

血清 C-反应蛋白 / 白蛋白比值评估 成人脓毒症患者预后的回顾性研究

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DOI: 10.3760/cma.j.issn.2095-4352.2016.05.007

【摘要】目的 探讨血清 C-反应蛋白与白蛋白比值(CRP/ALB)对成人脓毒症患者预后的预测价值。**方法** 采用回顾性研究方法,选择 2013 年 9 月至 2015 年 9 月河南省郑州大学第一附属医院重症医学科收治的年龄 ≥ 18 岁且重症加强治疗病房(ICU)住院时间 ≥ 3 d 的脓毒症患者,根据 28 d 预后将患者分为存活组和死亡组,分析其治疗即刻(0 h)及治疗后 24 h、72 h 血清 CRP、ALB 和 CRP/ALB 的变化,绘制受试者工作特征曲线(ROC),评价不同时间点各指标对预后的预测价值。**结果** 入选 69 例脓毒症患者,28 d 死亡 28 例,病死率为 40.6%。两组患者基线资料均衡,死亡组入院第一个 24 h 急性生理学与慢性健康状况评分系统 II (APACHE II)评分、序贯器官衰竭评分(SOFA)较存活组显著升高[APACHE II (分): 25.18 ± 3.18 比 17.88 ± 3.20 , SOFA (分): 11.71 ± 1.78 比 9.17 ± 2.38 , 均 $P < 0.05$], ICU 住院时间显著延长[d: $9.0(2.5)$ 比 $8.0(3.0)$, $P < 0.05$]。随治疗时间延长,两组患者血清 ALB 逐渐升高,血清 CRP 及 CRP/ALB 逐渐下降;死亡组治疗后 0、24、72 h ALB 均明显低于存活组,CRP 及 CRP/ALB 均明显高于存活组[ALB (g/L): 0 h 为 $23.40(4.20)$ 比 $25.20(8.20)$, 24 h 为 24.18 ± 4.33 比 28.54 ± 4.88 , 72 h 为 25.50 ± 4.88 比 34.88 ± 7.23 ; CRP (mg/L): 0 h 为 179.32 ± 34.04 比 159.55 ± 36.82 , 24 h 为 160.08 ± 22.91 比 146.23 ± 30.31 , 72 h 为 159.36 ± 25.81 比 142.53 ± 36.30 ; CRP/ALB: 0 h 为 7.52 ± 1.32 比 6.04 ± 1.46 , 24 h 为 6.77 ± 1.42 比 5.23 ± 1.24 , 72 h 为 6.40 ± 1.34 比 4.19 ± 1.21 ; 均 $P < 0.05$]。ROC 曲线分析显示,治疗后各时间点 CRP/ALB 的 AUC 均大于同期 ALB 和 CRP 的 AUC,且有更高的敏感度和特异度;0、24、72 h CRP/ALB 的 AUC 分别为 0.767、0.807、0.895,截断值分别为 6.96、5.44、4.91,敏感度分别为 71.4%、85.7%、89.3%,特异度分别为 73.2%、63.4%、82.9%。**结论** 成人脓毒症患者血清 CRP、CRP/ALB 较高及血清 ALB 较低均可提示预后不良,CRP/ALB 对预后的预测价值明显优于单用 CRP 或 ALB。用 72 h CRP/ALB 评估脓毒症患者临床疗效及预后更佳。

【关键词】 脓毒症; C-反应蛋白; 白蛋白; 预后

基金项目: 国家临床重点专科建设项目(2011-873)

Retrospective analysis of serum C-reactive protein/albumin ratio for the prognosis of the adult patients with sepsis Sun Rongqing, Sun Xiaoge, Yang Hongfu, Liu Qilong

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【Abstract】 Objective To explore the prognostic value of serum C-reactive protein/albumin (CRP/ALB) ratio in the adult patients with sepsis. **Methods** A retrospective study was conducted. Clinical data were collected from septic patients who were at least 18 years old and whose intensive care unit (ICU) lengths of stay were at least 3 days, and who were admitted in the Department of Critical Care Medicine of the First Affiliated Hospital of Zhengzhou University in Henan Province from September 2013 to September 2015. These patients were divided into survival group and death group according to 28-day outcome. The serum CRP, ALB, and CRP/ALB ratio levels at the start of treatment (0 hour), 24 hours and 72 hours after treatment in ICU were analyzed. And the receiver-operating characteristic (ROC) curve was plotted to assess the value of CRP, ALB and CRP/ALB ratio at different time points for predicting the outcome. **Results** Sixty-nine patients with sepsis were selected, among whom 28 cases were in the death group and the mortality was 40.6%. The characteristic of the baseline data in the two groups was balanced. The acute physiology and chronic health evaluation II (APACHE II) score and sequential organ failure assessment (SOFA) score at the first 24 hours of ICU admission in the death group were significantly higher than those in the survival group (APACHE II score: 25.18 ± 3.18 vs. 17.88 ± 3.20 , SOFA score: 11.71 ± 1.78 vs. 9.17 ± 2.38 , both $P < 0.05$). And the ICU length of

stay in the death group was significantly longer than that in the survival group [days: 9.0 (2.5) vs. 8.0 (3.0), $P < 0.05$]. The ALB level increased gradually as the treatment was extended in both groups while the levels of CRP and CRP/ALB declined gradually. The ALB levels at 0, 24, 72 hours after treatment in the death group were significantly lower, and the CRP and CRP/ALB levels were significantly higher than those in survival group [ALB (g/L): 23.40 (4.20) vs. 25.20 (8.20) at 0 hour, 24.18 ± 4.33 vs. 28.54 ± 4.88 at 24 hours, 25.50 ± 4.88 vs. 34.88 ± 7.23 at 72 hours; CRP (mg/L): 179.32 ± 34.04 vs. 159.55 ± 36.82 at 0 hour, 160.08 ± 22.91 vs. 146.23 ± 30.31 at 24 hours, 159.36 ± 25.81 vs. 142.53 ± 36.30 at 72 hours; CRP/ALB: 7.52 ± 1.32 vs. 6.04 ± 1.46 at 0 hour, 6.77 ± 1.42 vs. 5.23 ± 1.24 at 24 hours, 6.40 ± 1.34 vs. 4.19 ± 1.21 at 72 hours; all $P < 0.05$]. ROC curves analysis showed that the area under ROC curves (AUC) of CRP/ALB at all time points were larger than those of CRP and ALB, with higher sensitivity and specificity; the AUC of CRP/ALB at 0, 24, 72 hours were 0.767, 0.807, 0.895, respectively; the cut-off values were 6.96, 5.44, 4.91, the sensitivity were 71.4%, 85.7% and 89.3%, and the specificity were 73.2%, 63.4% and 82.9%, respectively. **Conclusions** High serum CRP, CRP/ALB and low ALB in adult patients with sepsis indicate a poor prognosis, while the prognostic value of CRP/ALB is obviously better than the single value of CRP or ALB. CRP/ALB at 72 hours may be one of the best indicators for the assessment of clinical therapy and prognosis of patients with sepsis.

[Key words] Sepsis; C-reactive protein; Albumin; Prognosis

Fund program: National Clinical Key Specialty Construction Projects (2011-873)

脓毒症是全世界范围内重症患者的首要死因,病死率占院内死亡患者的30%~50%^[1-4]。全身炎症反应是脓毒症发生发展的重要病理生理机制,研究显示,C-反应蛋白(CRP)升高程度与早期感染的严重程度相关^[5],可作为脓毒症的诊断指标,并可用于评价感染患者的疗效以判定患者是否可转出重症加强治疗病房(ICU)^[6-8];血清白蛋白(ALB)作为评估患者营养状态的指标,同样与感染所致炎症反应相关^[9]。近来有研究将CRP/ALB比值作为评价急性重症患者预后的指标^[10],并有学者称之为“渗透指数”^[11]。本研究旨在探讨CRP/ALB对成人脓毒症患者病情严重程度及预后的评估价值。

1 资料与方法

1.1 研究对象的选择:采用回顾性研究方法,收集2013年9月至2015年9月本院重症医学科收治的脓毒症患者的临床资料。

1.1.1 纳入标准:符合2012年脓毒症诊断标准^[12];年龄 ≥ 18 岁;ICU住院时间 ≥ 3 d;临床资料完整。

1.1.2 排除标准:在液体复苏期间应用白蛋白;恶性肿瘤终末期;严重肝肾疾病;严重心功能不全;风湿免疫性疾病;活动性大出血;血栓性疾病(如急性心肌梗死、肺栓塞);妊娠。

1.1.3 伦理学:本研究符合医学伦理学标准,并通过本院伦理委员会审查,治疗及检测均获得过患者或亲属的知情同意。

1.2 病例分组及观察指标:收集患者的一般资料,如性别、年龄、体质指数、感染部位;入ICU第一个24h的急性生理学与慢性健康状况评分系统II(APACHE II)评分、序贯器官衰竭评分(SOFA)及

ICU住院时间;记录治疗即刻(0h)及治疗后24h、72h血清CRP(免疫比浊法)、ALB(溴甲酚绿法)水平,并计算CRP/ALB比值。根据28d预后将患者分为存活组和死亡组。

1.3 统计学处理:采用SPSS 21.0软件处理数据,正态分布计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较用 t 检验;非正态分布计量资料以中位数(四分位数间距)[$M(Q_R)$]表示,组间比较用秩和检验;绘制各指标受试者工作特征曲线(ROC),计算曲线下面积(AUC); $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组一般资料比较(表1):最终69例患者入选,男性39例,女性30例;年龄26~81岁,平均(56.61 ± 14.67)岁;全部患者在确诊1h内接受初始经验性抗感染治疗,覆盖所有可能的致病微生物。28d存活41例,死亡28例,病死率为40.6%。两组性别、年龄、体质指数及感染部位比较差异均无统计学意义(均 $P > 0.05$),说明基线资料均衡,具有可比性。死亡组24h APACHE II和SOFA评分、ICU住院时间均明显高于存活组(均 $P < 0.05$)。

2.2 两组患者血清CRP、ALB及CRP/ALB的变化比较(表2):随治疗时间延长,两组患者血清CRP及CRP/ALB呈下降趋势,血清ALB呈上升趋势;死亡组各时间点CRP、CRP/ALB均高于存活组,ALB均低于存活组(均 $P < 0.05$)。

2.3 血清CRP、ALB及CRP/ALB对脓毒症预后的预测价值(表3;图1):治疗后各时间点CRP/ALB的AUC均大于同期CRP和ALB,72h CRP/ALB的AUC最大,对预后评价的敏感度及特异度也最高。

表1 不同预后两组成人脓毒症患者基线资料及ICU住院时间比较

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)	体质指数 ($\text{kg}/\text{m}^2, \bar{x} \pm s$)	感染部位(例)				APACHE II评分 (分, $\bar{x} \pm s$)	SOFA评分 (分, $\bar{x} \pm s$)	ICU住院时间 [d, $M(Q_R)$]
		男性	女性			肺部	腹部	血流	其他			
存活组	41	22	19	56.63 ± 12.59	22.23 ± 2.25	19	11	5	6	17.88 ± 3.20	9.17 ± 2.38	8.0(3.0)
死亡组	28	17	11	56.57 ± 17.53	22.43 ± 2.56	14	7	3	4	25.18 ± 3.18 ^a	11.71 ± 1.78 ^a	9.0(2.5) ^a

注:ICU为重症加强治疗病房,APACHE II为急性生理学与慢性健康状况评分系统II,SOFA为序贯器官衰竭评分;与存活组比较,^a $P < 0.05$

表2 不同预后两组成人脓毒症患者治疗各时间点血清CRP、ALB及CRP/ALB的变化比较

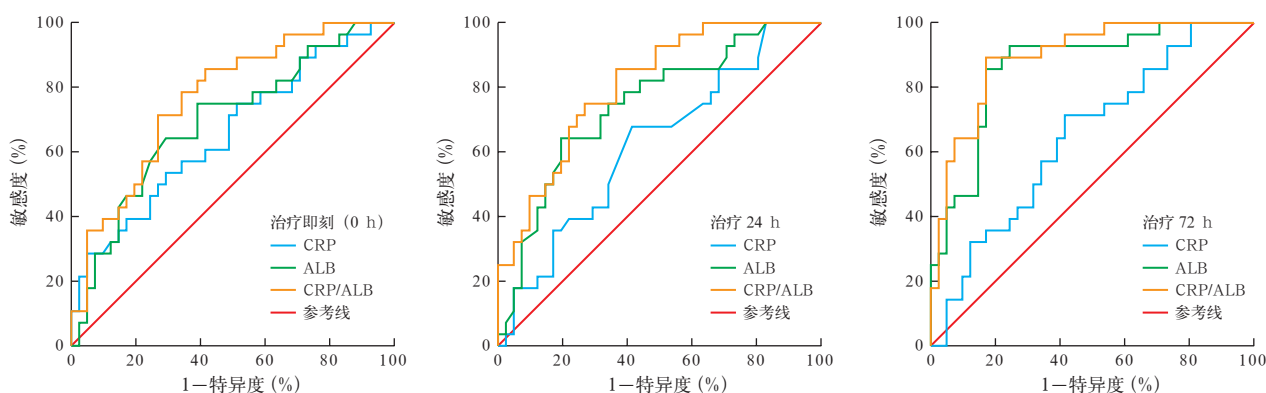
组别	例数 (例)	CRP($\text{mg}/\text{L}, \bar{x} \pm s$)			ALB [$\text{g}/\text{L}, M(Q_R)$ 或 $\bar{x} \pm s$]			CRP/ALB($\bar{x} \pm s$)		
		0h	24h	72h	0h	24h	72h	0h	24h	72h
存活组	41	159.55 ± 36.82	146.23 ± 30.31	142.53 ± 36.30	25.20(8.20)	28.54 ± 4.88	34.88 ± 7.23	6.04 ± 1.46	5.23 ± 1.24	4.19 ± 1.21
死亡组	28	179.32 ± 34.04 ^a	160.08 ± 22.91 ^a	159.36 ± 25.81 ^a	23.40(4.20) ^b	24.18 ± 4.33 ^b	25.50 ± 4.88 ^b	7.52 ± 1.32 ^b	6.77 ± 1.42 ^b	6.40 ± 1.34 ^b

注:CRP为C-反应蛋白,ALB为白蛋白;与存活组比较,^a $P < 0.05$,^b $P < 0.01$

表3 治疗后各时间点血清ALB、CRP、CRP/ALB对成人脓毒症患者28d预后的预测价值

指标	AUC	95%CI	P值	敏感度(%)	特异度(%)	截断值	约登指数	阳性预测值	阴性预测值
0h ALB	0.695	0.567 ~ 0.822	0.006	60.7	73.2	23.65	0.339	0.607	0.731
24h ALB	0.747	0.628 ~ 0.865	0.001	64.3	80.5	24.95	0.448	0.692	0.767
72h ALB	0.864	0.776 ~ 0.953	0.000	85.7	82.9	29.40	0.686	0.774	0.895
0h CRP	0.657	0.525 ~ 0.789	0.027	53.6	70.7	181.70	0.243	0.556	0.690
24h CRP	0.623	0.490 ~ 0.757	0.084	67.9	58.5	155.40	0.264	0.528	0.727
72h CRP	0.646	0.534 ~ 0.795	0.040	71.4	58.5	145.00	0.300	0.541	0.750
0h CRP/ALB	0.767	0.655 ~ 0.878	0.000	71.4	73.2	6.96	0.446	0.645	0.789
24h CRP/ALB	0.807	0.707 ~ 0.907	0.000	85.7	63.4	5.44	0.491	0.615	0.867
72h CRP/ALB	0.895	0.821 ~ 0.969	0.000	89.3	82.9	4.91	0.722	0.781	0.919

注:ALB为白蛋白,CRP为C-反应蛋白,AUC为受试者工作特征曲线下面积,95%CI为95%可信区间



注:ALB为白蛋白,CRP为C-反应蛋白,ROC曲线为受试者工作特征曲线

图1 治疗后各时间点血清ALB、CRP、CRP/ALB对成人脓毒症患者28d预后评估的ROC曲线

3 讨论

多种炎症因子参与了脓毒症的发生发展,如CRP、白细胞介素(IL-1、IL-6)、正五聚蛋白3、肝素结合蛋白等^[13-14],其中CRP在临床应用最为广泛且易于监测^[15]。本研究排除了合并风湿免疫性疾病、

严重肝肾功能不全等影响血清CRP水平的脓毒症患者,结果显示,死亡组血清CRP水平明显高于存活组,说明CRP水平越高,患者病情越严重,与国内学者的研究结果一致^[15-16]。另有动物实验表明,应用清瘟败毒饮降低脓毒症大鼠血清CRP、降钙素原

(PCT)水平,能够显著改善其肺组织和肠组织的病理学表现,调节脓毒症的免疫反应^[17]。

ALB对维持血浆胶体渗透压起重要作用,疾病状态下患者血清ALB半衰期明显缩短^[15,18]。故本研究排除了恶性肿瘤、严重肝肾功能不全等能导致低蛋白血症的疾病。结果显示,死亡组血清ALB水平明显低于存活组,提示ALB水平与脓毒症病情严重程度相关。脓毒症时,单核-巨噬系统、内皮细胞和中性粒细胞过度激活产生肿瘤坏死因子、IL-1、IL-6、内毒素等大量炎性介质,作用于肝细胞可抑制ALB mRNA表达,导致低蛋白血症^[19]。同时,大量炎性介质释放入血损伤毛细血管内皮,增加血管通透性,致使毛细血管渗漏,大量血浆蛋白渗漏至组织间隙,从而出现血液浓缩、低蛋白血症^[20-21]。严重感染所致应激状态下,ALB的分解代谢加快,血清ALB从血管内到血管外的分布速率增加,合成速率减慢,同样能使血清ALB水平下降^[22]。

Fairclough等^[10]对盖茨黑德市伊利沙伯医院2004年至2006年急诊科收治的患者进行了回顾性研究,最先发现CRP/ALB对评估慢性疾病急性发作老年患者的预后较改良早期预警评分(MEWS)更准确。随后有文献报道,CRP/ALB与食管鳞状细胞癌的肿瘤大小、异质性及病理分期相关,且比值升高提示预后更差^[23]。CRP/ALB能独立预测小细胞肺癌患者的预后^[24]。近年来,Ranzani等^[25]对229例严重脓毒症和111例脓毒性休克患者的血清CRP及CRP/ALB进行logistic回归分析显示,患者入ICU和出ICU时CRP/ALB较高均与90d不良预后相关,且评价预后的敏感度较CRP高,并且CRP/ALB是90d病死率的独立预测因子。Kim等^[26]对接受早期目标导向治疗的670例严重脓毒症或脓毒性休克患者进行多因素回归分析显示,入急诊科时的CRP/ALB是180d全因病死率的独立预测因子;生存分析结果提示,CRP/ALB>5.09时患者180d病死率更高。本研究关注的是脓毒症患者的28d病死率,结果表明,患者入ICU治疗后各时间点CRP/ALB的AUC均大于同期CRP和ALB,提示CRP/ALB能更准确地评估患者预后,其中72h CRP/ALB的AUC最大,截断值为4.91。脓毒症时ALB和CRP呈反向变化,而CRP/ALB综合了两项指标,能够更敏感地反映患者病情的微小改变,因此能协助临床医生评估患者预后,指导临床治疗。

综上,动态监测血清CRP及ALB能使临床医生

及时了解脓毒症患者病情变化,为评估预后提供依据。脓毒症患者血清ALB较低、CRP和CRP/ALB较高均可提示预后不良,CRP/ALB对预后的预测价值明显优于单用ALB或CRP,72h CRP/ALB对评估临床疗效及预后具有更高的应用价值。由于本研究为单中心回顾性研究,样本量较小,有必要进行多中心前瞻性研究来进一步探讨CRP/ALB在脓毒症或其他重症患者治疗中的应用价值。

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(收稿日期: 2015-11-29)

(本文编辑: 保健媛, 李银平)

• 科研新闻速递 •

一项有关开放性骨折初步处理中伤口冲洗的研究

开放性骨折治疗时要求采用伤口冲洗和清创术以去除坏死组织及污染物,但目前关于冲洗伤口时压力和冲洗液的选择仍存在争议。因此,有学者进行了一项研究,比较橄榄肥皂水与生理盐水在高、低、极低压力下对开放性骨折伤口的冲洗效果。该研究在41个临床中心进行,将存在四肢开放性骨折的患者随机分组,分别在高压[>9.1 kg(>20磅)],低压[2.3~4.5 kg(5~10磅)]或极低压[0.5~0.9 kg(1~2磅)]下,采用橄榄肥皂水或生理盐水冲洗伤口。研究主要终点指标为12个月内因促进创面或骨愈合或治疗伤口感染而再次手术的发生率。最终共2447例患者纳入该研究,高压组患者再次手术的发生率为13.2%(109/826),低压组为12.7%(103/809),极低压组为13.7%(111/812)。3组患者再次手术的风险相似[低压组与高压组:风险比(HR)=0.92,95%可信区间(95%CI)=0.70~1.20,P=0.53;高压组与极低压组:HR=1.02,95%CI=0.78~1.33,P=0.89;低压组与极低压组:HR=0.93,95%CI=0.71~1.23,P=0.62]。橄榄肥皂水组再次手术发生率为14.8%(182/1229),生理盐水组为11.6%(141/1218);生理盐水组再次手术的风险低于橄榄肥皂水组(HR=1.32,95%CI=1.06~1.66,P=0.01)。研究者由此得出结论,采用不同压力冲洗开放性骨折伤口的效果相似,各压力组间再次手术发生率接近;极低压冲洗成本低,可作为处理开放性骨折伤口的方法;橄榄肥皂水冲洗比生理盐水冲洗的再次手术发生率更高。

喻文, 罗红敏, 编译自《N Engl J Med》, 2015, 373(27): 2629-2641