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脓毒症患者炎性因子、凝血功能与 APACHE Ⅱ 评分和预后的关系 *

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摘要 目的：研究脓毒症患者炎性因子、凝血功能与急性生理学和慢性健康状况Ⅱ（APACHE Ⅱ）评分和预后的关系。**方法：**选取 2017 年 1 月至 2018 年 1 月我院收治的脓毒症患者 150 例为脓毒症组，所有患者根据预后结果分为死亡组（n=49）和存活组（n=101），选择同期在我院住院的非脓毒症患者 98 例为非脓毒症组，比较脓毒症组与非脓毒症组患者炎性因子、凝血功能指标水平及 APACHE Ⅱ 评分，同时比较死亡组和存活组患者炎性因子、凝血功能指标水平及 APACHE Ⅱ 评分，并分析脓毒症患者 APACHE Ⅱ 评分与炎性因子、凝血功能指标的相关性。**结果：**脓毒症组患者降钙素原（PCT）、活化部分凝血酶原时间（APTT）、凝血酶原时间（PT）水平及 APACHE Ⅱ 评分均高于非脓毒症组，血小板计数（PLT）低于非脓毒症组（P<0.05），两组 C- 反应蛋白（CRP）比较差异无统计学意义（P>0.05）。死亡组患者 PCT、APTT、PT 水平及 APACHE Ⅱ 评分均高于存活组，PLT 水平低于存活组（P<0.05），两组 CRP 比较差异无统计学意义（P>0.05）。经 Spearman 相关性分析结果显示，脓毒症患者 APACHE Ⅱ 评分与 PCT、APTT、PT 均呈正相关关系，与 PLT 呈负相关关系（P<0.05），与 CRP 无相关性（P>0.05）。**结论：**脓毒症患者 PCT、APTT、PT 水平明显上升，PLT 水平明显下降，且均与患者的 APACHE Ⅱ 评分密切相关，临床可通过调节炎症因子水平及凝血功能指标从而改善患者的病情和预后。

关键词：脓毒症；炎性因子；凝血功能；APACHE Ⅱ 评分；预后；关系

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Relationship Between Inflammatory Factors, Coagulation Function and APACHE II Score and Prognosis in Patients with Sepsis*

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ABSTRACT Objective: To study the relationship between inflammatory factors, coagulation function and acute physiology and chronic health status II (APACHE II) score and prognosis in patients with sepsis. **Methods:** A total of 150 patients with sepsis, who were treated in the Fifth Affiliated Hospital of Xinjiang Medical University from January 2017 to January 2018, were selected as sepsis group and were further divided into death group (n=49) and survival group (n=101) according to the outcome of the prognosis. Another 98 patients without sepsis, who were hospitalized in the hospital during the same period, were selected as non sepsis group. The levels of inflammatory factors, coagulation function indexes and APACHE II score were compared between sepsis group and non sepsis group; at the same time, the levels of inflammatory factors, coagulation function indexes and the APACHE II score were compared between the death group and the survival group, and the correlation of APACHE II score with inflammatory factors and coagulation function indexes in the patients with sepsis was analyzed. **Results:** The levels of procalcitonin (PCT), activated partial thromboplastin time (APTT), prothrombin time (PT) and APACHE score of patients in sepsis group were higher than those in non sepsis group, but platelet count (PLT) in sepsis group was lower than that in non sepsis group (P<0.05). There was no significant difference in C-reactive protein (CRP) between the two groups (P>0.05). The levels of PCT, APTT, PT and APACHE II score in the death group were all higher than those in the survival group, and the level of PLT was lower than that in the survival group (P<0.05). There was no significant difference in CRP between the two groups (P>0.05). The correlation analysis of Spearman showed that there was a positive correlation between APACHE II score and PCT, APTT and PT in the patients with sepsis, which was negatively correlated with PLT (P<0.05), and there was no correlation with CRP(P>0.05). **Conclusion:** The levels of PCT, APTT and PT are increased significantly in the patients with sepsis, and the level of PLT is decreased significantly, which are closely related to the APACHE II score of the patients. It is possible to improve the patient's condition and prognosis by controlling the levels of inflammatory factors and coagulation function.

Key words: Sepsis; Inflammatory factors; Coagulation function; APACHE II score; Prognosis; Relationship

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前言

脓毒症是感染、烧伤、创伤等临床上急危重患者的严重并发症之一，其病情凶险，可以进展为多器官功能衰竭、严重脓毒症以及脓毒症休克等，具有较高的发生率和病死率[1,2]。脓毒症的病理生理变化主要表现为全身炎性反应综合征和凝血功能紊乱，有报道显示[3-5]，脓毒症的实质是炎性反应，当患者发生感染和创伤时，机体细胞在病原体的入侵下产生大量的炎性因子，在炎性因子的作用下，其凝血系统被激活，此时会持续消耗大量的抗凝血因子，进而使血液处于高凝状态，最终造成患者凝血系统紊乱。同时，凝血因子的活化将通过多种途径促进炎症反应的进展，两者相互作用、相互影响共同导致病情的进一步加剧，对患者的预后造成严重的影响[6,7]。急性生理学和慢性健康状况Ⅱ（Acute Physiology and Chronic Health EvaluationⅡ，APACHEⅡ）是临床上常用于评估急危重患者病情和预后的评分体系，其主要是通过收集患者的体征、临床症状以及一些有预测价值的生化指标进行判定，具有应用范围广、操作简单、科学可靠等优点，已在全世界范围内被推广使用[8-10]。本研究通过探讨脓毒症患者炎性因子、凝血功能与APACHEⅡ评分和预后的关系，旨在为临床脓毒症的治疗及预后的改善提供数据参考。

1 资料与方法

1.1 一般资料

选取2017年1月至2018年1月我院收治的脓毒症患者150例为脓毒症组，纳入标准：(1)所有患者均符合2014年中华医学会重症医学分会制定的关于脓毒症的诊断标准[11]；(2)入院后存活时间≥24 h；(3)年龄≥18岁；(4)患者及其家属对本研究知情同意并签署知情同意书。排除标准：(1)伴有血液系统疾病者；(2)呼吸衰竭、肝硬化等严重慢性疾病者；(3)自身免疫性疾病者；(4)临床资料不全者。脓毒症组中男性91例，女性59例；年龄18-81岁，平均(58.23± 9.56)岁；原发病类型：肺炎33例，严重创伤57例，重症胆管炎21例，重症胰腺炎18例，血流感染12例，弥漫性腹膜炎9例。将脓毒症组患者根据治疗后28天的预后结果分为死亡组(n=49)和存活组(n=101)。选择同期在我院住院的非脓毒症患者98例为非脓毒症组，男性57例，女性41例；年龄20-82岁，平均(57.93± 9.22)岁；疾病类型：胃肠道癌34例，脑血管意外30例，气胸12例，高血压12例，呼吸衰竭10例。脓毒症组与非脓毒症组患者年龄、性别比较差异无统计学意义(P>0.05)，均衡可比。本研究获得我院伦理委员会的批准。

1.2 方法

两组患者均在入院当天抽取空腹静脉血10 mL，均分成两份，一份在常温下静置30 min后，以3500 r/min的离心速度、7.5 cm的离心半径离心10 min，分离上层血清，并于-80℃的冰箱中保存待测。采用酶联免疫吸附试验(试剂盒购自北京华夏远洋科技有限公司)检测C-反应蛋白(C-reactive protein, CRP)水平；采用免疫发光夹心法(试剂盒购自上海拜力科技有限公司)检测降钙素原(procalcitonin, PCT)水平；以上所有检测步骤均按照试剂盒指南进行。另一份血液样本用于凝血功能指标的检测，凝血功能指标包括血小板计数(platelet count, PLT)、活化部分凝血酶原时间(activated partial thromboplastin time, APTT)、凝血酶原时间(prothrombin time, PT)，PLT、APTT、PT均采用全自动血液分析仪(贝克曼库尔，型号：LH 750)进行测定。所有患者入院后24小时内均通过APACHEⅡ评分评价疾病严重程度，内容包括急性生理评分、年龄评分和慢性健康评分，总分为71分，分值越高表示病情越严重。

1.3 统计学处理

所有数据均采用SPSS19.0软件进行统计分析，性别比例等计数资料以率(%)的形式表示，采用x^2检验，炎症因子、凝血功能指标及APACHEⅡ评分等计量资料以均值± 标准差($\bar{x}$± s)的形式表示，采用t检验。采用Spearman相关性分析法分析APACHEⅡ评分与CRP、PCT、PLT、APTT、PT的相关性。检验标准设置为α=0.05。

2 结果

2.1 脓毒症组与非脓毒症组患者炎症因子、凝血功能指标及APACHEⅡ评分比较

脓毒症组患者PCT、APTT、PT水平及APACHEⅡ评分均高于非脓毒症组，PLT水平低于非脓毒症组（P<0.05），两组CRP比较差异无统计学意义(P>0.05)。见表1。

表1 脓毒症组与非脓毒症组患者炎症因子、凝血功能指标及APACHEⅡ评分比较($\bar{x}$± s)

Table 1 Comparison of inflammatory factors, coagulation function indexes and APACHE II score between sepsis group and non sepsis group ($\bar{x}$± s)

Groups	n	CRP(mg/L)	PCT(ng/L)	PLT(× 10^9/L)	APTT(s)	PT(s)	APACHEⅡ score (scores)
Sepsis group	150	118.36± 98.05	30.23± 7.85	157.45± 39.25	108.52± 26.24	17.21± 4.69	26.33± 6.31
Non sepsis group	98	117.89± 23.65	6.98± 2.39	209.42± 72.31	59.46± 18.36	9.58± 2.97	19.98± 6.78
t		0.047	28.454	6.513	16.106	14.331	7.522
P		0.963	0.000	0.000	0.000	0.000	0.000

2.2 死亡组和存活组患者炎症因子、凝血功能指标及APACHEⅡ评分比较

死亡组患者PCT、APTT、PT水平及APACHEⅡ评分均高于存活组，PLT水平低于存活组(P<0.05)，两组CRP比较差异无统计学意义(P>0.05)。见表2。

2.3 脓毒症患者APACHEⅡ评分与炎症因子、凝血功能指标的相关性分析

经Spearman相关性分析结果显示，脓毒症患者APACHEⅡ评分与PCT、APTT、PT均呈正相关关系，与PLT呈负相关关系(P<0.05)，与CRP无相关性(P>0.05)。见表3。

表 2 死亡组和存活组患者炎症因子、凝血功能指标及 APACHEⅡ评分比较($\bar{x}\pm$ s)

Table 2 Comparison of inflammatory factors, coagulation function indexes and APACHE II score between death group and survival group ($\bar{x}\pm$ s)

Groups	n	CRP(mg/L)	PCT(ng/L)	PLT(× 109/L)	APTT(s)	PT(s)	APACHEⅡ score (scores)
Death group	49	119.14± 95.12	40.89± 5.13	171.12± 41.03	150.23± 29.03	20.35± 5.12	29.25± 7.91
Survival grotup	101	115.12± 59.36	20.14± 4.05	287.06± 74.31	73.98± 20.78	12.36± 3.15	10.03± 2.65
P		0.317	26.909	12.306	11.661	11.769	22.063
		0.752	0.000	0.000	0.000	0.000	0.000

表 3 脓毒症患者 APACHEⅡ评分与炎症因子、凝血功能指标的相关性分析

Table 3 Correlation analysis of APACHE II score with inflammatory factors and coagulation function indexes in patients with sepsis

Indexes	CRP		PCT		PLT		APTT		PT	
	r	P	r	P	r	P	r	P	r	P
APACHE Ⅱ score	0.158	0.697	0.751	0.000	-0.598	0.004	0.565	0.005	0.426	0.009

3 讨论

随着多发伤的增多和有创操作的发展,脓毒症发病率呈逐渐上升趋势,其已成为威胁人类健康的主要危重疾病之一[12,13]。脓毒症患者病情变化迅速,预后差,因此积极探讨与其预后有关的因素将有利于其病情的控制和预后的改善。既往报道显示[14,15],凝血功能紊乱和炎症反应贯穿了脓毒症的整个发生、发展过程,研究两者相关指标与脓毒症患者预后的关系具有重要的意义。PCT 可以反映全身炎症的活跃程度,CRP 是临床上常用的炎症反应指标,而 PLT、APTT、PT 均是反映机体凝血状态的有效指标,且均具有较强的敏感度[16],APACHEⅡ评分则与急危重患者预后密切相关[17],因此探讨 PCT、PLT、APTT、PT 等与脓毒症患者 APACHEⅡ评分的关系可以有效地诊断患者病情及预后。

本研究结果显示,脓毒症组患者 PCT、APTT、PT 水平及 APACHEⅡ评分均高于非脓毒症组,PLT 低于非脓毒症组($P<0.05$),死亡组患者 PCT、APTT、PT 水平及 APACHEⅡ评分均高于存活组,PLT 低于存活组($P<0.05$),说明脓毒症患者炎症因子水平和凝血功能均存在异常,且随着病情的加重,其炎症指标、凝血功能指标水平也发生相应变化。PCT 是一种糖蛋白,是特异性较高的全身炎症指标,主要产生于肝、肺、肾以及脂肪组织中,在正常人机体中,其水平较低。当机体发生感染、创伤时,其水平迅速升高,因此其可以作为脓毒症患者病情判定的特异性指标[18,19]。PLT 是只存在于哺乳动物中的最小的血细胞,是血液的有形成分之一,当机体发生创伤时,PLT 被活化并迅速黏附于创伤处,参与了凝血功能的启动,同时其在止血、炎症反应、伤口愈合等生理病理过程中也起到重要作用,有研究显示,其水平升高越缓慢,说明预后越差[20,21]。APTT 是内源性凝血途径较敏感的指标,处于感染状态时的患者 APTT 延长,从而使患者发生凝血微循环障碍,导致患者预后较差[22,23]。PT 是外源性凝血途径较敏感和最常用的指标,可反映凝血因子Ⅱ、Ⅴ、Ⅶ、Ⅹ和Ⅰ的活性,当以上凝血因子缺乏时,导致其数值升高[24,25]。脓毒症组和非脓毒症组、死亡组和存活组 CRP 水平比较差异均无统计学意义($P>0.05$),说明 CRP 虽然是反映炎症的敏感指标,但在脓毒症患者中缺乏特异性。分析原因可能与脓毒症患者病情复杂有关,单独的 CRP 检测对病原体感染与创伤等非感染性疾病缺乏特异性,因此临床上需与其他指标联合使用共同判定脓毒症病情和预后[26-28]。Spearman 相关性分析结果显示,脓毒症患者 APACHEⅡ评分与 PCT、APTT、PT 呈正相关关系,与 PLT 呈负相关关系($P<0.05$),与 CRP 无相关性($P>0.05$)。这也再次证实脓毒症患者炎症反应、凝血功能与 APACHEⅡ评分和预后存在密不可分的关系。APACHEⅡ评分能实地反映出患者的病情严重程度,并与预后密切相关,借助 PCT、APTT、PT、PLT 水平与 APACHEⅡ评分的关系,可以很好地反映出脓毒症患者中炎症反应、凝血功能的具体情况,从而可以通过治疗控制以上各指标水平的变化,进而改善患者预后[29,30]。

综上所述,脓毒症患者炎症因子及凝血功能指标水平异常,且 PCT、APTT、PT 与 APACHEⅡ评分呈正相关关系,PLT 与 APACHEⅡ评分呈负相关关系,临床可通过调节 PCT、APTT、PT、PLT 水平以控制患者病情并改善预后。

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