

# 新型冠状病毒肺炎患者血液 CRP,CREA,ALB,IL-6 水平检测对疾病预后的应用价值分析

闫美田<sup>1,2</sup>, 郑雨桐<sup>1,2</sup>, 孙艳美<sup>3</sup>, 栾亮<sup>2</sup>, 刘静<sup>2</sup>, 田笑<sup>2</sup>, 万楠<sup>2</sup>

(1. 大连医科大学, 辽宁大连 116044; 2. 北部战区总医院检验科, 沈阳 110016;

3. 吉林医药学院, 吉林吉林 132013)

**摘要:**目的 探讨性别、年龄以及血液指标联合检测在预测新型冠状病毒肺炎(COVID-19)患者预后的应用价值。方法 选择2020年2~3月在泰康同济(武汉)医院的145例COVID-19确诊患者,根据出院预后状况分为治愈组(130例)和死亡组(15例),对两组患者的性别、年龄及血液中淋巴细胞绝对值(LYMPH)、C反应蛋白(CRP)、肌酸激酶MB同工酶(CK-MB)、肌酐(CREA)、清蛋白(ALB)、白细胞介素6(IL-6)和降钙素原(PCT)表达水平进行比较。应用多因素logistic回归分析和受试者工作曲线(ROC曲线)评价相关检测指标对COVID-19预后的判断价值。结果 治愈组、死亡组患者性别之间差异无统计学意义( $\chi^2=0.412, P>0.05$ ),年龄之间差异有统计学意义( $t=-4.341, P<0.05$ ),LYMPH, CRP, CK-MB, CREA, ALB, IL-6和PCT之间差异均有统计学意义( $U=97.000\sim 1\ 907.000$ , 均 $P<0.05$ ),而经多因素logistic回归分析仅筛选出CRP, CREA, ALB和IL-6四项是死亡的独立危险因素。CRP, CREA, ALB, IL-6以及CRP+CREA+ALB+IL-6联合检测的ROC曲线下面积(AUC值)分别为0.978, 0.881, 0.950, 0.979和0.988,敏感度分别为100%, 86.7%, 91.5%, 100%和100%,特异度分别为93.8%, 84.6%, 86.7%, 88.5%和95.4%。结论 CRP, CREA, ALB和IL-6可以作为COVID-19患者预后的判断指标,CRP+ALB+CRP+CREA联合检测能够提高COVID-19患者预后的评估能力。

**关键词:**新型冠状病毒肺炎; C反应蛋白; 肌酐; 清蛋白; 白细胞介素6

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## Analysis of the Value of Detection of Blood CRP,CREA,ALB and IL-6 Level in Patients with New Coronavirus Pneumonia to the Prognosis of the Disease

YAN Mei-tian<sup>1,2</sup>, ZHENG Yu-tong<sup>1,2</sup>, SUN Yan-mei<sup>3</sup>, LUAN Liang<sup>2</sup>, LIU Jing<sup>2</sup>, TIAN Xiao<sup>2</sup>, WAN Nan<sup>2</sup>

(1. Dalian Medical University, Liaoning Dalian 116044, China; 2. Department of Clinical Laboratory, Northern Theater General Hospital, Shenyang 110016, China; 3. Jilin Medical College, Jilin Jilin 132013, China)

**Abstract: Objective** To explore the value of sex, age and blood indexes in predicting the prognosis of patients with COVID-19. **Methods** A total of 145 patients diagnosed with COVID-19 in Taikang Tongji (Wuhan) Hospital from February to March in 2020 were selected. They were divided into cure group ( $n=130$ ) and death group ( $n=15$ ) according to the prognosis of discharge. The sex, age and the expression levels of lymphocyte absolute value (LYMPH), C-reactive protein (CRP), creatine kinase MB isoenzyme (CK-MB), creatinine (CREA), albumin (ALB), interleukin6 (IL-6) and procalcitonin (PCT) in blood were compared between the two groups. Multivariate logistic regression analysis and receiver working curve (ROC curve) were used to evaluate the prognostic value of related indexes in COVID-19. **Results** The differences in sex between the two groups were not statistically significant ( $\chi^2=0.412, P>0.05$ ). The differences in ages between the two groups were statistically significant ( $t=-4.341, P>0.05$ ). The differences in LYMPH, CRP, CK-MB, CREA, ALB, IL-6 and PCT between the two groups were statistically significant ( $U=97.000\sim 1\ 907.000$ , all  $P<0.05$ ). Only CRP, CREA, ALB and IL-6 were independent risk factors of death by multivariate logistic regression analysis. The area under the ROC curve (AUC value) of CRP, CREA, ALB, IL-6 and CRP+CREA+ALB+IL-6 were 0.978, 0.881, 0.950, 0.979 and 0.988, the sensitivity were 100%, 86.7%, 91.5%, 100% and 100%, and the specificity were 93.8%, 84.6%, 86.7%, 88.5% and 95.4%, respectively. **Conclusion** CRP, CREA, ALB and IL-6 can be used as prognostic indicators in patients with COVID-19. Combined detection of CRP+ALB+CRP+CREA can

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作者简介: 闫美田(1993-),女,在读研究生,研究方向:病原生物与分子生物学, E-mail: ymt19930425@163.com。

通讯作者: 万楠(1978-),男,副主任技师,硕士生导师, E-mail: wannan@outlook.com。

improve the ability to evaluate the prognosis of patients with COVID-19.

**Keywords:** COVID-19; C-reactive protein; creatinine; albumin; interleukin 6

2019年12月,湖北武汉市陆续出现新型冠状病毒肺炎(COVID-19)患者<sup>[1-2]</sup>,并在中国多个地区及境外多个国家相继暴发,具有极强的传染性<sup>[3-4]</sup>。截至3月27日,我国累计确诊病例81439例、死亡病例3300例(国家卫生健康委发布)<sup>[5]</sup>。引发COVID-19的病毒是一种新型冠状病毒,国际病毒分类委员会将其命名为严重急性呼吸综合征冠状病毒2(SARS-CoV-2)。严重的SARS-CoV-2感染者可快速引发呼吸窘迫综合征、脓毒血症、多脏器功能衰竭等,最终导致死亡<sup>[6-7]</sup>。但目前未见相关预测患者预后的研究,因此本研究旨在探讨性别、年龄以及血液中淋巴细胞绝对值(LYMPH),C-反应蛋白(CRP),肌酐(CREA),清蛋白(ALB),白细胞介素-6(IL-6),降钙素原(PCT),肌酸激酶MB同工酶(CK-MB)表达水平是否与患者预后相关,并评估对预后判断的应用价值,为COVID-19早期支持性诊疗和预后提供理论依据,从而降低COVID-19患者死亡率。

## 1 材料与与方法

**1.1 研究对象** 经武汉泰康同济医院医学伦理委员会批准,对2020年2~3月泰康同济(武汉)医院收治的145例COVID-19患者进行回顾性分析,根据预后情况分为治愈组和死亡组。治愈患者130例,女性72例(55.38%),男性58例(44.62%),平均年龄 $59.74 \pm 15.82$ 岁;死亡患者15例,女性7例(46.67%),男性8例(53.33%),平均年龄 $77.87 \pm 9.40$ 岁。

**纳入标准:**根据《新型冠状病毒肺炎诊疗方案(试行第七版)》临床分型标准<sup>[6]</sup>,经实时荧光定量PCR检测鼻咽拭子新型冠状病毒核酸阳性,或者血清特异性IgM, IgG抗体阳性,血清IgG由阴转阳或恢复期较急性期4倍及以上增高,并且均具有明确的流行病学史及典型的临床症状和(或)肺部CT特征。

**1.2 仪器与试剂** 使用SysmexXN-1000全自动血细胞分析仪及配套试剂检测LYMPH;使用普门PA-900特定蛋白分析仪及配套试剂检测CRP;使用贝克曼AU5811全自动生化分析仪及配套试剂检测CREA, ALB;使用罗氏Combos E602全自动电化学发光分析仪及配套试剂检测IL-6, PCT, CK-MB。

**1.3 方法** 抽取晨起空腹静脉血2~5ml,严格按照各仪器的操作流程和试剂说明书进行LYMPH和CRP的检测,3500 r/min离心10 min,分离上层血清,进行CREA, ALB, IL-6, PCT和CK-MB的检测。

各项指标正常参考值范围:LYMPH:  $(1 \sim 3.2) \times 10^9/L$ , CRP:0~10 mg/L, CREA:49~90  $\mu\text{mol/L}$ , ALB:35~55g/L, IL-6:0~7 pg/ml, PCT:0.00~0.05 ng/ml, CK-MB:0~4.87 ng/ml。

**1.4 统计学分析** 应用SPSS26.0软件进行数据分析,计数资料比较采用 $\chi^2$ 检验,以率表示;正态分布的计量资料比较应用独立样本 $t$ 检验,以均数 $\pm$ 标准差( $\bar{x} \pm s$ )表示;偏态分布的计量资料比较应用 $U$ 检验,以 $M(P_{25}, P_{75})$ 表示;应用多因素logistic回归筛选死亡的独立危险指标,再应用ROC曲线评估logistic回归预测模型的诊断能力。 $P < 0.05$ 为差异具有统计学意义。

## 2 结果

**2.1 患者临床资料** 治愈组130例患者中,从发病入院到出院的中位时间9天(IQR 7.0, 21.3),最短住院时间为4天,最长为38天;死亡组15例患者,从发病入院到死亡的中位时间为9天(IQR 6.0,18.0),最短时间为2天,最长为24天。

**2.2 治愈组与死亡组性别、年龄、血液检测结果的比较** 见表1。治愈组患者中女性72例(55.38%)、男性58例(44.62%),死亡组患者女性7例(46.67%)、男性8例(53.33%),两组性别差异无统计学意义( $\chi^2=0.412, P > 0.05$ );死亡组年龄明显高于治愈组,两组之间差异有统计学意义( $t = -4.341, P < 0.05$ ),死亡组LYMPH, ALB水平明显低于治愈组,死亡组以及CRP, CK-MB, CREA, IL-6水平明显高于治愈组,并且两组之间差异均有统计学意义( $U = 97.000 \sim 1907.000, P < 0.01$ )。

表1 治愈组和死亡组性别、年龄、血液检测结果的比较

指标	治愈组 (n=130)	死亡组 (n=15)	$t/\chi^2/U$	P
男[n(%)]	58(44.62)	8(53.33)	0.412	0.521
年龄(岁)	$59.74 \pm 15.82$	$77.87 \pm 9.40$	-4.341	0.000
LYMPH( $\times 10^9/L$ )	1.47(1.1,1.8)	0.32(0.3,0.7)	224.500	0.000
CRP(mg/L)	0.50(0.5,3.8)	44.68(31.1,133.8)	1907.000	0.000
CK-MB(ng/ml)	1.08(0.8,1.7)	4.20(2.3,9.7)	1765.000	0.000
CREA(ng/ml)	59.54(49.8,66.9)	122.87(83.2,194.8)	1718.000	0.000
ALB(g/L)	37.73(35.3,39.8)	25.91(23.8,29.9)	97.000	0.000
IL-6(pg/ml)	3.66(1.8,8.6)	204.60(52.0,2932.0)	1897.500	0.000
PCT(ng/ml)	0.05(0.0,0.1)	1.99(0.4,17.9)	1850.500	0.000

**2.3 多因素逐步logistic回归分析** 见表2。对表1差异有统计学意义的指标进行多因素逐步logistic回归分析,筛选出CRP, CREA, ALB和IL-6四项是死亡的独立危险因素( $P < 0.05$ ),将表2中参数进行拟

合,得到 CRP+CREA+ALB+IL-6 四项指标联合的回归预测模型,公式为:  $0.437+0.002 \times \text{CRP}+0.002 \times \text{CREA}-0.014 \times \text{ALB}+0.000 \times \text{IL-6}$ 。

2.4 ROC 曲线的绘制 见表 3,图 1。CRP, CREA, ALB, IL-6 以及 CRP+CREA+ALB+IL-6 联合检测的回归预测模型纳入 ROC 曲线中,结果显示 CRP, CREA, ALB, IL-6 以及 CRP+CREA+ALB+IL-6 联合检测的 ROC 曲线下面积(AUC 值)分别为 0.978, 0.881, 0.950, 0.979 和 0.988; 灵敏度分别为 100%, 86.7%, 91.5%, 100% 和 100%; 特异度分别为 93.8%, 84.6%, 86.7%, 88.5% 和 95.4%; CRP, CREA,

表 3 CRP, CREA, ALB, IL-6 及四项联合检测对于预测患者死亡的诊断效能

变量	AUC	标准误	P	最大约登数	临界值
CRP	0.978	0.011	0.000	0.938	22.99
CREA	0.881	0.055	0.000	0.713	72.995
ALB	0.950	0.026	0.000	0.782	31.055
IL-6	0.979	0.011	0.000	0.885	14.38
CRP+CREA+ALB+IL-6	0.988	0.007	0.000	0.954	

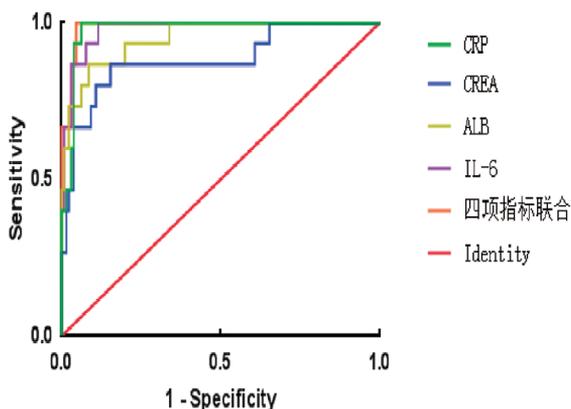


图 1 CRP, CREA, ALB, IL-6 及四项联合判断预后的 ROC 曲线

### 3 讨论

部分 COVID-19 患者病情发展极其迅速,可引起肺部和全身炎症反应,呼吸窘迫综合征、脓毒血症、多脏器功能衰竭等,会严重威胁患者的生命安全,因此探讨临床医生如何在诊疗过程中及时预测患者病情发展及预后尤为重要。

由单因素分析结果可知患者年龄、CRP, CK-MB, CREA, IL-6, PCT, LYMPH 和 ALB 在病情进展以及预后中起着一定的推动作用,但经多因素逐步 logistic 回归分析,仅筛选出 CRP, CREA, ALB 和 IL-6 四项是死亡的独立危险因素,ALB 对于死亡具有负相关,CRP, CREA 和 IL-6 对死亡具有正相关。通过 ROC 曲线对预测能力进一步分析,CRP+CREA+ALB+IL-6 联合的 AUC 值最高为 0.988,表明这四项指标联合检测对于评估

ALB, IL-6 最大约登指数截止点对应的临界值分别为 22.99 mg/L, 72.995  $\mu\text{mol/L}$ , 31.055 g/L 和 14.38 pg/ml。

表 2 多因素逐步 logistic 回归分析 COVID-19 患者预后的影响因素

变量	回归系数	标准误	P	95% 可信区间
CRP	0.002	0.001	0.004	0.002 ~ 0.005
CREA	0.002	0.000	0.000	0.001 ~ 0.003
ALB	-0.014	0.004	0.000	-0.002 ~ -0.007
IL-6	0.000	0.000	0.003	0.000 ~ 0.000

COVID-19 患者预后具有相当高的诊断价值。

IL-6 是一种具有广泛功能的细胞因子,参与发热和炎症反应,它的表达水平升高会促进肝脏分泌 CRP<sup>[8]</sup>, CRP 是一种急性时相反应蛋白,在机体感染时会显著增高,它可反映病毒所致炎症疾病的严重程度,并与呼吸衰竭呈正相关<sup>[9]</sup>。有研究表明严重的 COVID-19 患者大多引发肾损伤<sup>[10]</sup>,故临床医生需密切关注肾脏指标,例如 CREA,避免严重的肾损伤导致死亡; COVID-19 引发的肝损伤以及发热等应激反应会导致 ALB 大量消耗<sup>[11]</sup>。故 CRP, CREA, ALB 和 IL-6 可以成为很好的预示预后不良的主要标志物。

但是 CREA 的 AUC 值仅有 0.881,分析其原因,血清 CREA 虽是急性肾损伤常用的标志物,但缺乏特异性,检测结果易受年龄、药物等因素的影响<sup>[12]</sup>,若 CREA 检测结果再联合其他肾脏相关指标诊断能力会有很大程度提高。

综上所述,CRP, CREA, ALB 和 IL-6 可作为以 COVID-19 患者预后的判断指标,CRP+ALB+CRP+CREA 联合检测能够提高 COVID-19 患者预后的评估能力,可为 COVID-19 早期支持性诊疗和预后提供理论依据,从而降低 COVID-19 患者死亡率。

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(上接第102页)

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