

·论著·

血清 C 反应蛋白、白介素-6 和降钙素原 对小儿急性复杂性阑尾炎的诊断价值研究



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【摘要】目的 探索血清 C 反应蛋白(C-reactive protein, CRP)、白介素-6(interleukin 6, IL-6)和降钙素原(procalcitonin, PCT)水平对小儿急性复杂性阑尾炎的诊断价值。**方法** 以 2016 年 1 月至 2017 年 5 月包头市第四医院小儿外科收治并进行手术治疗的 96 例急性阑尾炎患者为研究对象,分为两组:单纯性阑尾炎组 30 例,复杂性阑尾炎(包括化脓性阑尾炎及坏疽性阑尾炎)组 66 例,两组患者年龄、性别、体重差异均无统计学意义($P > 0.05$),检测两组患者术前血清 CRP、IL-6、和 PCT 浓度,并绘制 ROC 曲线分析 CRP、IL-6 和 PCT 对小儿急性复杂性阑尾炎的诊断价值。**结果** 复杂性阑尾炎组 CRP、IL-6 及 PCT 水平均显著高于单纯性阑尾炎组($P < 0.05$);以手术后病理结果为金标准,CRP、PCT、IL-6 及三者联合检验 ROC 曲线下面积分别为 0.906(95% 置信区间:0.829~0.956),0.953(95% 置信区间:0.889~0.986),0.765(95% 置信区间:0.668~0.846),0.973(95% 置信区间:0.971~0.995)。曲线下面积值由大到小排序:PCT+CRP+IL-6 > PCT > CRP > IL-6,通过两两比较发现,联合检验曲线下面积与 CRP、IL-6 单独检验曲线下面积比较差异具有统计学意义($Z = 2.932, P = 0.003; Z = 3.854, P = 0.0001$);联合检验曲线下面积与 PCT 单独检验曲线下面积比较差异无统计学意义($Z = 1.861, P = 0.063$);CRP 与 PCT 单独检验曲线下面积差异无统计学意义($Z = 1.668, P = 0.095$),IL-6 单独检验与 CRP 单独检验、PCT 单独检验比较曲线下面积差异具有统计学意义($Z = 2.312, P = 0.021; Z = 3.371, P = 0.001$);得到最佳临界点分别为 11.47(95% 置信区间:11.42~14.48)mg/L,0.87(95% 置信区间:0.63~0.98)ng/L,88.60(95% 置信区间:87.12~170.83)pg/mL。**结论** CRP、IL-6 和 PCT 有助于临床医师对阑尾炎严重程度进行早期判断,从而早期争取家长配合,尽早手术治疗并减少并发症的发生。

【关键词】 阑尾炎/诊断; 阑尾炎/免疫学; C 反应蛋白; 白介素-6; 降钙素原; 儿童

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Applicable value of serum c-reactive protein, interleukin 6 and procalcitonin in acute complex pediatric appendicitis. Xu Yongkang¹, Yun Ye¹, Zhao Yongxiang¹, Jiang Haishan¹, Zhao Jungang², Zhang Jianguo¹, Wu Xiangming¹. 1. Department of Pediatric Surgery, Fourth Municipal Hospital, Baotou 014000, China; 2. Affiliated Children's Hospital, Soochow University, Suzhou 215003, China. Corresponding author: Zhao Yongxiang, Email:121418388@qq.com; Jiang Haishan, Email:584955375@qq.com

【Abstract】Objective To explore the correlation between serum C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT) and acute complex appendicitis in children and examine their diagnostic values.
Methods A total of 96 hospitalized children with acute appendicitis underwent operations from 2016 to 2017. They were divided into two groups of simple appendicitis ($n = 30$, A1) and complex suppurative/gangrenous appendicitis ($n = 60$, A2). The preoperative serum concentrations of CRP, IL-6, and PCT were measured and compared for two groups. The receiver operating characteristic (ROC) curves were plotted for analyzing the diagnostic values of CRP, IL-6 and PCT in children with acute complex appendicitis. **Results** No statistical significance existed in age, gender or weight between two groups ($P > 0.05$). The levels of CRP, IL-6 and PCT

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were significantly higher in group A2 than those in group A1 ($P < 0.05$). ROC curve was plotted according to the postoperative pathological results for analyzing the diagnostic efficiency of CRP, PCT and IL-6 for complicated appendicitis. AUC of CRP, PCT, IL-6 and their combined test were 0.906 (95% CI: 0.829 – 0.956), 0.953 (95% CI: 0.889 – 0.986), 0.765 (95% CI: 0.668 – 0.846) and 0.973 (95% CI: 0.971 – 0.995) respectively. Value of AUC was PCT + CRP + IL-6 > PCT > CRP > IL-6. AUC of combined test was statistically different from that of CRP/IL-6 ($Z = 2.932, P = 0.003$; $Z = 3.854, P = 0.0001$). No statistical difference existed between AUC of combined test and that of PCT ($Z = 1.861, P = 0.063$) or between AUC of CRP and that of PCT ($Z = 1.668, P = 0.095$); and statistical difference existed between AUC of IL-6 and that of CRP/PCT ($Z = 2.312, P = 0.021$; $Z = 3.371, P = 0.001$). The obtained optimal critical points were 11.47 (95% CI: 11.42 – 14.48) mg/L, 0.87 (95% CI: 0.63 – 0.98) ng/L and 88.60 (95% CI: 87.12 – 170.83) pg/ml respectively.

Conclusion Clinicians can judge the severity of appendicitis during an early stage by CRP, IL-6 and PCT so as to win the cooperation of parents, perform operations as early as possible and reduce the occurrence of complications.

【Key words】 Appendicitis/DI; Appendicitis/IM; C-Reactive Protein; Interleukin 6; Procalcitonin; Child

急性阑尾炎是儿童常见的急腹症之一。小儿阑尾壁相对较薄,炎症侵犯容易造成穿孔,较成人炎症穿孔率高,易引起腹膜炎,迅速导致严重的全身中毒症状,甚至危及生命^[1]。C反应蛋白(C-reactive protein, CRP)、白介素-6(interleukin 6, IL-6)和降钙素原(procalcitonin, PCT)均属于机体炎症标志物,目前研究表明,上述指标在多种感染性疾病的诊断中均具有一定意义。CRP不受患者免疫功能、肝肾功能等多种因素的影响,故其灵敏度和稳定性均较高^[2-5]。IL-6是参与脓毒症及脓毒血症发生过程的一种炎性介质,在机体发生炎症2~3 h后即可达到血浓度高峰。PCT作为人体重要的感染标记物,当细菌感染导致系统发生炎症反应时,血清PCT浓度可迅速升高^[6-8]。本研究旨在探讨CRP、IL-6和PCT与小儿急性复杂性阑尾炎的关系,并量化其诊断价值。

材料与方法

一、一般资料

本研究经医院伦理委员会审批,研究对象及监护人皆知情并签署同意书。收集2016年1月至

2017年5月包头市第四医院小儿外科收治并接受手术治疗的小儿急性阑尾炎患者,术式均为腹腔镜下阑尾切除术。排除标准:①心肺功能不全、肝肾功能异常、自身免疫性疾病或罹患肿瘤;②近期接受过手术或发生重大创伤;③近期使用过抗生素、糖皮质激素或免疫抑制剂。最终纳入符合条件的患者96例,年龄2~12岁,平均年龄5.5岁,其中男60例,女36例。根据本院病理科对术后标本做出的最终病理诊断,将患者按照病理类型分为两组:单纯性阑尾炎组30例,复杂性阑尾炎组66例。两组患者年龄、性别、体重差异无统计学意义($P > 0.05$),具有可比性,见表1。

二、研究方法

(一) 血样采集

所有患者于入院当天术前2 h采集外周静脉血3 mL于干燥管中,2 000 r/min 离心15 min,样品置于-70°C冰箱待测。

(二) 分析方法

CRP采用全自动微量蛋白分析仪及其配套试剂进行检测,IL-6、PCT检测分别采用相应的酶联免疫吸附法,试剂盒购自武汉博士德生物工程公司,检测时严格按照试剂说明书操作。

表1 两组患者一般资料比较

Table 1 Comparison of general data for two groups

分组	性别(男/女,例)	年龄(岁, $\bar{x} \pm s$)	身高(cm, $\bar{x} \pm s$)	体重(kg, $\bar{x} \pm s$)
单纯性阑尾炎组	16/14	5.73 ± 2.22	116.38 ± 38.95	25.15 ± 8.35
复杂性阑尾炎组	33/33	4.97 ± 2.13	113.38 ± 39.99	23.82 ± 7.13
χ^2/t 值	0.092	1.603	0.326	0.801
P值	0.762	0.112	0.745	0.425

三、统计学处理

采用SPSS19.0进行统计学分析,计量资料采用($\bar{x} \pm s$)进行描述,两组间比较采用独立样本t检验;计数资料采用频数和构成比进行描述,组间比较采用 χ^2 检验;通过绘制ROC曲线,计算曲线下面积(area under the curve, AUC),获得各检测指标及联合指标的敏感性、特异性;AUC之间的显著性差异采用单一变量Z检验, $P < 0.05$ 表示差异具有统计学意义。

结 果

一、复杂性阑尾炎与单纯性阑尾炎炎性指标水平比较

复杂性阑尾炎组CRP、IL-6、PCT水平均明显高于单纯性阑尾炎组,差异具有统计学意义($P < 0.05$),见表2。

二、CRP、IL-6、PCT对复杂性阑尾炎诊断效能以手术后病理结果为金标准绘制ROC曲线,分

析CRP、PCT、IL-6对复杂性阑尾炎诊断效能,得到CRP、PCT、IL-6及三者联合检验曲线下面积分别为0.906(95%置信区间:0.829~0.956)、0.953(95%置信区间:0.889~0.986)、0.765(95%置信区间:0.668~0.846)、0.973(95%置信区间:0.971~0.995)。曲线下面积值由大到小排序:PCT+CRP+IL-6>PCT>CRP>IL-6。经两两比较发现,联合检验的曲线下面积与CRP单独检验、IL-6单独检验曲线下面积差异存在统计学意义($Z = 2.932, P = 0.003$; $Z = 3.854, P = 0.0001$);联合检验的曲线下面积与PCT单独检验比较差异无统计学意义($Z = 1.861, P = 0.063$);CRP单独检验与PCT单独检验的曲线下面积差异无统计学意义($Z = 1.668, P = 0.095$),IL-6单独检验与CRP单独检验、PCT单独检验比较曲线下面积差异具有统计学意义($Z = 2.312, P = 0.021$; $Z = 3.371, P = 0.001$);得到最佳临界点分别为11.47(95%置信区间:11.42~14.48)mg/L,0.87(95%置信区间:0.63~0.98)ng/L,88.60(95%置信区间:87.12~170.83)pg/mL,见表3、图1。

表2 两组炎性指标水平比较

Table 2 Comparison of levels of inflammatory markers for two groups

分组	CRP(mg/L, $\bar{x} \pm s$)	IL-6(pg/mL, $\bar{x} \pm s$)	PCT(ng/mL, $\bar{x} \pm s$)
单纯性阑尾炎组	9.51 ± 2.15	71.48 ± 40.26	0.44 ± 0.34
复杂性阑尾炎组	14.73 ± 3.48	128.39 ± 64.61	1.46 ± 0.56
t值	8.96	10.96	5.26
P值	<0.001	<0.001	<0.001

表3 CRP、IL-6、PCT及联合检验对复杂性阑尾炎诊断效能的比较

Table 3 Comparison of diagnostic efficacy of CRP, IL-6, PCT and combined tests for complex appendicitis

诊断效能	CRP单独检验	PCT单独检验	IL-6单独检验	联合指标
最佳判断点	11.47 mg/L	0.87 ng/L	88.60 pg/mL	-
灵敏度	81.82%	87.88%	72.73%	98.48%
特异度	86.67%	90.00%	83.33%	90.00%
Youden指数	0.685	0.779	0.561	0.885
曲线下面积	0.906	0.953	0.765	0.973

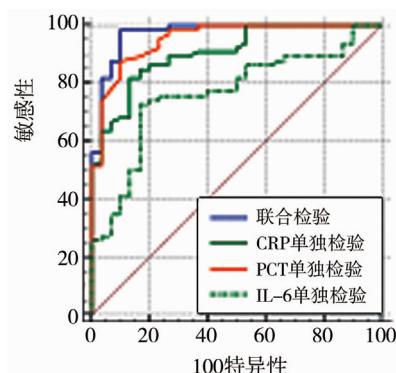


图1 CRP、IL-6、PCT及联合检验的ROC曲线

Fig. 1 ROC curves of CRP, IL-6, PCT and combined tests

讨 论

小儿阑尾壁薄,管腔狭窄,容易造成阑尾腔梗阻和血运障碍,加上大网膜发育不全,故更容易发生化脓、坏疽,临床主张早期诊断后尽早进行手术^[9]。但目前部分专家学者认为阑尾切除后可能导致消化系统、心血管系统、内分泌系统异常,早期急性单纯性阑尾炎大部分可选择内科治疗^[10]。因此,需要尽早进行诊断并对阑尾炎病理类型进行区分^[11~13]。

CRP 不受患者免疫功能、肝肾功能等因素的影响,所以其灵敏度和稳定性均较高^[14]。本研究发现,急性复杂性阑尾炎患者的 CRP 水平明显高于急性单纯性阑尾炎患者,在诊断效能的评价中,其灵敏度为 81.82%,特异度为 86.67%,曲线下面积为 0.906,对急性复杂性阑尾炎具有较高的诊断效能。

PCT 是一种血清降钙素的前体物,在人体内部很稳定,正常生理情况下,通过双抗夹心法检测正常人群血液中的 PCT 浓度,一般都在 0.1 ng/mL 以下。研究表明,PCT 往往在感染发生的 2 h 之内迅速升高,约 6 h 左右达到顶峰^[15]。IL-6 是一种功能广泛的多效性细胞因子,机体受炎症刺激后由 T 细胞、B 细胞、单核巨噬细胞及内皮细胞等分泌,是炎症介质网络的关键成分,也是急性期反应的主要调节因子之一,可调节局部、全身的炎症反应及免疫应答。有研究报道,IL-6 的主要作用是放大和催化炎症反应,也是临幊上诊断急慢性炎症常用的标志物,其含量越高代表感染越严重^[16]。本研究表明,急性复杂性阑尾炎患者的 IL-6 水平明显高于单纯性阑尾炎组,但在诊断效能的评价中,其特异性及敏感度要低于 CRP 及 PCT。

综上,CRP、IL-6 和 PCT 与阑尾炎的严重程度均存在相关性,对小儿复杂性阑尾炎具有一定的诊断价值,且联合诊断的诊断效能更高,有助于医师对术前病情严重程度预判。

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