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血清 PCT、CRP 及 IL-6 联合检测诊断细菌性血流感染的临床价值分析*

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摘要 目的:探讨血清降钙素原(PCT)、C 反应蛋白(CRP)及白介素-6(IL-6)联合检测诊断细菌性血流感染(BSI)的临床价值。**方法:**选取我院 2015 年 8 月到 2016 年 10 月收治的疑似细菌性 BSI 患者 216 例,入院后均送检血培养,根据培养结果将其分为阳性组(102 例)和阴性组(114 例)。统计细菌性 BSI 阳性率、革兰阳性菌感染率和革兰阴性菌感染率;检测血清 PCT、CRP、IL-6 水平,并比较两组患者的差异,同时绘制 ROC 曲线并计算出各指标及联合检测的灵敏度、特异度、阳性预测值、阴性预测值及约登指数值。**结果:**所有疑似 BSI 患者的细菌阳性检出率为 47.22%,革兰阳性菌感染率与革兰阴性菌感染率对比无差异($P>0.05$);阳性组的血清 PCT、CRP、IL-6 水平均明显高于阴性组($P<0.05$);血清 IL-6 的 AUC 明显大于 PCT 和 CRP($P<0.05$);PCT、CRP 及 IL-6 联合检测的灵敏度、特异度、阳性预测值、阴性预测值及约登指数均明显高于单项检测($P<0.05$)。**结论:**血清 PCT、CRP 及 IL-6 对于 BSI 均有着一定诊断价值,而各指标联合检测诊断 BSI 的临床价值更高。

关键词:PCT;CRP;IL-6;BSI;诊断价值

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Analysis of the Clinical Value of Combined Detection of Serum PCT, CRP and IL-6 for the Diagnosis of Bacterial Bloodstream Infection*

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ABSTRACT Objective: To study the clinical value of combined detection of serum calcitonin (PCT), c-reactive protein (CRP) and interleukin-6 (il-6) for the diagnosis of bacterial bloodstream infection (BSI). **Methods:** From August 2015 to October 2015, 216 cases of patients with suspected bacterial BSI were selected for this study, blood culture were performed after admission, according to the result of blood culture, the patients were divided into the positive group (102 cases) and the negative group (114 cases). The bacterial BSI positive rate, gram-positive bacteria infection and gram-negative bacteria infection rate were calculated. The serum PCT and CRP, IL - 6 levels were compared between the two groups of patients. The ROC curve and the sensitivity, specific, positive predictive value, negative predictive value were drawn and compared. **Results:** The positive detection rate of all suspected BSI patients was 47.22%, among which there was no difference in the infection rate of gram-positive bacteria ($P>0.05$). The serum PCT, CRP and il-6 levels of positive groups were significantly higher than those of the negative group ($P<0.05$). The AUC of il-6 was significantly larger than PCT and CRP($P<0.05$). The sensitivity, specificity, positive predictive value, negative predictive value and Jordan index of PCT, CRP and il-6 were significantly higher than those of the single test ($P<0.05$). **Conclusion:** Serum PCT, CRP and IL-6 had some diagnostic value for the diagnosis of BSI, the combined detection can obviously improve the diagnostic value for BSI.

Key words: PCT; CRP; IL-6; BSI; Diagnostic value

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前言

血流感染(Bloodstream Infection, BSI)是一种机体血液由于金黄色葡萄球菌、肺炎链球菌、大肠埃希菌、凝固酶阴性葡萄球菌等入侵引发的全身性感染疾病,常发生于社区或医院等公共场所,寒战、发热、呼吸急促、皮疹、器官肿大等为该类疾病的主要临床症状^[1,2],严重者可引起休克、多器官衰竭、甚至死亡的不

良后果。因此,及时、有效地诊断 BSI 对确保患者生活质量和保证生命安全均具有重要的临床意义。

目前,临床上多采用血培养诊断 BSI,但该方式具有检测周期长、影响因素多、阳性率偏低等缺点^[3-5],易导致患者错过最佳治疗时机,增加治疗难度。近年来,有研究表明降钙素(PCT)作为一种免疫调节蛋白在机体正常情况下并无激活性,但机体一旦受到细菌感染,PCT 的含量便会显著增加^[6,7]。因此,PCT

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可作为诊断 BSI 的临床检测指标。白介素 -6(IL-6)是主要参与机体炎症反应的细胞因子,血流被细菌感染后,其水平变化可明显反映病情的严重程度。C 反应蛋白(CRP)是一种由肝细胞合成的炎症标志物之一。上述各指标在单独检测时,存在特异度较低的缺点^[8-10]。为提高细菌性 BSI 的临床诊断率,本研究主要探讨了血清 PCT、CRP 及 IL-6 联合检测诊断 BSI 的临床价值,现将结果报道如下:

1 材料与方法

1.1 一般资料

选取我院 2015 年 8 月到 2016 年 10 月收治的疑似细菌性 BSI 患者 216 例,入院后均送检血培养,根据培养结果将其分为阳性组(102 例)和阴性组(114 例)。阳性组男性患者有 65 例、女性患者有 37 例,年龄在 18-73 岁,平均年龄计算为(52.2±7.8)岁,阴性组男性患者有 69 例、女性患者有 33 例,年龄在 20-74 岁,平均年龄计算为(53.1±6.5)岁,统计学比较上述基础资料,两组间无差异($P>0.05$)。本研究得到了我院医学伦理委员会的批准,并获得患者的知情同意。

1.2 纳入及排除标准

纳入标准:①临床表现符合细菌性血流感染(BSI)指征者(体温高于 38℃或低于 36℃并伴有寒战,合并白细胞计数在 10^{10} 以上、昏迷或皮肤黏膜出血之一者);②临床资料完整者;③患者对本研究知情且已签署知情同意书。

排除标准:①患有血液疾病者;②依从性较差、不能完全配合本次研究者;③患有严重免疫系统疾病者;④研究前期服用过抗菌药物者;⑤患有严重精神类疾病者;⑥患有恶性肿瘤者。

1.3 方法

使用 BACTEC9050 全自动血培养仪(美国 BD 公司)和 VITEKI2_compact 全自动微生物分析仪(法国生物梅里埃公司)进行细菌培养和鉴定。所有患者于晨起空腹抽取静脉血 2 mL,在 37℃水浴箱中放置 30 min,于转速为 3000 r/min 的条件下离心 5 min,分离出血清备用,采用罗氏 e_601 化学发光免疫分析

仪(瑞士罗氏公司)检测患者的 IL-6 水平,当 IL-6 的含量 >2 ng/L 时,即可判断为阳性。血清 CRP 使用免疫比浊法进行检测,经国赛 Astep 蛋白分析仪(深圳市国赛生物技术有限公司),当 CRP 的含量 >5.0 mg/L 时,即可判断为阳性。PCT 检测经试剂及其配套的比色仪(罗氏 e_411,瑞士罗氏公司)采用上转发光法进行测定,当 PCT 的含量 >0.5 ng/mL 时,即可判断为阳性。所有操作均严格根据试剂盒要求进行。

1.4 观察指标

1.4.1 血培养结果 根据血培养结果统计患者的阳性检出率、革兰阳性菌感染率和革兰阴性菌感染率。

1.4.2 血清 PCT、CRP 和 IL-6 水平对比 检测并比较两组患者的血清 PCT、CRP 和 IL-6 水平。

1.4.3 不良反应的发生情况 绘制 ROC 曲线,并计算各指标的 ROC 曲线下面积 AUC。

1.4.4 各指标诊断 BSI 的价值评价 计算并比较两组患者的血清 PCT、CRP、IL-6 各指标单项检测和联合检测的灵敏度、特异度、阳性预测值、阴性预测值及约登指数。

1.5 统计学方法

采用 SPSS19.0 统计学软件,计数资料使用百分比表示,经卡方检验;计量资料使用($\bar{x}\pm s$)表示,经 t 检验或秩和检验;各指标的价值评价使用 ROC 曲线下面积 AUC 进行判断,经 Z 检验; $P<0.05$ 即存在统计学差异。

2 结果

2.1 血培养结果

血培养结果显示:216 例疑似细菌性 BSI 患者的细菌阳性检出率为 47.22%(102/216);其中,革兰阳性菌感染率为 52.94%(54/102),革兰阴性菌感染率为 47.06%(48/102),统计学对比无差异($P>0.05$)。

2.2 两组患者的血清 PCT、CRP 和 IL-6 水平比较

阳性组的血清 PCT、CRP、IL-6 水平均明显高于阴性组($P<0.05$),如表 1。

表 1 两组血清 PCT、CRP、IL-6 水平比较($\bar{x}\pm s$)

Table 1 Comparison of the serum PCT, CRP, IL-6 levels between the two groups($\bar{x}\pm s$)

Groups	n	PCT(ng/L)	CRP(mg/L)	IL-6(ng/L)
Positive group	102	9.31± 2.10*	112.97± 31.05*	162.27± 42.51*
Negative group	114	3.21± 0.84	74.69± 20.16	5.17± 0.34

Note: compared with the Negative group, $*P<0.05$.

2.3 血清 PCT、CRP 和 IL-6 水平诊断 BSI 的 ROC 曲线分析

血清 PCT、CRP、IL-6 水平诊断 BSI 的 AUC 分别为 0.732、0.695 和 0.798。其中,IL-6 的 AUC 明显大于 PCT 和 CRP ($P<0.05$),如图 1。

2.4 各指标诊断 BSI 的价值评价

血清 PCT、CRP 及 IL-6 联合检测的灵敏度、特异度、阳性预测值、阴性预测值及约登指数均明显高于单项检测($P<0.05$),如表 2。

3 讨论

BSI 是一种由于病原微生物侵入机体血液循环进而引发的严重全身性感染疾病,具有发病率高、病情严重、死亡率高的特点^[11,12],发病因素主要包括年龄、性别、疾病种类、免疫状态等机体因素和创伤、手术、血液透析、气管插管等医院因素。患者的临床症状主要包括持续高热、骤发寒战、呼吸急促、心率加快等,若不及时给予有效诊断和治疗,易导致患者出现脓毒血症、感染性休克、全身性器官功能不全等不良后果^[13-15],严重威胁着患者的生命安全。近年来,随着介入治疗、透析治疗、抗生素和激素类药物的大量应用,BSI 的发病率呈逐年上升趋势^[16-18],血培养为临床上诊断 BSI 的金标准。全自动血培养仪虽可有效降

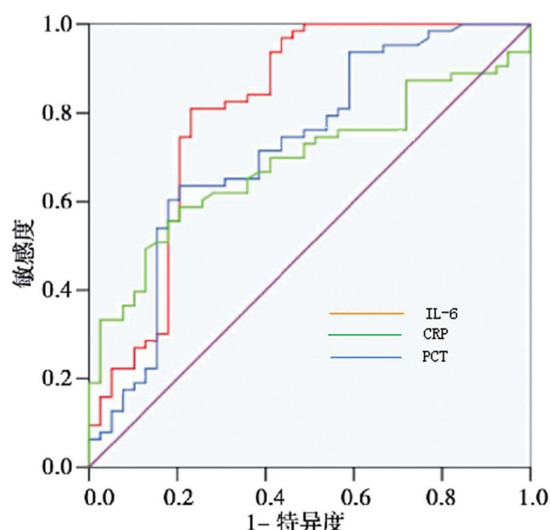


图1 血清PCT、CRP、IL-6诊断BSI的ROC曲线

Fig.1 ROC curve of serum PCT, CRP and IL-6 for the diagnosis of BSI

表2 各指标诊断BSI的价值评价

Table 2 Evaluation of the diagnostic value of each index for BSI

Test	PCT	CRP	IL-6	PCT+CRP+IL-6
Sensitivity(%)	78.31	87.50	89.53	94.79
Specificity(%)	72.18	76.47	80.47	92.37
Positive prediction(%)	63.73	68.63	75.49	89.22
Negative prediction(%)	84.21	91.22	90.35	95.61
Youden index	0.5049	0.6397	0.7000	0.8716

低传统手工操作的污染风险、提高阳性检出率^[19],但检测周期尚未明显缩短,对于具有发病急、病情凶险特点的BSI还存在一定的使用弊端^[20]。为提高BSI患者的治疗效率,降低患者的死亡率,积极寻找快速、有效的检测指标对及时、准确地诊断BSI具有重要的临床意义。

BSI的病原菌主要分为革兰阳性菌、革兰阴性菌和真菌。其中,革兰阳性菌感染主要以金黄色葡萄球菌、凝固酶阴性葡萄球菌、肠球菌为主^[21,22],发病原因主要为外科伤口、留置导管、人工装置、生殖系统感染等^[23,24]。本研究血培养结果显示所有疑似BSI患者的细菌阳性检出率为47.22%,革兰阳性菌感染率与革兰阴性菌感染率对比无差异。近年来,为提高BSI的诊断效率,人们不断在寻找新的细菌性血流感染标记物,PCT、CRP和细胞因子等作为新的标记物正逐步被人们关注。细胞因子是一种信号小分子蛋白,主要作用于机体的防御系统和损伤愈合过程中,具有调节固有免疫和适应性免疫、血细胞生成、细胞生长、APSC多能细胞以及损伤组织修复等多种功能。其中,单核细胞因子IL-6作为参与全身炎症反应综合征的重要炎症介质之一。研究表明机体产生感染时,血液中该指标的浓度会显著增高,可作为评估BSI的潜在指标^[25,26]。CRP是一种广泛存在于人体体液中由肝细胞合成的急性时相反应蛋白,该蛋白是急性时相反应的一个极灵敏的炎性指标。在机体受到细菌感染的4-6h后,CRP的浓度便开始升高,可于36-50h达到最大值,通过检测浓度变化,可明显判断机体的炎症程度^[27-29]。PCT是一种由甲状腺C细胞生成的降钙素前体,是一种无激素活性的糖蛋

白,在健康机体血液中含量极低,一旦机体出现细菌感染,3-4h便可被检测到含量明显升高,且稳定性较好^[30,31]。

本研究结果显示阳性组的血清PCT、CRP、IL-6水平均明显高于阴性组,血清IL-6的AUC明显大于PCT和CRP,血清PCT、CRP及IL-6联合检测的灵敏度、特异度、阳性预测值、阴性预测值及约登指数均明显高于单项检测。血清PCT、CRP与IL-6均属于非特异性感染指标,在单独使用时,易受到创伤、胰腺炎、手术等非感染条件的影响,特异度较低,将三种指标联合应用于细菌性BSI的检测过程中,可有效提高诊断准确率。

综上所述,血清PCT、CRP及IL-6对于BSI均有着一定诊断价值,而各指标联合检测诊断BSI的临床价值更高。

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