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不同分级及转归脓毒症患者血清 PCT、D-D、CRP 及血小板相关参数检测的临床意义*

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摘要 目的:探讨不同分级及转归脓毒症患者的血清降钙素原(PCT)、D-二聚体(D-D)、C反应蛋白(CRP)及血小板相关参数检测的临床意义。**方法:**回顾性分析 2015 年 3 月至 2018 年 8 月期间中国人民解放军西部战区总医院收治的 92 例脓毒症患者的临床资料,分析不同分级及转归脓毒症患者的血清中 PCT、D-D 和 CRP 水平、急性病生理与慢性健康评价系统 II (APACHE II) 评分及血小板相关参数[血小板计数(PLT)、血小板平均容积(MPV)、血小板分布宽度(PDW)、大型血小板比率(P-LCR)],并分析脓毒症患者 PCT、D-D、CRP 水平以及血小板相关参数与 APACHE II 评分的相关性。**结果:**全身炎症反应综合征组、轻度脓毒症组、严重脓毒症组、脓毒性休克组血清 PCT、D-D 和 CRP 水平、MPV、PDW、P-LCR、APACHE II 评分逐渐升高 ($P<0.05$), PLT 逐渐降低 ($P<0.05$)。存活组患者血清 PCT、D-D、CRP 水平、MPV、PDW、P-LCR、APACHE II 评分均低于死亡组 ($P<0.05$), PLT 高于死亡组 ($P<0.05$)。Pearson 相关分析显示,脓毒症患者血清 PCT、D-D、CRP、MPV、PDW、P-LCR 与 APACHE II 评分呈正相关 ($P<0.05$), PLT 与 APACHE II 评分呈负相关 ($P<0.05$)。**结论:**脓毒症患者血清 PCT、D-D、CRP 及血小板相关指标可能参与了脓毒症的发展,通过检测其血清 PCT、D-D、CRP 水平及血小板相关参数可评估脓毒症患者的病情和预后。

关键词:脓毒症;降钙素原;D-二聚体;C反应蛋白;血小板;急性病生理与慢性健康评价系统 II

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Clinical Significance of Serum PCT, D-D, CRP and Platelet-related Parameters in Sepsis Patients with Different Grades and Prognosis*

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ABSTRACT Objective: To investigate the clinical significance of serum procalcitonin (PCT), D-dimer (D-D), C-reactive protein (CRP) and platelet parameters in sepsis patients with different grades and prognosis. **Methods:** The clinical data of 92 patients with sepsis who were admitted to General Hospital of the Western War Zone of the Chinese People's Liberation Army from March 2015 to August 2018 were retrospectively analyzed. The levels of serum PCT, D-D and CRP, acute physiology and chronic health evaluation II (APACHE II) score and platelet-related parameters [(platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), platelet-large platelet ratio (P-LCR)] in patients with sepsis of different conditions and different prognosis were analyzed. The correlation between PCT, D-D, CRP levels, platelet-related parameters and APACHE II score in sepsis patients were analyzed. **Results:** The levels of serum PCT, D-D and CRP, MPV, PDW, P-LCR and APACHE II in systemic inflammatory response syndrome group, mild sepsis group, severe sepsis group and septic shock group increased gradually ($P<0.05$). PLT decreased gradually ($P<0.05$). The levels of serum PCT, D-D, CRP, MPV, PDW, P-LCR and APACHE II in survival group were lower than those in death group ($P<0.05$). PLT was higher than that in the death group ($P<0.05$). Pearson correlation analysis showed that serum PCT, D-D, CRP, MPV, PDW, P-LCR were positively correlated with APACHE II score in patients with sepsis ($P<0.05$). PLT was negatively correlated with APACHE II score ($P<0.05$). **Conclusion:** The serum PCT, D-D, CRP and platelet-related parameters may be involved in the development of sepsis. Serum PCT, D-D, CRP levels and platelet-related parameters can be used to evaluate the condition and prognosis of sepsis patients.

Key words: Sepsis; Procalcitonin; D-dimer; C reactive protein; Platelet; Acute physiology and chronic health evaluation II

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前言

脓毒症是指因感染引起的宿主反应失调导致危及生命的器官功能障碍,涉及体内多个器官和系统,其连续发展过程为全身性炎症反应综合征、轻度脓毒症、严重脓毒症、脓毒性休克、多器官功能障碍综合征^[1-3]。脓毒症的死亡率约为25%-40%^[4],病原学结果可作为诊断脓毒症的可靠依据,但其在早期诊断中阳性率较低、需时较长,因此寻找更加准确、有效的脓毒症诊断指标成为当前研究的热点。血清降钙素原(Procalcitonin, PCT)作为炎症指标,其可以反映机体炎性反应的严重程度^[5-7];D-二聚体(D-D)是纤溶酶与交联纤维蛋白相互作用的降解产物,其水平的升高表明机体内形成了血栓及纤溶^[8,9];C反应蛋白(C-reactive protein, CRP)是一种由肝脏细胞合成、能结合肺炎球菌细胞壁C-多糖的急性蛋白,其水平变化可敏感反映机体是否合并感染及感染严重程度^[10];此外,以血小板相关参数为代表的血液系统指标在脓症患者疾病的早期阶段就会表现出异常,且随着患者病情的恶化其水平也会发生变化。鉴于此,本研究通过探讨不同分级及转归脓症患者血清PCT、D-D、CRP以及血小板相关参数的变化,以期对脓毒症病情的评估及治疗提供参考依据,现报告如下。

1 资料与方法

1.1 一般资料

回顾性分析2015年3月至2018年8月期间中国人民解放军西部战区总医院收治的92例脓毒症患者的临床资料。脓毒症分级诊断标准^[11]:(1)满足下列条件2项以上者即可诊断为全身炎症反应综合征:①体温 $>38^{\circ}\text{C}$ 或者 $<36^{\circ}\text{C}$;②心率 >90 次/分;③白细胞计数 $>12\times 10^9/\text{L}$ 或者 $<4\times 10^9/\text{L}$;(2)满足全身炎症反应综合征诊断标准的同时伴有可疑或明确的感染时可诊断为轻度脓毒症;(3)轻度脓毒症伴有器官功能障碍和/或组织灌注不足时可诊断为严重脓毒症;(4)当出现严重感染导致循环衰竭,虽经充分液体复苏但仍未能纠正低组织灌注和低血压等情况时,即诊断为脓毒性休克。纳入标准:①所有患者均符合《中国严重脓毒症/脓毒性休克治疗指南(2014)》^[12]的诊断标准;②住院时间在72h以上;③有完整的临床档案资料;④进入正式研究前7天未服用阿司匹林等影响血小板功能的药物;⑤肝肾功能无障碍,无糖尿病、高血压等慢性疾病史,无血液病病史。排除标准:①患有恶性肿瘤者;②正在接受糖皮质激素或免疫抑制剂治疗者;③长期或重症心源性休克者;④长期重症器官灌注异常者。根据脓毒症分级诊断标准分为全身炎症反应综合征组33例、轻度脓毒症组28例、严重脓毒症组19例、脓毒性休克组12例。其中全身炎症反应综合征组男19例,女14例,年龄43-69岁,平均年龄 (57.44 ± 3.17) 岁;轻度脓毒症组男12例,女16例,年龄45-68岁,平均年龄 (57.23 ± 2.98) 岁;严重脓毒症组男11例,女8例,年龄44-71岁,平均年龄 (57.67 ± 4.22) 岁;脓毒性休克组男8例,女4例,年龄43-70岁,平均年龄 (57.43 ± 3.98) 岁。收集92例患者的转归资料,其中存活者71例,记为存活组,死亡者21例,记为死亡组。

1.2 观察指标

(1)采集所有患者入院后空腹静脉血5 mL,3200 r/min离

心10 min,离心半径12 cm,分离血清,送至检验科检测。采用化学发光免疫测定法(试剂盒购自武汉默沙克生物科技有限公司)进行血清PCT水平检测;采用免疫过滤胶体金显色反应法(试剂盒购自江苏鸿恩医疗器械有限公司)进行D-D及CRP水平检测。(2)采用血细胞分析仪(迪瑞医疗科技股份有限公司,型号BCC-3900)检测血小板相关参数,包括血小板计数(Platelet count, PLT)、血小板平均容积(Mean platelet volume, MPV)、血小板分布宽度(Platelet distribution width, PDW)以及大型血小板比率(Platelet-large platelet ratio, P-LCR)。(3)所有患者于入院24h内完成急性病生理与慢性健康评价系统II(Acute physiology and chronic health evaluation II, APACHE II)评分^[13],从急性生理学、年龄和慢性健康状况等方面进行评分,各部分评分之和记为总分,分值越高表示病情越严重。

1.3 统计学方法

应用SPSS 20.0软件进行数据统计,以[n(%)]表示计数资料,采用 χ^2 检验;以 $(\bar{x}\pm s)$ 表示计量资料,采用单因素方差分析多组间数据,使用t检验分析两组独立样本差异;采用Pearson相关分析法分析脓症患者血清PCT、D-D、CRP、血小板相关参数与APACHE II评分的相关性。以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 不同脓毒症分级患者血清PCT、D-D、CRP水平及APACHE II评分比较

各组患者血清PCT、D-D和CRP水平和APACHE II评分整体比较差异有统计学意义($P<0.05$)。随着病情的加重,患者血清PCT、D-D和CRP水平及APACHE II评分随之升高,组间比较差异均有统计学意义($P<0.05$)。如表1所示。

2.2 不同脓毒症分级患者血小板相关参数比较

各组患者PLT、MPV、PDW和P-LCR整体比较差异有统计学意义($P<0.05$)。随着病情的加重,患者MPV、PDW和P-LCR随之升高,PLT随之下降,组间比较差异均有统计学意义($P<0.05$)。如表2所示。

2.3 不同转归患者血清PCT、D-D、CRP水平及APACHE II评分比较

存活组患者血清PCT、D-D、CRP水平及APACHE II评分低于死亡组($P<0.05$)。如表3所示。

2.4 不同转归患者血小板相关参数比较

存活组患者MPV、PDW、P-LCR低于死亡组,PLT高于死亡组($P<0.05$)。如表4所示。

2.5 脓症患者PCT、D-D、CRP及血小板相关参数与APACHE II评分的相关性分析

Pearson相关分析显示,脓症患者PCT、D-D、CRP、MPV、PDW、P-LCR与APACHE II评分呈正相关($r=0.583$ 、 0.472 、 0.287 、 0.487 、 0.491 、 0.372 , $P=0.000$ 、 0.000 、 0.027 、 0.000 、 0.000 、 0.011),PLT与APACHE II评分呈负相关($r=-0.657$, $P=0.000$)。

3 讨论

脓毒症是由感染所引起的全身性炎症反应,可能诱发感

表 1 不同脓毒症分级患者血清 PCT、D-D、CRP 水平及 APACHE II 评分比较($\bar{x}\pm s$)Table 1 Comparison of serum PCT, D-D, CRP levels and APACHE II score in sepsis patients with different grades($\bar{x}\pm s$)

Groups	n	PCT(ng/mL)	D-D(mg/L)	CRP(μ g/mL)	APACHE II score (scores)
Systemic inflammatory response syndrome group	33	1.92 $\pm$ 0.98	0.99 $\pm$ 3.15	52.76 $\pm$ 11.92	4.77 $\pm$ 1.87
Mild sepsis group	28	3.58 $\pm$ 1.16*	3.31 $\pm$ 3.34*	77.91 $\pm$ 12.27*	12.65 $\pm$ 2.13*
Severe sepsis group	19	9.27 $\pm$ 1.01* [#]	5.18 $\pm$ 2.11* [#]	98.45 $\pm$ 11.56* [#]	15.52 $\pm$ 1.99* [#]
Septic shock group	12	15.27 $\pm$ 1.33* [#] ^Δ	7.37 $\pm$ 2.37* [#] ^Δ	150.33 $\pm$ 10.21* [#] ^Δ	23.69 $\pm$ 2.18* [#] ^Δ
F		542.200	20.380	216.600	259.800
P		0.000	0.000	0.000	0.000

Note: Compared with the systemic inflammatory response syndrome group, * $P<0.05$; Compared with mild sepsis group, [#] $P<0.05$; Compared with septic shock group, ^Δ $P<0.05$.

表 2 不同脓毒症分级患者血小板相关参数比较($\bar{x}\pm s$)Table 2 Comparison of platelet-related parameters in sepsis patients with different grades($\bar{x}\pm s$)

Groups	n	PLT($\times 10^9/L$)	MPV(fL)	PDW(%)	P-LCR(%)
Systemic inflammatory response syndrome group	33	220.31 $\pm$ 33.53	8.66 $\pm$ 1.11	9.89 $\pm$ 1.41	0.18 $\pm$ 0.07
Mild sepsis group	28	165.21 $\pm$ 38.37*	9.44 $\pm$ 1.02*	11.97 $\pm$ 1.46*	0.23 $\pm$ 0.07*
Severe sepsis group	19	108.87 $\pm$ 29.32* [#]	10.64 $\pm$ 1.28* [#]	14.48 $\pm$ 1.78* [#]	0.30 $\pm$ 0.09* [#]
Septic shock group	12	37.61 $\pm$ 11.78* [#] ^Δ	12.71 $\pm$ 1.15* [#] ^Δ	16.53 $\pm$ 1.95* [#] ^Δ	0.42 $\pm$ 0.08* [#] ^Δ
F		110.500	42.450	66.600	32.920
P		0.000	0.000	0.000	0.000

Note: Compared with the systemic inflammatory response syndrome group, * $P<0.05$; Compared with mild sepsis group, [#] $P<0.05$; Compared with septic shock group, ^Δ $P<0.05$.

表 3 不同转归患者血清 PCT、D-D、CRP 水平及 APACHE II 评分比较($\bar{x}\pm s$)Table 3 Comparison of serum PCT, D-D, CRP levels and APACHE II score in patients with different prognosis($\bar{x}\pm s$)

Groups	n	PCT(ng/mL)	D-D(mg/L)	CRP(μ g/mL)	APACHE II score (scores)
Death group	21	18.44 $\pm$ 0.64	6.39 $\pm$ 2.16	151.06 $\pm$ 12.42	15.70 $\pm$ 1.53
Survival group	71	1.91 $\pm$ 0.67	1.72 $\pm$ 1.99	62.32 $\pm$ 11.69	7.79 $\pm$ 1.60
t		100.300	9.266	30.130	20.120
P		0.000	0.000	0.000	0.000

表 4 不同转归患者血小板相关参数比较($\bar{x}\pm s$)Table 4 Comparison of platelet-related parameters in patients with different prognosis($\bar{x}\pm s$)

Groups	n	PLT($\times 10^9/L$)	MPV(fL)	PDW(%)	P-LCR(%)
Death group	21	60.17 $\pm$ 22.17	12.73 $\pm$ 1.72	17.09 $\pm$ 3.34	0.52 $\pm$ 0.11
Survival group	71	185.24 $\pm$ 28.30	8.98 $\pm$ 1.66	10.93 $\pm$ 2.83	0.17 $\pm$ 0.09
t		18.610	9.021	8.404	14.860
P		0.000	0.000	0.001	0.000

染性休克及多器官功能障碍综合征, 具有较高发病率和病死率^[13-15]。及时、准确地评估脓毒症患者的病情可以为其治疗提供合理的手段。APACHE II 评分以其简便、可靠的特点成为世界范围内普遍使用的危重病病情评价系统, 对患者的病情危重程度及其预后评估有重要的参考价值^[16-18]。PCT 是降钙素的前肽

物质, 生理情况下由甲状腺细胞产生, 在正常人中 PCT 水平低于 0.5 g/L, 而脓症患者体内水平相当于正常人的 2000 倍, 可达到 1000 g/L^[19]。D-D 水平升高与多种原因引起的血栓性疾病有关, 当患者体内出现血栓性疾病的继发性纤溶亢进时, D-D 水平也随之升高, 因此其可将其作为体内凝血功能的标志物

之一^[20-22]。脓毒症患者体内炎性介质剧增,其可启动凝血系统,形成微血栓,导致 D-D 水平升高,同时纤溶性增强。有研究表明^[23],D-D 水平在妊娠、先兆子痫、新生儿窒息、急性心梗深静脉血栓等疾病中均呈高表达。D-D 水平的升高虽然能够反映患者的凝血功能状况,但是不能说明血栓形成的原因及位置,必须结合其他临床指标进行分析。CRP 在机体感染后 2h 内可由肝脏细胞快速合成,在 48h 时到达高峰,当感染被控制后,CRP 迅速下降^[24,25],然而由于在手术、应激、意外创伤等发生时,CRP 浓度也将升高^[26],其并不是诊断脓毒症的特异性指标,因此,结合其他临床指标进行综合评估才能更准确地评估脓毒症患者的病情。

在脓毒症早期阶段的凝血机制激活、炎症反应等过程中,血小板受到刺激而活化,其功能及结构均随之发生变化^[27,28]。同时,脓毒症发生过程中,由于患者体内血小板被吞噬,因而 PLT 可较为客观地反应脓毒症患者的病情程度。MPV 能够代表巨核细胞在骨髓中的增生代谢以及血小板的产生情况,在骨髓衰竭等骨髓抑制严重的情况下,MPV 随患者血小板的破坏而持续下降^[29,30]。PDW 可反映血小板容积大小差异的程度,其值降低代表患者血小板均一性较高。P-LCR 的变化则反映了血小板的成熟程度,其比率降低,说明血小板成熟程度较高,而患者出血时,由于血小板数量和大血小板比值同时减少,可导致 P-LCR 数值降低。因此,联合 MPV、PDW 和 P-LCR 等血小板相关参数,便于较全面地分析患者体内的血小板生成状况,从而可以反映出脓毒症患者的病情严重程度。本研究结果中,随着病情的加重,脓毒症患者的血清 PCT、D-D、CRP 水平及 APACHE II 评分逐渐升高;存活组患者的上述四个指标均低于死亡组,PCT、D-D、CRP 与 APACHE II 评分呈正相关,脓毒症患者体内 MPV、PDW 和 P-LCR 均迅速升高,PLT 降低,存活组 MPV、PDW 和 P-LCR 低于死亡组,而 PLT 高于死亡组,MPV、PDW 和 P-LCR 与 APACHE II 评分呈正相关,PLT 与 APACHE II 评分呈负相关。这可能是由于病情较严重患者或死亡患者体内会出现高浓度的菌落刺激因子,导致血小板被消耗、破坏,说明随着病情的加重,脓毒症患者体内炎症反应加重,严重损伤机体机能,PCT、D-D、CRP 和血小板相关参数等指标出现剧烈变化,因此,检测上述指标可对脓毒症患者病情进行综合评估。

综上所述,脓毒症患者血清 PCT、D-D、CRP 水平及血小板相关参数与 APACHE II 评分相关,检测血清 PCT、D-D、CRP 水平及血小板相关参数,可在一定程度上评估脓毒症患者的病情发展和预后。

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(上接第 3456 页)

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