment

2.4 血清PCT、CRP及乳酸对脓毒症患者预后的评估价值

血清PCT_{d1}、PCT_{d3}、PCT_{d7}评估脓毒症患者预后的AUC(95% *CI*)分别为0.682(0.612~0.757)、0.884(0.817~0.958)、0.836(0.765~0.907),其中PCT_{d3}截断点为9.83 μg/L时,敏感度(81.7%)和特异度(85.3%)较好。血清CRP_{d1}、CRP_{d3}、CRP_{d7}评估脓毒症患者预后的AUC(95% *CI*)分别为0.628

(0.563 ~ 0.692)、0.793 (0.727 ~ 0.861)、0.724 (0.658 ~ 0.792),其中 CRP_{d3} 截断点为 86.42 mg/L 时,敏感度(77.5%)和特异度(79.8%)较好。乳酸$_{d1}$、乳酸$_{d3}$、乳酸$_{d7}$ 评估脓毒症患者预后的 AUC(95% *CI*)分别为 0.647 (0.582 ~ 0.717)、0.841(0.773 ~ 0.913)、0.805(0.736 ~ 0.875),其中乳酸$_{d3}$ 截断点为 3.72 mmol/L 时,敏感度(86.3%)和特异度(76.2%)较好(表 4)。

2.5 死亡组血清 PCT、CRP 及乳酸水平与 APACHE Ⅱ、SOFA 评分的相关性分析

Pearson 相关分析显示,死亡组血清 PCT、CRP 及乳酸水平与 APACHE Ⅱ、SOFA 评分均呈显著正相关($P < 0.05$),其中血清 PCT_{d3} 与 APACHE Ⅱ 评分、SOFA 评分的相关性较好($r = 0.703$, $P < 0.001$; $r = 0.802$, $P < 0.001$;表 5)。

3 讨 论

近年来老年脓毒症的发病率和病死率呈持续上升趋势,其病死率高达 30% ~ 70%,已成为 ICU 和急诊病房主要的死亡原因[6]。因此,寻找脓毒症早期诊断及病情评估的可靠指标对降低患者的病死率具有重要意义。

PCT 是降钙素的前肽物质,在严重感染及全身炎症反应患者中显著升高,是鉴别细菌感染和病毒感染的良好指标[7]。近期研究表明,血清 PCT 水平检测有助于脓毒症的早期诊断和治疗[8],但其对预测脓毒症患者的预后价值仍存在争议。CRP 是一种急性期反应蛋白,常用来反映感染的严重程度,已经成为临床上应用广泛的炎症和组织损伤标志物[9]。动脉血乳酸是反映组织灌注及细胞缺氧的重要指标,脓毒症患者由于机体存在着不同程度的组织低灌注和氧合障碍导致无氧代谢而产生大量乳酸[10]。本研究显示,死亡组不同时间点血清 PCT、CRP 及乳酸水平均明显高于存活组,且死亡组第 7 天血清 PCT、CRP 及乳酸水平均明显高于第 1 天和第 3 天,而存活组第 7 天血清 PCT、CRP 及乳酸水平则呈明显下降趋势。分析其原因可能是死亡组患者病情严重,感染无法得到有效地控制,出现肾衰竭

表 4 血清 PCT、CRP 及乳酸对脓毒症患者预后的评估价值

Table 4 Prognostic value of serum PCT, CRP and lactate in patients with sepsis

Item	Optimal cut-off	AUC	95% *CI*	Sensitivity (%)	Specificity (%)	Positive predictive value(%)	Negative predictive value(%)
PCT_{d1}	6.38 μg/L	0.682	0.612 – 0.757	78.4	62.8	66.7	75.3
PCT_{d3}	9.83 μg/L	0.884	0.817 – 0.958	81.7	85.3	88.6	78.2
PCT_{d7}	14.27 μg/L	0.836	0.765 – 0.907	82.5	79.3	83.4	78.7
CRP_{d1}	65.73 mg/L	0.628	0.563 – 0.692	70.5	60.2	63.5	67.4
CRP_{d3}	86.42 mg/L	0.793	0.727 – 0.861	77.5	79.8	83.6	74.2
CRP_{d7}	102.56 mg/L	0.724	0.658 – 0.792	71.6	77.5	80.7	68.3
$Lactate_{d1}$	3.04 mmol/L	0.647	0.582 – 0.717	74.6	59.6	64.2	70.8
$Lactate_{d3}$	3.72 mmol/L	0.841	0.773 – 0.913	86.3	76.2	79.5	83.1
$Lactate_{d7}$	4.28 mmol/L	0.805	0.736 – 0.875	83.7	74.5	77.8	80.5

PCT: procalcitonin; CRP: C-reactive protein; AUC: area under curve

表 5 死亡组血清 PCT、CRP 及乳酸水平与 APACHE Ⅱ、SOFA 评分的相关性分析

Table 5 Correlation analysis of serum PCT, CRP and lactate levels with APACHE Ⅱ and SOFA scores in the death group

Item	APACHE Ⅱ score		SOFA score	
	r	*P* value	*r*	*P* value
PCT_{d1}	0.507	0.006	0.541	0.003
PCT_{d3}	0.703	<0.001	0.802	<0.001
PCT_{d7}	0.659	<0.001	0.743	<0.001
CRP_{d1}	0.408	0.014	0.375	0.016
CRP_{d3}	0.594	<0.001	0.637	<0.001
CRP_{d7}	0.558	<0.001	0.604	<0.001
$Lactate_{d1}$	0.512	0.005	0.433	0.012
$Lactate_{d3}$	0.672	<0.001	0.758	<0.001
$Lactate_{d7}$	0.605	<0.001	0.663	<0.001

PCT: procalcitonin; CRP: C-reactive protein; APACHE Ⅱ: acute physiology and chronic health scoring system Ⅱ; SOFA: sequential organ failure assessment

或严重的脓毒症休克,血清 PCT、CRP 及乳酸水平显著升高;而存活组患者的感染得到有效控制,循环、呼吸等脏器功能逐渐稳定,血清 PCT、CRP 及乳酸水平呈显著下降趋势。Li 等[11]研究表明,血清 PCT 及 CRP 水平在脓毒症患者中明显升高,两者联合检测对早期诊断脓毒症具有重要价值。另有研究证实,动脉血乳酸水平与脓毒症患者的死亡率显著相关,可有效地评估脓毒症的严重程度及预后情况[12]。

本文对老年脓毒症患者预后影响因素进行logistic回归分析,结果显示,PCT、CRP、乳酸及SOFA评分是影响老年脓毒症患者预后不良的危险因素,与既往研究[13,14]结果相似,提示影响老年脓毒症患者预后不良的危险因素较多,血清 PCT、CRP、乳酸水平及 SOFA 评分高的患者预后较差,临床上应尽早采取有效的治疗措施,以降低患者的病死率。Ryu 等[15]研究表明,血清 PCT 和 CRP 水平的检测不仅可反映脓毒症患者的病情严重程度,也可作为预测脓毒症患者死亡的独立危险因素。本研究中,不同时间点 PCT、CRP 及乳酸水平对评估老年脓毒症患者预后的敏感度和特异度不同,其中 PCT_{d3}、CRP_{d3}及乳酸$_{d3}$的截断点分别为 9.83 μg/L、86.42 mg/L 和 3.72 mmol/L 时,对评估老年脓毒症患者预后的敏感度和特异度相对较好,说明 PCT、CRP 及乳酸水平有助于判断老年脓毒症患者的病情严重程度,对预测患者预后不良具有较好的效能。Schuetz 等[16]研究表明,PCT 可以有效预测脓毒症患者病情恶化和病情持续不稳定状态,对判断治疗效果及预后具有重要价值。Hegazy 等[17]研究认为,CRP 水平在脓毒症的诊断及预后评估中具有一定的价值,联合 PCT 及 SOFA 评分的变化可更好地评估脓毒症患者的预后。李晓晶等[18]研究也发现,脓毒症患者动脉血乳酸水平和 SOFA 评分越高,患者预后越差;乳酸水平检测是判断脓毒症患者病情严重程度和预后的良好指标。相关研究表明,APACHE Ⅱ评分对脓毒症和其他危重症患者有较好的临床评估效果,已广泛应用于危重患者的病情评估[19]。SOFA 评分操作简单快捷,临床广泛应用,能较好地评估危重病患者的预后[20]。目前对于脓毒症死亡患者血清 PCT、CRP 及乳酸水平与 APACHE Ⅱ、SOFA 评分的相关性研究较少。本研究显示,死亡组血清 PCT、CRP 及乳酸水平与 APACHE Ⅱ、SOFA评分均呈正相关,其中血清 PCT_{d3}与 APACHE Ⅱ评分、SOFA 评分的相关性较好,这进一步说明血清 PCT、CRP 及乳酸水平与老年脓毒症患者预后不良密切相关,第 3 天血清 Copeptin 水平变化能准确预测患者的预后,联合 APACHE Ⅱ、SOFA 评分可提高患者的预后评估准确性。因此,血清 PCT、CRP 及乳酸水平显著升高可能是老年脓毒症患者病情加重的早期预警信号,临床上应尽早采取有效治疗措施阻止病情进一步发展。

综上所述,血清 PCT、CRP 及乳酸水平升高是老年脓毒症患者预后不良的危险因素,动态观察 PCT、CRP 及乳酸水平对评估脓毒症患者病情严重程度及预后具有一定的价值,其中第 3 天血清 PCT 水平预测老年脓毒症患者预后不良的敏感度和特异度最好,但本研究为单中心的病例对照研究,其研究结果尚需大规模、多中心的前瞻性研究来进一步证实。

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· 消　息 ·

《中华老年多器官疾病杂志》论文优先发表快速通道

为加快重大医学研究成果的交流推广，促进医学事业的发展，我刊对符合下列条件的论文开设快速通道，优先发表：(1)国家、军队、省部级基金资助项目；(2)其他具有国内领先水平的创新性科研成果论文；(3)相关领域各类最新指南解读。凡要求以“快速通道”发表的论文，作者应提供关于论文科学性和创新性的说明。我刊对符合标准的稿件，即快速审核及刊用。

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