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PCT 与 IL-6 联合检测鉴别诊断脓毒性和非脓毒性全身炎症反应综合征的临床价值

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摘要 目的：探讨降钙素原(PCT)与白细胞介素 -6(IL-6)联合检测鉴别诊断 ICU 患者脓毒性和非脓毒性全身炎症反应综合征(SIRS)的临床价值。**方法：**选择 2013 年 ~2016 年入住我院 ICU 的 100 例患者，包括 61 例非脓毒性 SIRS 患者与 39 例脓毒症患者，同时选择同期 50 例健康者作对照，分别设为非脓毒性组、脓毒血症组及对照组，采用电化学发光分析法检测三组血清 PCT 与 IL-6 水平，并以 PCT 为 2 μg/L 和 IL-6 为 50 ng/L 为临界值来鉴别非感染性 SIRS 和脓毒血症，评价联合检测的临床诊断价值。结**果：**非脓毒性组 PCT 与 IL-6 最大值分别为 0.91± 0.54μg/L、62.77± 11.75 ng/L，脓毒血症组为 24.49± 5.00 μg/L、1542.69± 361.66 ng/L，对照组为 0.08± 0.06 μg/L、3.68± 1.11 ng/L，非脓毒性组与脓毒血症组 PCT 与 IL-6 最大值均显著高于对照组(P＜0.05)；与非脓毒性组比较，脓毒血症组 PCT 与 IL-6 均显著升高 (P＜0.05)。非脓毒性组 PCT＞2 μg/L、IL-6＞50 ng/L 的占比分别为 21.31%、65.57%，脓毒血症组为 92.31%、87.18%，脓毒血症组 PCT＞2 μg/L、IL-6＞50 ng/L 的占比均显著提高于非脓毒性组(P＜0.05)。PCT 的阳性预期值、灵敏度、特异度均显著高于 IL-6，而联合检测的阳性预期值、特异度显著高于 IL-6 及 PCT，联合检测的灵敏度显著高于 IL-6，P 均 <0.05。**结论：**PCT 与 IL-6 联合检测有助于脓毒性和非脓毒性 SIRS 的鉴别诊断。

关键词：降钙素原；白细胞介素 -6；全身炎症反应综合征；脓毒症；鉴别诊断

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The Clinical Value of Combined Detection of PCT and IL-6 in the Differential Diagnosis Septic and Non-septic SIRS in ICU

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ABSTRACT Objective: To explore the value of combined detection of PCT and IL-6 in differential diagnosis SIRSin ICU patients. **Methods:** 100 patients with ICU admitted to our hospital from 2013 to 2016 were choosen, including 61 cases with non septic SIRS and 39 cases with sepsis, and 50 healthy persons over the same period were selected as control, and they were divided into non-septic group, sepsis group and control group. The levels of serum PCT and IL-6 were detected by electrochemiluminescence assay, and took PCT of 2 g/L and IL-6 of 50 ng/L for the critical value to identify non infectious SIRS and sepsis, to evaluate the clinical diagnostic value of combined detection. **Results:** The maximum values of PCT and IL-6in the non-septic group respectively were 0.91± 0.54 μg/L and 62.77± 11.75 ng/L, in the septic group respectively were 24.49± 5.00 μg/L and 1542.69± 361.66 ng/L, in the control group respectively were 0.08± 0.06 μg/L and 3.68± 1.11 ng/L, the maximum values of PCT and IL-6 in the non-sepsis group and the sepsis group were significantly higher than control group (P<0.05). Compared with the non-septic group, the maximum valuesin sepsis group were significantly increased (P<0.05). The proportions of PCT＞2 g/L and IL-6＜50ng/L in the non-septic group respectively were 21.31% and 65.57%, in the septic group respectively were 92.31% and 87.18%, the proportions of PCT＞2 g/L, IL-6＜50 ng/L in the sepsis groupwere significantly higher chan those in the non-septic group (P<0.05). The positive predictive values, sensitivity and specificity of PCT were higher than IL-6, the positive value, specificity of combined detection was higher than IL-6 and PCT, while the sensitivity of combined detection was higher than IL-6, P<0.05. **Conclusions:** Combined detection of PCT and IL-6 is helpful for differential diagnosis of sepsis and non-septic SIRS.

Key words: Procalcitonin; Interleukin-6; Systemic inflammatory response syndrome; Sepsis; Differential diagnosis

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前言

全身炎症反应综合征(SIRS)和脓毒症是同一病理过程的不同阶段[1]，常发生于 ICU 患者中。一般认为合并有明确原发

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感染灶症状及体征的 SIRS 即为脓毒症，但 2001 年 " 国际脓毒症专题讨论会 " 提出 " 感染 +SIRS 表现 " 的诊断标准太过敏感，对于有确切感染或可疑感染的情况应结合患者的全身状况、炎症指标、血流动力学指标及器官功能障碍参数等综合的评估与诊断[2-4]，以合理有效的干预治疗。尽管目前出现的生物标记物已有不少，但在 ICU 患者中的应用未被广泛接受。血清降钙素原(PCT)＞2ng/L 与脓毒血症的发生密切相关[5]。正常情况下，血清白细胞介素 -6(IL-6)＜7.0 ng/L，但在炎症急性期，肿瘤坏死因子 -α(TNF-α)可刺激 IL-6 的生成，引起血清 IL-6 水平升高，在脓毒血症患者中甚至可高达 500 ng/L 以上，但用于非感染性 SIRS 与脓毒血症鉴别诊断的特异性较差[6,7]。为了对脓毒性和非脓毒性 SIRS 的鉴别诊断提供更多依据，本研究主要探讨了 PCT 与 IL-6 联合检测鉴别诊断 ICU 患者脓毒性和非脓毒性 SIRS 的临床价值。

1 对象与方法

1.1 研究对象

选择 2013 年 ~2016 年我院入住 ICU＞24 h 的患者 100 例，其中非脓毒性 SIRS 患者 61 例，男 33 例，女 28 例，年龄 27~71 岁，平均年龄(57.3± 6.1)岁；脓毒症患者 39 例，男 24 例，女 15 例，年龄 30~70 岁，平均年龄(60.4± 8.4)岁；并选择同期 50 例健康人作为对照组，男 27 例，女 23 例，年龄 25~68 岁，平均年龄 (51.4± 7.4) 岁。三组一般资料对比差异无统计学意义(P＞0.05)。

1.2 诊断标准

① 低温(36℃)或发热(＞38℃)；② 呼吸频率过快(＞20 次 /min)，$PaCO_2$＜32 mmHg；③ 心率增快(＞90 次 /min)；④ WBC 增多(＞12.0× 10^9/L)或过少＜4.0× 10^9/L)或未成熟粒细胞＞10%，SIRS 符合至少两点[8]。脓毒血症为 SIRS 的基础上根据培养结果证实合并有细菌感染。

1.3 研究方法

患者入 ICU 24 h 内及健康者于健康体检时抽取静脉血 4 mL，离心 10 min，速率 4000 r/min，取上清液待检。采用电化学发光分析法检测 PCT 和 IL-6，试剂盒均购于德国 BRAHMS 公司，操作严格按照说明书进行。以 PCT 为 2 μg/L 和 IL-6 为 50 ng/L 为临界值来鉴别非感染性 SIRS 和脓毒血症。以入 ICU 24 h 内的 PCT 与 IL-6 的最大值计算阳性预期值(全身性感染例数 / 检查阳性例数)、阴性预期值(非感染性 SIRS 例数 / 检查阴性例数)、灵敏度(全身感染例数 / 全身感染例数 + 检查阴性例数)、特异度(非感染性 SIRS 例数 / 非感染 SIRS+ 检查阴性例数)。

1.4 统计学方法

采用 SPSS18.0 统计，x^2 检验分析计数资料；t 检验分析计量资料，以 P<0.05 为差异有统计学意义。

2 结果

2.1 三组入 ICU 24 h 内 PCT 与 IL-6 的最大值比较

脓毒性和非脓毒性 SIRS 患者的 PCT 及 IL-6 最大值显著高于对照组 (P＜0.05)；且脓毒血症组显著高于非脓毒血症组(P＜0.05)，见表 1。

表 1 三组入 ICU 24 h 内 PCT 及 IL-6 的最大比较

Table 1 PCT and IL-6 maximum comparison in three groups in ICU for 24 h

Groups	PCT(μg/L)	IL-6(ng/L)
No septic group(n=61)	0.91± 0.54[a]	62.77± 11.75[a]
Sepsis group(n=39)	24.49± 5.00[a,b]	1542.69± 361.66[a,b]
Control group(n=50)	0.08± 0.06	3.68± 1.11

Note: Compared with control group, [a] P＜0.05; Compared with no septic group, [b] P＜0.05.

2.2 两组入 ICU 24 h 内 PCT 与 IL-6 水平高于临界值的占比

脓毒血症组 PCT＞2 μg/L、IL-6＞50 ng/L 的占比均显著高于非脓毒性组(P＜0.05)。

表 2 两组入 ICU 24 h 内 PCT 与 IL-6 水平高于临界值的占比(%)

Table 2 The percentage of PCT and IL-6 level higher than critical value in ICU of two groups for 24 h(%)

Groups	PCT＞2 μg/L	IL-6＞50 ng/L
No septic group(n=61)	21.31(13/61)	65.57(40/60)
Septic group(n=39)	92.31(36/39)[a]	87.18(34/39)[a]

Note: Compared with no septic group, [a] P＜0.05.

2.3 联合检测 PCT 与 IL-6 水平对脓毒性 SIRS 的临床诊断价值

PCT 的阳性预期值、灵敏度、特异度均显著高于 IL-6，而联合检测的阳性预期值、特异度显著高于 IL-6 及 PCT，联合检测的灵敏度显著高于 IL-6(P 均 <0.05)，见表 3。

表 3 PCT 与 IL-6 最大值的阳性预期值、阴性预期值(%)

Table 3 The positive expectations and negative expectations of PCT and IL-6 maximum value(%)

Indexs	Positive expectations	Negative expectations	Sensitivity	Specificity
PCT	73.46[a]	91.31	89.42[a]	77.47[a]
IL-6	45.95	92.42	77.80	61.65
PCT combined with IL-6	84.55[a,b]	92.03	91.39[a]	85.63[a,b]

Note: Compared with IL-6, [a] P＜0.05; compared with PCT, [b] P＜0.05.

3 讨论

SIRS 通常是由于感染或非感染因素使机体不受控制地自我持续放大和自我破坏而引起的全身性炎症反应 [9]，ICU 患者由于机体的代偿性抗炎反应能力减弱，代谢功能改变，因而十分容易发生 SIRS。脓毒症是由感染引起的 SIRS，在 ICU 患者中的发生率约 42%，死亡率约 35%~75%[10]。正确鉴别诊断出脓毒症有利于临床及时采取相应的干预措施，减少死亡率。传统的临床指标如体温升高、白细胞计数增加、C 反应蛋白升高等虽然可用于诊断感染，但受限因素较多，如体温的改变可由多

种因素引起;全身性感染时可能引起白细胞增多也可能导致白细胞减少;C 反应蛋白通常在炎症出现后 8~12 h 才可在血中检测到。因此这些指标或多或少都会影响诊断的准确性[11-14]。近些年,越来越趋向于认同血中某些炎症介质和中性粒细胞可能是 SIRS 的特征性标志物[15]。

PCT 是最近广被关注的一个感染标志物,它是上世纪晚期被发现的一个无激素活性的降钙素前肽物质,一般不会释放入血,所以在健康机体中的检测水平很低,此时主要由甲状腺 C 细胞产生,然而对于细菌感染的机体,肝、肾上腺、胰腺、脑等多个其它组织也会分泌 PCT,所以血中 PCT 的含量会急剧上升,且感染越严重,上升的幅度越明显[16-19]。外国学者 Assicot 等首先报道了 PCT 在细菌感染患儿血中的浓度异常增高,之后亦有研究发现 PCT 能够帮助急性胰腺炎患者鉴别感染和非感染性炎症[20,21]。Uchida 等[22]研究认为 PCT 可作为细菌感染的特异性指标。PCT 作为急性期反应蛋白,具有两个明显的优点:① 在严重全身性细菌感染患者中,其水平开始变化的时间早(2~3 h 内),并在 24~48 h 达峰值,因而十分利于疾病的早期诊断;② 对细菌感染与非细菌感染有良好的敏感度和特异度,临床鉴别诊断价值高[23-26]。目前尚不知 PCT 鉴别诊断感染与非感染性 SIRS 的最佳临界值,按多数学者的看法,本研究将临界值取在 2 μg/L,从而获知脓毒血症患者入 ICU24 h 内 PCT>2 μg/L 的占比为 92.31%,阳性预期值为 73.46%,阴性预期值为 95.31%,提示当 PCT<2 μg/L 大部分可排除脓毒症。虽然一些非感染因素也可能引起 PCT 的生成和释放增多,但多个研究认为非感染性 SIRS 和全身性感染患者血清 PCT 水平间的差异仍是十分明显的,提示 PCT 能够很好地鉴别脓毒症和非感染性 SIRS[27-30]。

IL-6 能够通过作用于多种免疫细胞参与炎症反应,是感染后炎性反应中释放较早的介质,在水平持续上升的状态下,发生多脏器功能不全和死亡的风险增高[31]。Pang X H 等[32]研究显示,脓毒症患者血清 IL-6 水平远远高于非感染性 SIRS 患者。Gökce M I 等[33]研究认为用 PCT 联合 IL-6 构成感染评分可能有利于更好地提高对脓毒症的鉴别能力。目前常以 50 ng/L 作为 IL-6 鉴别诊断感染与非感染性 SIRS 的临界值,本研究中脓毒血症患者 IL-6>50 ng/L 的占比为 87.18%,阳性预期值为 45.95%,阴性预期值为 92.42%,灵敏度为 77.80%,特异度为 61.65%。IL-6 的阳性预期值较低,可能是脓毒血症患者入院后,随着干预治疗,IL-6 水平迅速降低,从而出现假阴性结果。联合检测 PCT 与 IL-6 的阳性预期值能够达到 86.89%,阴性预期值为 92.03%,灵敏度为 91.39%,特异度为 85.63%。PCT 的阳性预期值、灵敏度、特异度均显著高于 IL-6,而联合检测的阳性预期值、特异度显著高于 IL-6 及 PCT,联合检测的灵敏度显著高于IL-6,P 均 <0.05。比较之下,联合检测更有利于辅助诊断脓毒血症。

综上所述,PCT 与 IL-6 联合检测有助于脓毒性和非脓毒性 SIRS 的鉴别诊断,但在临床实际中还应结合其它异常指标及具体病情变化以提高诊断的准确性。

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