



DOI: 10.3978/j.issn.2095-6959.2023.22586

血清C反应蛋白、前白蛋白和红细胞体积分布宽度对重症肺炎合并呼吸衰竭患者预后的预测价值

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[摘要] 目的: 探讨血清C反应蛋白(C-reactive protein, CRP)、前白蛋白(prealbumin, PAB)和红细胞体积分布宽度(red cell volume distribution width, RDW)对重症肺炎合并呼吸衰竭患者预后的预测价值。方法: 回顾性分析2020年1月至2022年1月南通大学附属肿瘤医院收治的228例重症肺炎合并呼吸衰竭患者的临床资料。根据患者入院后28 d转归情况将其分为存活组与死亡组。比较2组血清CRP、PAB水平及RDW等临床资料, 采用多因素logistic回归分析患者预后的独立影响因素, 同时通过绘制受试者操作特征(receiver operating characteristic, ROC)曲线分析血清CRP、PAB水平及RDW对重症肺炎合并呼吸衰竭预后的预测价值。结果: 相比存活组, 死亡组急性生理学和慢性健康状况评价II(acute physiology and chronic health evaluation II, APACHE II)评分, 白细胞计数, 动脉血二氧化碳分压(arterial partial pressure of carbon dioxide, PaCO₂), 血清CRP、降钙素原(procalcitonin, PCT)水平, RDW均显著增高(均 $P<0.001$ 或 $P<0.05$), 动脉血氧分压(arterial partial pressure of oxygen, PaO₂)及PAB水平显著降低($P<0.001$), 机械通气时间及ICU住院时间较长(均 $P<0.001$)。多因素logistic回归分析显示: APACHE II评分、CRP、PAB、RDW是预测患者死亡的独立影响因素(均 $P<0.05$)。ROC曲线显示: APACHE II评分预测患者预后的曲线下面积(area under the curve, AUC)为0.813; CRP的AUC为0.668, 相比APACHE II评分较低($P=0.007$); PAB的AUC为0.794, 与APACHE II评分相比差异无统计学意义($P=0.662$); RDW的AUC为0.871, 与APACHE II评分相比差异无统计学意义($P=0.153$); 而CRP+PAB+RDW的AUC为0.919, 相比APACHE II评分明显提高($P=0.004$)。结论: 血清CRP和PAB水平及RDW对预测重症肺炎合并呼吸衰竭患者预后有一定参考价值, 三者联合可以其高临床预测价值。

[关键词] 重症肺炎; 呼吸衰竭; C反应蛋白; 前白蛋白; 红细胞体积分布宽度; 预后

Prognostic value of serum C-reactive protein, prealbumin, and red cell volume distribution width in patients with severe pneumonia complicated with respiratory failure

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收稿日期(Date of reception): 2022-03-28

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ABSTRACT

Objective: To investigate the prognostic value of serum C-reactive protein (CRP), prealbumin (PAB), and red cell volume distribution width (RDW) in patients with severe pneumonia complicated with respiratory failure.

Methods: The clinical data of 228 patients with severe pneumonia complicated with respiratory failure admitted to Tumor Hospital Affiliated to Nantong University from January 2020 to January 2022 were retrospectively analyzed. According to the outcome of 28 days after admission, the patients were divided into a survival group and a death group. The baseline data, serum level of CRP and PAB, and RDW were compared between the 2 groups. Multivariate logistic regression was used to analyze the independent influencing factors of prognosis. At the same time, the predictive value of serum level of CRP and PAB, and RDW on the prognosis of severe pneumonia complicated with respiratory failure was analyzed by drawing the receiver operating characteristic (ROC) curve.

Results: Compared with the survival group, acute physiology and chronic health evaluation II (APACHE II) score, white blood cell count, arterial partial pressure of carbon dioxide (PaCO_2), serum level of CRP and procalcitonin (PCT), and RDW in the death group were significantly increased ($P < 0.001$ or $P < 0.05$), arterial partial pressure of oxygen (PaO_2) and serum level of PAB were significantly decreased (both $P < 0.001$), mechanical ventilation time and ICU stay were longer (both $P < 0.001$). Multivariate logistic regression analysis showed that APACHE II score, CRP, PAB, and RDW were independent predictors of death (all $P < 0.05$). ROC curve showed that area under the curve (AUC) of APACHE II score for predicting the prognosis of patients was 0.813; AUC of CRP was 0.668, which was lower than APACHE II score ($P = 0.007$); AUC of PAB was 0.794, and the difference was not statistically significant compared with APACHE II score ($P = 0.662$); AUC of RDW was 0.871, and the difference was not statistically significant compared with APACHE II score ($P = 0.153$); the AUC of CRP + PAB + RDW was 0.919, which was significantly higher than APACHE II score ($P = 0.004$).

Conclusion: Serum level of CRP and PAB, and RDW have certain reference value in predicting the prognosis of patients with severe pneumonia complicated with respiratory failure, and the combination of the three can have high clinical predictive value.

KEY WORDS

severe pneumonia; respiratory failure; C-reactive protein; prealbumin; red cell volume distribution width; prognosis

重症肺炎是临床常见的危急病症, 极易引起呼吸衰竭, 由于病情进展快、预后差, 如果不及时对症治疗, 将严重威胁患者生命健康^[1]。因此, 提前预测重症肺炎合并呼吸衰竭患者预后极为重要。C反应蛋白(C-reactive protein, CRP)是急性期炎症反应指标, 具有灵敏度高、检测快捷的优点, 也是目前临床评估炎症性疾病常用指标之一^[2]。在重症疾病中, 机体处于高分解状态, 营养消耗快, 极易导致营养不良, 从而影响病情转归。前白蛋白

(prealbumin, PAB)是反映机体营养状况的重要指标, 有研究^[3]显示血清PAB水平可用于预测炎症反应及重症肺炎病情严重程度。红细胞体积分布宽度(red cell volume distribution width, RDW)指红细胞大小的异质性, 在评估贫血方面有重要价值^[4]。近年研究^[5]显示RDW与CRP水平升高有相关性, 可用于预测肺部疾病预后。为进一步改善重症肺炎合并呼吸衰竭患者预后, 本研究探讨CRP、PAB和RDW对这类患者死亡的预测价值。

1 对象与方法

1.1 对象

回顾性分析2020年1月至2022年1月南通大学附属肿瘤医院收治的228例重症肺炎合并呼吸衰竭患者的临床资料。其中,男146例,女82例;年龄26~78(59.92±9.74)岁;体重指数(body mass index, BMI)19~28(24.99±3.50) kg/m²;合并高血压27例,糖尿病32例,高血脂29例;38例有吸烟史;入院后28 d存活168例,死亡60例。根据患者入院后28 d转归情况将其分为存活组与死亡组。本研究符合伦理相关规定并获得南通大学附属肿瘤医院批准(审批号:LW2022120)。

1.2 纳入及排除标准

纳入标准:1)年龄≥18岁。2)经临床确诊为重症肺炎。主要诊断标准^[6]:需行机械通气;合并感染性休克需使用血管活性药物治疗。次要标准:呼吸频率超过30次/min;氧合指数不超过250;体温低;血小板计数低;白细胞计数低;需要进行液体复苏;存在意识障碍或者定向障碍。满足1个主要标准,且符合3个次要标准即可诊断为重症肺炎。3)符合呼吸衰竭临床诊断标准^[7]:动脉血氧分压(arterial partial pressure of oxygen, PaO₂)不足60 mmHg(1 mmHg=0.133 kPa),伴随或者不伴随动脉血二氧化碳分压(arterial partial pressure of carbon dioxide, PaCO₂)超过50 mmHg。4)病史资料及随访资料完整。排除标准:1)恶性营养不良;2)恶性肿瘤;3)合并严重血液系统疾病;4)合并器官移植。

1.3 资料收集

收集患者基线资料,包括:1)一般资料。性别、年龄、BMI、基础疾病(高血压、糖尿病、高血脂)、吸烟情况、饮酒情况及入院时急性生理学和慢性健康状况评价II(acute physiology and chronic health evaluation II, APACHE II)评分、PaO₂、PaCO₂、氧合指数。2)实验室指标。血小板计数、白细胞计数、淋巴细胞计数、谷丙转氨酶(glutamic-pyruvic transaminase, GPT)、谷草转氨酶(glutamic-oxaloacetic transaminase, GOT)、降钙素原(procalcitonin, PCT)、红细胞沉降率、CRP、PAB和RDW等。于入院后次日,采集患者清晨空腹肘静脉血5 mL,采用全自动生化分析仪进行实验室

指标的检测。

1.4 统计学处理

采用SPSS 22.0统计软件对数据进行分析。计量资料符合正态分布且方差齐,用均数±标准差($\bar{x}\pm s$)表示,采用独立样本 t 检验;计数资料用例(%)表示,采用 χ^2 检验;采用logistic回归分析影响患者预后的独立影响因素;通过绘制受试者操作特征(receiver operating characteristic, ROC)曲线分析CRP、PAB、RDW及三者联合预测患者预后的临床价值,曲线下面积(area under the curve, AUC)的比较用秩和检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组基线资料比较

相比存活组,死亡组APACHE II评分、白细胞计数、PaCO₂、血清CRP和PCT水平、RDW均显著增高($P<0.001$ 或 $P<0.05$),PaO₂、氧合指数、PAB水平均显著降低($P<0.001$ 或 $P<0.05$),机械通气时间及ICU住院时间较长(均 $P<0.001$)。两组性别、年龄、BMI、高血压占比、糖尿病占比、高血脂占比、吸烟占比、血小板计数等一般资料比较,差异均无统计学意义(均 $P>0.05$,表1)。

2.2 多因素logistic回归分析

以患者入院后28 d转归为因变量,以单因素分析中有统计学意义的因素为自变量,行多因素logistic回归分析,结果显示:APACHE II评分、CRP、PAB、RDW是预测患者死亡的独立影响因素(均 $P<0.05$,表2)。

2.3 CRP、PAB、RDW对重症肺炎合并呼吸衰竭预后的诊断效能

ROC曲线显示:APACHE II评分预测患者预后的AUC为0.813;CRP的AUC为0.668,相比APACHE II评分,CRP的预测效能较低($Z=2.677$, $P=0.007$);PAB的AUC为0.794,与APACHE II评分相比差异无统计学意义($Z=0.437$, $P=0.662$);RDW的AUC为0.871,与APACHE II评分相比差异无统计学意义($Z=1.428$, $P=0.153$);而CRP+PAB+RDW的AUC为0.919,相比APACHE II评分,CRP、PAB、RDW三者联合的预测效能明显提高($Z=2.891$, $P=0.004$;表3,图1)。

表1 两组基线资料比较

Table 1 Comparison of baseline data between the 2 groups

组别	n	性别/[例(%)]		年龄/岁	BMI/(kg·m ⁻²)	高血压/[例(%)]	糖尿病/[例(%)]	高血脂/[例(%)]
		男	女					
存活组	168	104 (61.90)	64 (38.10)	59.52±9.81	25.01±3.87	21 (12.50)	25 (14.88)	24 (14.29)
死亡组	60	42 (70.00)	18 (30.00)	61.03±9.44	24.92±3.56	6 (10.00)	7 (11.67)	5 (8.33)
χ^2/t		1.258		1.033	0.158	0.265	0.379	1.411
P		0.262		0.303	0.875	0.607	0.538	0.235

组别	吸烟史/[例(%)]	饮酒史/[例(%)]	APACHE II评分	血小板计数/($\times 10^9 \cdot L^{-1}$)	白细胞计数/($\times 10^9 \cdot L^{-1}$)	淋巴细胞计数/($\times 10^9 \cdot L^{-1}$)
存活组	30 (17.86)	21 (12.50)	28.59±5.01	102.68±15.72	13.60±4.02	0.79±0.24
死亡组	8 (13.33)	9 (15.00)	34.62±5.17	101.43±14.58	19.81±4.35	0.73±0.20
χ^2/t	0.241	0.242	7.936	0.539	10.050	1.733
P	0.623	0.623	<0.001	0.591	<0.001	0.085

组别	PaO ₂ /mmHg	PaCO ₂ /mmHg	氧合指数	ALT/(U·L ⁻¹)	AST/(U·L ⁻¹)	CRP/(mg·L ⁻¹)
存活组	54.29±6.74	58.23±7.15	156.59±35.28	52.79±11.26	57.58±9.26	66.14±11.09
死亡组	46.08±7.31	67.96±8.04	144.75±32.65	53.84±10.19	58.46±8.76	75.95±17.55
χ^2/t	7.919	8.751	2.274	0.635	0.641	4.984
P	<0.001	<0.001	0.024	0.526	0.522	<0.001

组别	PCT/($\mu g \cdot L^{-1}$)	红细胞沉降率/(mm·h ⁻¹)	PAB/(mg·L ⁻¹)	RDW/%	机械通气时间/d	ICU住院时间/d
存活组	8.74±1.25	16.71±3.19	183.64±56.00	13.45±3.03	7.56±0.98	13.41±3.12
死亡组	9.34±1.56	17.65±4.59	121.78±48.79	17.96±2.71	10.69±1.58	15.74±4.26
χ^2/t	2.982	1.732	7.587	10.166	17.837	4.485
P	0.003	0.085	<0.001	<0.001	<0.001	<0.001

1 mmHg=0.133 kPa。BMI: 体重指数; APACHE II: 急性生理学和慢性健康状况评价 II; PaO₂: 动脉血氧分压; PaCO₂: 动脉血二氧化碳分压; GPT: 谷丙转氨酶; GOT: 谷草转氨酶; CRP: C 反应蛋白; PCT: 降钙素原; PAB: 前白蛋白; RDW: 红细胞体积分布宽度。

表2 多因素 logistic 回归分析

Table 2 Multiple logistic regression

指标	β	SE	Wald χ^2	OR	95% CI	P
APACHE II评分	0.359	0.126	8.118	1.432	1.119~1.833	0.005
白细胞计数	0.408	0.227	3.230	1.504	0.964~2.346	0.073
PaO ₂	-0.316	0.324	0.951	0.726	0.386~1.376	0.330
氧合指数	-0.258	0.176	2.149	0.773	0.547~1.091	0.143
CRP	0.529	0.243	4.739	1.697	1.054~2.733	0.030
PAB	-0.138	0.057	5.861	0.871	0.779~0.974	0.016
RDW	1.064	0.341	9.736	2.898	1.485~5.654	0.038

APACHE II: 急性生理学和慢性健康状况评价 II; PaO₂: 动脉血氧分压; CRP: C 反应蛋白; PAB: 前白蛋白; RDW: 红细胞体积分布宽度。

表3 CRP、PAB、RDW对重症肺炎合并呼吸衰竭预后的诊断效能

Table 3 Diagnostic efficacy of CRP, PAB, and RDW on prognosis of severe pneumonia complicated with respiratory failure

指标	最佳截断值	AUC	灵敏度/%	特异度/%	95% CI	P
APACHE II评分	33	0.813	61.7	82.7	0.757~0.862	<0.001
CRP	70.76*	0.668	61.67	66.67	0.602~0.728	<0.001
PAB	166.89*	0.794	85.00	63.10	0.736~0.845	<0.001
RDW	15.34	0.871	85.00	73.21	0.820~0.911	<0.001
CRP+PAB+RDW	—	0.919	88.33	80.95	0.875~0.951	<0.001

*单位为mg/L。AUC: 曲线下面积; APACHE II: 急性生理学和慢性健康状况评价II; CRP: C反应蛋白; PAB: 前白蛋白; RDW: 红细胞体积分布宽度。

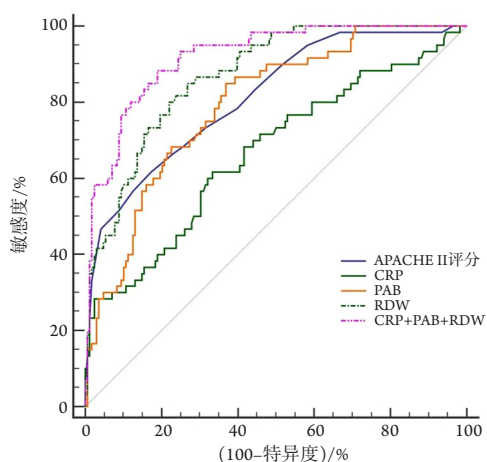


图1 APACHE II评分、CRP、PAB、RDW预测重症肺炎合并呼吸衰竭预后的ROC曲线

Figure 1 ROC curve of APACHE II score, CRP, PAB, and RDW in predicting prognosis of severe pneumonia complicated with respiratory failure

APACHE II: Acute physiology and chronic health evaluation II; CRP: C-reactive protein; PAB: Prealbumin; RDW: Red cell volume distribution width; ROC: Receiver operating characteristic.

3 讨论

数据^[8]显示: 中国每年肺炎感染人数高达300万, 其中约有15万人因重症肺炎感染死亡, 是导致居民死亡的5大原因之一。重症肺炎首要攻击对象为人肺间质细胞, 因此重症肺炎患者多合并呼吸衰竭, 其病情进一步进展还会以引起多器官功能衰竭, 导致死亡。目前, 临床主要采取常规抗炎、平喘、止咳、化痰等对症治疗手段, 但效果有限。临床^[9]发现提前预测重症肺炎合并呼吸衰竭患者预后对调整治疗方案有一定参考价值, 可有效改善患者预后。

本研究以入院后28 d转归情况为终点事件, 发现本组患者28 d病死率为26.32%, 且存活组与死亡组性别、年龄、BMI、合并症、吸烟状况、血小板计数等一般资料比较无明显差异, 存活组APACHE II评分、白细胞计数、PaCO₂、血清CRP和PCT水平、RDW均显著低于死亡组, PaO₂、氧合指数、PAB显著高于死亡组。APACHE II评分是临床评估危重患者病情程度及预后的“金标准”, 分数越高患者病情越严重, 对重症肺炎合并呼吸衰竭患者预后同样有较高预测价值^[10]。白细胞计数是嗜中性粒细胞、淋巴细胞、单核细胞、嗜酸性粒细胞、嗜碱性粒细胞的总和, 其水平升高可能与细菌性炎症、病毒性感染有关^[11]。既往研究^[12]显示: 在重症肺炎合并呼吸衰竭发病过程中, 患者免疫功能处于异常激活状态, 持续过度的免疫防御导致患者病情加重, 引起血气指标变化(PaO₂、氧合指数降低及PaCO₂升高), 严重时可诱发多器官功能衰竭甚至死亡。

本研究显示: 存活组与死亡组血清CRP、PAB和RDW比较差异显著, 表明血清CRP和PAB水平及RDW与重症肺炎合并呼吸衰竭患者预后有关。CRP是一种急性时象反应蛋白, 当机体受到损伤或存在炎症性疾病时, 其血清水平急剧升高。张玲等^[13]研究显示: 随重症肺炎患者病情进展, 其肺功能、凝血功能逐渐下降, 炎症反应逐渐增强, 通过检测炎症反应指标CRP可以鉴别重症肺炎的病情程度。重症肺炎合并呼吸衰竭患者炎症反应更强, CRP变化更为明显。PAB与血清白蛋白(serum albumin, SA)一样, 都是临床判断机体营养状况的常用指标, 且PAB半衰期为2.5 d, 比SA监测更为灵敏^[14]。重症肺炎合并呼吸衰竭患者存在不同程度的营养不良, 有研究^[15]显示: 当PAB≤14.0 mg/dL时, 急性心力衰竭(acute congestive heart failure, AHF)患者全因死亡、复合终点事件发生率明显升高, 提示血清PAB可作

为AHF患者风险分层指标,且低PAB水平可能与患者长期预后不良有关。RDW反映的是红细胞体积,数值越大表示红细胞体积异质性越大,在鉴别造血异常、先天性红细胞异常、贫血方面有极高的价值。近年报道^[16]显示:RDW与多种血清前炎症因子、炎症指标水平密切相关,可作为机体炎症反应的新型标志物。随着重症肺炎合并呼吸衰竭患者病情发展,机体血液循环减慢,血液中的红细胞数量及体积减小,导致RDW水平升高。因此, RDW与重症肺炎合并呼吸衰竭患者预后有关。

重症肺炎合并呼吸衰竭疾病进展是多因素共同作用的结果。本研究采用logistic回归分析,结果显示:白细胞计数、PaO₂、氧合指数与患者预后不独立相关,APACHE II评分、CRP、RDW是预测患者预后不良的独立危险因素,PAB是预测患者预后不良的独立保护因素。分析原因为白细胞计数、PaO₂、氧合指数不能全面反应患者病情变化。APACHE II评分对重症患者预后的预测价值已得到证实并被广泛应用^[17]。因此本研究以APACHE II评分为参照,探讨血清CRP、PAB和RDW对重症肺炎合并呼吸衰竭患者预后的预测价值,结果显示:CRP、PAB、RDW预测患者预后不良的AUC分别为0.668、0.794、0.871,灵敏度分别为61.67%、85.00%、85.00%,特异度分别为66.67%、63.10%、73.21%,CRP的AUC低于APACHE II评分,而PAB、RDW与APACHE II评分相比差异无统计学意义,这提示CRP、PAB、RDW可作为重症肺炎合并呼吸衰竭患者预后不良的预测指标,尤其以PAB、RDW效能较高。韩振坤等^[18]研究则显示血清CRP与重症肺炎合并呼吸衰竭患者预后不独立相关。本研究表明CRP对重症肺炎合并呼吸衰竭预后有一定预测价值,但灵敏度、特异度不高,可能的原因是在肺炎感染早期CRP即开始升高,发展到重症肺炎时可能达到达峰值,变化水平不明显。本研究还显示CRP、PAB、RDW联合可以提高重症肺炎合并呼吸衰竭患者预后不良的预测价值,优于APACHE II评分,与既往类似研究^[19]结果类似,联合检测可提高单一指标的诊断效能。

综上所述,CRP、PAB、RDW与重症肺炎合并呼吸衰竭患者预后相关,三者联合检测对患者预后评估有较高的应用价值。本研究为回顾性研究,仅对患者基线CRP、PAB、RDW进行分析,未来有待通过前瞻性设计观察患者CRP、PAB、RDW动态变化,以更好地指导临床诊治。

利益冲突声明:作者声称无任何利益冲突。

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本文引用: 刘锦茂, 张小林, 胡敏. 血清C反应蛋白、前白蛋白和红细胞体积分布宽度对重症肺炎合并呼吸衰竭患者预后的预测价值[J]. 临床与病理杂志, 2023, 43(1): 22-28. DOI:10.3978/j.issn.2095-6959.2023.22586

Cite this article as: LIU Jinmao, ZHANG Xiaolin, HU Min. Prognostic value of serum C-reactive protein, prealbumin, and red cell volume distribution width in patients with severe pneumonia complicated with respiratory failure[J]. Journal of Clinical and Pathological Research, 2023, 43(1): 22-28. DOI: 10.3978/j.issn.2095-6959.2023.22586