

doi: 10.13241/j.cnki.pmb.2019.16.013

• 临床研究 •

中心静脉 - 动脉二氧化碳分压差与动脉 - 中心静脉氧含量差的比值
(Pcv-aCO₂/Ca-cvO₂)变化率

对急诊重症监护室脓毒症患者预后的评估价值 *

倪主昂[#] 吕 丹[#] 张柯基[△] 龚 好 徐欣晖 朱长清

(上海交通大学医学院附属仁济医院急诊科 上海 200127)

摘要 目的:探讨中心静脉动脉二氧化碳分压差 / 氧含量差(Pcv-aCO₂/Ca-cvO₂)变化率在急诊重症监护室(EICU)高乳酸脓毒血症患者病情及预后评估中的临床应用价值。**方法:**选择 2017 年 1 月到 2018 年 9 月入住急诊重症监护室的 48 例高乳酸(乳酸大于 4 mmol/h)脓毒血症患者,均按 2016 年脓毒症指南进行液体复苏治疗。采集复苏前(T0h)和开始复苏后 6h(T6h)、24h(T24h)的动脉血、上腔静脉血气分析以及动脉血乳酸浓度。计算并记录各时间点的乳酸、乳酸清除率,中心静脉动脉二氧化碳分压差(Pcv-aCO₂)值,中心静脉动脉二氧化碳分压差 / 氧含量(Pcv-aCO₂/Ca-cvO₂)值及其变化率。根据治疗 24h 改良 SOFA 评分是否改善将患者分为两组,即改良 SOFA 改善组和未改善组,观察和比较两组间基本临床资料及化验参数,并分析各时间点各参数之间的相关性,以及这些参数能否有效预测高乳酸脓毒血症患者病情危重程度和预后。**结果:**45 例患者纳入最终分析,3 例因为 24h 内死亡或者自动出院脱落。其中,17 例 24hSOFA 改善,28 例未改善;20 例死亡,25 例存活。两组患者复苏前各项一般临床资料指标比较差异均无统计学意义($P>0.01$)。24hSOFA 改善组与未改善组患者 Pcv-aCO₂/Ca-cvO₂(T24h)、Pcv-aCO₂/Ca-cvO₂ 变化率(0-24h)存在组间差异($P<0.01$)。45 例患者的乳酸清除率(0-24h)与 Pcv-aCO₂/Ca-cvO₂ 变化率(0-24h)呈显著相关性($r=0.906, P=0.034$)。ROC 分析显示 Pcv-aCO₂/Ca-cvO₂ 变化率(0-24h)能有效预测 24hSOFA 评分改善,同其他指标相比,曲线下面积最大(AUROC=0.851),最佳界值是 0.307(30.7%),敏感度是 76.5%,特异度是 92.9%;Pcv-aCO₂/Ca-cvO₂ 变化率(0-24h)也能有效预测脓毒症患者院内死亡,AUROC=0.696,AUROC 较 24h 乳酸值小,但不存在统计学差异,最佳界值是 0.181(18.1%),敏感度是 65%,特异度是 68%。**结论:**液体复苏前到开始复苏后 24h 的 Pcv-aCO₂/Ca-cvO₂ 变化率可以有效预测高乳酸脓毒血症患者的器官功能改善情况,也能有效预测脓毒症患者院内死亡的发生。

关键词:脓毒症;中心静脉动脉二氧化碳分压差 / 氧含量差;中心静脉动脉二氧化碳分压差 / 氧含量差变化率;中心静脉动脉二氧化碳分压差;预后

中图分类号:R631.2 文献标识码:A 文章编号:1673-6273(2019)16-3073-07

The Change Rate of Central Venous-arterial Carbon Dioxide Tension
Difference to Arterial-central Venous Oxygen Content Difference Ratio for
Evaluating Progression and Prognosis in Patients with Sepsis
in the Emergency Intensive Care Unit*NI Zhu-ang[#], LV Dan[#], ZHANG Ke-ji[△], GONG Hao, XU Xin-hui, ZHU Chang-qing

(Department of emergency, Renji Hospital, School of medicine, Shanghai Jiaotong University, Shanghai, 200127, China)

ABSTRACT Objective: To investigate the clinical value of change rate of central venous-arterial carbon dioxide tension difference to arterial-central venous oxygen content difference ratio (Pcv-aCO₂/Ca-cvO₂) for evaluating the progression and the prognosis of septic patients with high level of lactate in the emergency intensive care unit (EICU). **Methods:** Forty-eight septic patients with high level of lactate (lactic acid >4 mmol/h) admitted to EICU from January 2017 to September 2018 were enrolled. All the patients were given an initial resuscitation therapy according to the 2016 sepsis guidelines. The arterial and central venous blood gases and lactate level were measured simultaneously at baseline (T0h), 6 hours after resuscitation (T6h) and 24 hours after resuscitation (T24h). The lactate level,

* 基金项目:上海市卫生和计划生育委员会科研项目(201640220)

作者简介:倪主昂(1988-),男,本科,主要研究方向:急诊常见病的诊治

吕丹(1984-),女,硕士研究生,主要研究方向:危重病的诊治

为共同第一作者

△ 通讯作者:张柯基, E-mail: zhangkejide@126.com

(收稿日期:2018-12-31 接受日期:2019-01-25)

lactate clearance rate (LCR), P_{cv-aCO_2} , $P_{cv-aCO_2}/Ca-cvO_2$ and P_{cv-aCO_2} , $P_{cv-aCO_2}/Ca-cvO_2$ change rate were calculated. The patients were classified into two groups according to the improvement of 24-hour sequential organ failure assessment (SOFA) score. The basic clinical data and laboratory parameters of each group were analyzed and compared, and the relationship among P_{cv-aCO_2} , $P_{cv-aCO_2}/Ca-cvO_2$, the change rate of $P_{cv-aCO_2}/Ca-cvO_2$ and lactate was analyzed. The relationship between the severity and prognosis of sepsis with hyperlactatemia and the above parameters was also analyzed. **Results:** Forty-five patients were included in the final analysis, and three patients were removed due to death or discharge within 24 hours. Twenty patients died and 25 survived eventually; 24-hour SOFA improved in 17 cases, and did not in 28 cases. There were no significant differences in the general clinical data between the two groups before resuscitation. The difference of $P_{cv-aCO_2}/Ca-cvO_2$ at 24 hours after resuscitation and its change rate at 0-24h were statistically significant between the SOFA improved group and the unimproved group (both $P < 0.01$). There was a good correlation between the 24-hour LCR and the change rate of $P_{cv-aCO_2}/Ca-cvO_2$ in 45 patients ($r=0.906$, $P=0.034$). For the prediction of SOFA improvement, the area under ROC curve (AUC) of the change rate of $P_{cv-aCO_2}/Ca-cvO_2$ during the 24 hours after the onset of resuscitation was 0.851. At the cut-off value of 0.307(30.7%), the change rate of $P_{cv-aCO_2}/Ca-cvO_2$ (0-24h) had a sensitivity of 76.5%, a specificity of 92.9% in the prediction of SOFA improvement. ROC analysis of death prediction showed that the area under the $P_{cv-aCO_2}/Ca-cvO_2$ (0-24h) was 0.696, which had no significant statistical difference with the lactate level at 24h. At the cut-off value of 0.181 (18.1%), the change rate of $P_{cv-aCO_2}/Ca-cvO_2$ (0-24h) had a sensitivity of 65%, a specificity of 68% in the prediction of the in-hospital death in septic patients. **Conclusion:** The change rate of $P_{cv-aCO_2}/Ca-cvO_2$ during the 24 hours after the onset of resuscitation can well predict the improvement of organ function in septic patients with hyperlactatemia and the death of septic patients with hyperlactatemia.

Key words: Sepsis; Central venous-arterial carbon dioxide tension to arterial-venous oxygen content ratio; The change rate of central venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference ratio; Central venous-to-arterial carbon dioxide difference; Prognosis

Chinese Library Classification(CLC):R631.2 **Document code:** A

Article ID:1673-6273(2019)16-3073-07

前言

脓毒症是机体对感染的特异性反应导致的危及生命的器官功能障碍,其病情加重和导致死亡重要的原因是组织低灌注^[1]。乳酸常被作为组织低灌注的重要标志^[2],已有多项研究显示乳酸值 ≥ 4 mmol/L与高死亡率相关^[3-5],而乳酸清除率则能进一步反映组织灌注的变化^[2,6,7]。中心静脉动脉二氧化碳分压差/氧含量差的比值($P_{cv-aCO_2}/Ca-cvO_2$)识别无氧代谢的敏感度和特异度均较高,也能反映组织灌注情况。

随着人们对脓毒症认识的深入,2016年SCCM/ESICM提出的Sepsis 3.0诊断标准首次将SOFA评分纳入脓毒症诊断标准,强调器官衰竭是导致脓毒症不良预后的重要原因,更注重早期对脓毒症预后的判断及对多器官功能不全的识别并且动态监测器官功能障碍的过程。Vincent等^[8]回顾分析了在1643例感染患者中最初的24hSOFA评分,发现其与病死率存在良好的相关性。有研究表明SOFA评分的动态变化可以很好评估脓毒症病情的严重程度及其预后^[9]。本研究以第24h的SOFA评分是否改善(改良SOFA评分)做为主要分组依据,主要探讨了 $P_{cv-aCO_2}/Ca-cvO_2$ 的变化率是否可以更好地评估合并高乳酸血症的脓毒症患者的病情严重程度及预测患者预后,以期帮助临床医师尽早制定合理的治疗策略,从而进一步改善脓毒症患者的预后。

1 材料与方法

1.1 研究对象和入选条件

纳入2017年1月到2018年9月就诊上海交通大学医学

院附属仁济医院并于急诊重症监护室住院治疗的合并高乳酸血症(血乳酸值 ≥ 4 mmol/L)的脓毒症患者48例,其中3例因24h内死亡或自动出院脱落,最终纳入45例。

纳入标准:符合严重脓毒症或脓毒症休克的相关诊断标准;年龄 >18 岁;合并高乳酸血症(乳酸 ≥ 4 mmol/L);确诊的24h内收治入住急诊重症监护室;排除标准:怀孕;系统性免疫疾病;恶性肿瘤晚期;急性冠脉综合征;入组24h内死亡;已经存在液体高负荷的临床症状;需要急诊手术的;急性脑血管意外;存在安置中心静脉导管的禁忌症或输血禁忌症。

1.2 治疗方法

收治入急诊重症监护室的准入患者第一时间留置颈内深静脉置管术;留置导尿并监测尿量,监测中心静脉压;进行液体复苏治疗,若液体复苏后如血流动力学仍不稳定,予以血管活性药物(首选去甲肾上腺素)。同时根据2016年脓毒症指南给予相应抗感染、合理的机械通气支持、监测及控制血糖、营养支持、器官功能保护、预防应激性溃疡、预防深静脉血栓以及其他相应治疗。

1.3 数据采集

观察并记录患者的一般资料,包括性别、年龄、APACHE II评分、感染的部位。分别记录液体复苏治疗前0h(T0h)、治疗后6h(T6h)及24h(T24h)等3个时间点的下列指标:中心静脉及动脉血气分析、血乳酸、心率、血压、中心静脉压(CVP)、全血细胞分析以及每h尿量。根据 $[C(a-v)O_2] = Hb \times 1.34 \times (SaO_2 - ScvO_2) + (PaO_2 - PcvO_2) \times 0.03$ 计算 $P_{cv-aCO_2}/CavO_2$ 的值。根据 $[P_{cv-aCO_2}/CavO_2(T0)-$

$P_{cv-aCO_2}/C_{avO_2}(T_{24h})/P_{cv-aCO_2}/C_{avO_2}(T_0)$ 计算 T24h 的 P_{cv-aCO_2}/C_{avO_2} 变化率(%). 根据[血乳酸(T0h)-血乳酸(T24h)]/血乳酸(T0h)计算 T24h 的血乳酸清除率(%).

1.4 统计学分析

应用 SPSS19.0 统计软件进行统计分析, 用 Shapiro-Wilk 法对计量资料进行正态性检验. 符合正态分布的数据以均数 $\pm$ 标准差($\bar{x}\pm s$)表示, 计量资料比较采用 t 检验和独立样本 t 检验. 非正态分布的变量以中位数(上下四分位数)表示, 数据比较采用 u 检验. 变量相关分析采用 Spearman 相关分析. 绘制受试者工作特征曲线(ROC 曲线)计算相关变量指标判断脓毒血症预后的曲线下面积(AUC)、灵敏度、特异度和约登指数, 曲线下面积比较采用 Z 检验. 当 $P<0.05$ 为差异具有统计学意义.

2 结果

2.1 两组患者一般临床资料的比较

共 45 例患者纳入本研究, 包括男性 26 例, 女性 19 例. 感

染部位以肺部最多(24 例), 第二位为泌尿系统(8 例), 次之则是胃肠道感染(6 例), 少见的感染部位有中枢系统(2 例)、皮肤软组织(1 例)以及其他部位感染(4 例). 由于格拉斯哥昏迷指数(GCS)评分主观性较强, 故通过使用 Vincent 的改良 SOFA 评分的变化来评估衰竭器官功能的变化, 改良 SOFA 评分去除了神经系统的 GCS 评分. 评估计算复苏前(T0h)、复苏后 24h(T24h)的 Vincent 改良 SOFA 评分, 前者和后者的差值为改善值 Δ SOFA, Δ SOFA ≥ 2 记为 24hSOFA 评分改善; 治疗前的改良 SOFA 评分=1, 但液体复苏启动后 24h 改良 SOFA 评分=0, 也记为 24hSOFA 评分改善; 其余的归为 24hSOFA 评分未改善. 本次研究中, 改善组 17 例, 未改善组 28 例. 两组复苏前 BMI、收缩压、舒张压、心率、血氧饱和度、中心静脉压、尿量、白细胞计数、血红蛋白、血小板计数、总胆红素、血肌酐比较差异无统计学意义(均 $P>0.05$). 两组患者的一般临床资料比较差异均无统计学意义, 具有可比性(表 1).

表 1 SOFA 评分改善组与未改善组复苏前的一般临床资料的比较

Table 1 Comparison of the general information between the improved and unimproved SOFA group

Variables	Improved group	Unimproved group	P value
BMI(kg/m ²)	20.980 $\pm$ 3.326	23.647 $\pm$ 4.386	0.270
Systolic blood pressure(mmHg)	129 $\pm$ 19.196	114.25 $\pm$ 30.198	0.354
Diastolic blood pressure(mmHg)	64 $\pm$ 14.866	61.375 $\pm$ 16.818	0.781
Heart rate(/min)	97.2 $\pm$ 14.873	97.2 $\pm$ 14.873	0.658
SPO ₂ (%)	100(96,100)	99(93.25,100)	0.622
Central venous pressure(mmH ₂ O)	8.8 $\pm$ 6.76	9.25 $\pm$ 6.756	0.909
Urine volume(mL/h)	42 $\pm$ 23.875	42.969 $\pm$ 27.564	0.950
White blood cells($\times 10^9/L$)	19.454 $\pm$ 8.0168	13.136 $\pm$ 10.698	0.283
Hemoglobin(g/L)	133.8 $\pm$ 39.859	117 $\pm$ 22.456	0.347
Platelets($\times 10^9/L$)	265.4 $\pm$ 95.204	169.5 $\pm$ 146.671	0.223
Total bilirubin(μ mol/L)	16.36 $\pm$ 3.299	19.075 $\pm$ 9.353	0.550
Serum creatinine(μ mol/L)	72(61,147)	108.5(64.5,188.5)	0.435

2.2 两组患者液体复苏不同时刻的乳酸 (Lac)、乳酸清除率 (LCR)、 $P_{cv-aCO_2}/P_{cv-aCO_2}/C_{avO_2}$ 值及其变化率的比较

两组患者间复苏后 24h 的乳酸 (Lac T24h) 及 6-24h(Lac 6-24h)和 0-24h(Lac 0-24h)的乳酸清除率比较均有统计学差异(分别为 $P<0.05$, $P<0.05$, $P<0.01$), 两组患者间复苏后 24h 的 P_{cv-aCO_2}/C_{avO_2} 的值(P_{cv-aCO_2}/C_{avO_2} T24h)及其 0-24h 变化率(P_{cv-aCO_2}/C_{avO_2} 0-24h)比较均有统计学差异意义(均 $P<0.01$), 见表 2。

2.3 复苏前后各时间点的 P_{cv-aCO_2} 值的变化、 P_{cv-aCO_2}/C_{avO_2} 的值及其变化率、乳酸及乳酸清除率之间的相关性分析

24h 的乳酸清除率与 24h P_{cv-aCO_2}/C_{avO_2} 变化率呈显著相关性($r=0.906$, $P=0.034$), P_{cv-aCO_2} 与复苏前、复苏 6h 及复苏 24h P_{cv-aCO_2}/C_{avO_2} 都有显著的相关性 (分别为 $r=0.749$, $P=0.003$; $r=0.707$, $P=0.007$; $r=0.952$, $P=0.012$), 复苏后 24h 的 P_{cv-aCO_2}/C_{avO_2} 的值与 0-24h P_{cv-aCO_2}/C_{avO_2} 变化率呈显

著负相关性($r=-0.813$, $P=0.001$), 复苏后 6h 的乳酸值与 0-6h 乳酸清除率呈显著负相关性($r=-0.894$, $P=0.000$), 而其他各时间点各指标间未发现存在明显相关性。

2.4 ROC 曲线分析

2.4.1 乳酸清除率与 P_{cv-aCO_2}/C_{avO_2} 0-24h 变化率预测改良 SOFA 改善的 ROC 曲线 评估计算复苏前(T0h)、复苏后 24h(T24h)的 Vincent 改良 SOFA 评分, 用 ROC 曲线评价乳酸、乳酸清除率、 P_{cv-aCO_2}/C_{avO_2} 以及 P_{cv-aCO_2}/C_{avO_2} 变化率对高乳酸脓毒症患者 24hSOFA 评分是否能得到改善的预测能力及最佳界值 (根据最大约登指数设立) 时发现: 复苏后 0-24h P_{cv-aCO_2}/C_{avO_2} 变化率、复苏后 6-24h 乳酸清除率以及复苏后 0-24h 乳酸清除率大于等于最佳界值时, 能有效预测 24hSOFA 评分的改善($P<0.05$); 而复苏后 24h P_{cv-aCO_2}/C_{avO_2} 和复苏后 24h 的乳酸小于等于最佳界值时可以有效预测 24hSOFA 评分的改善($P<0.05$)。这 5 个指标在预测 24hSOFA

表 2 两组患者液体复苏不同时刻的乳酸、Pcv-aCO₂、Pcv-aCO₂/Ca-cvO₂ 值及其变化率的比较

Table 2 Comparison of the lactate, Pcv-aCO₂, Pcv-aCO₂/Ca-cvO₂ values and the change rate of Pcv-aCO₂/Ca-cvO₂ at different times of fluid resuscitation between improved and unimproved SOFA group

Variables	Time	Groups		P value
		Improvement group (n=17)	Unimproved group (n=28)	
Lac	T0h	5.7(4.7, 6.8)	7.25(4.55, 9.825)	0.242
	T6h	2.7(1.75, 3.15)	2.5(1.7, 4.925)	0.879
	T24h	1.5(1.4, 2.05)	3.35(1.625, 4.575)	0.034
Lac	0-6h	0.537(0.399, 0.706)	0.616(0.374, 0.726)	1.000
	6-24h	0.348(0.179, 0.519)	0.117(-0.601, 0.291)	0.027
	0-24h	0.705(0.667, 0.761)	0.552(0.452, 0.699)	0.006
Pcv-aCO ₂	T0h	7(6, 9)	7.5(6, 10)	0.671
	T6h	7(5, 9.5)	7.5(6, 9)	0.646
	T24h	5.235± 1.678	6± 2.539	0.277
Pcv-aCO ₂ /Ca-cvO ₂	T0h	0.24(0.175, 0.433)	0.246(0.126, 0.291)	0.308
	T6h	0.169(0.135, 0.293)	0.198(0.138, 0.435)	0.406
	T24h	0.148(0.108, 0.172)	0.225(0.187, 0.287)	0.001
the change rate of Pcv-aCO ₂ /Ca-cvO ₂	0-6h	0.35(-0.351, 0.551)	-0.217(-0.767, 0.382)	0.087
	6-24h	0.233(-0.138, 0.491)	-0.053(-0.264, 0.417)	0.215
	0-24h	0.455(0.277, 0.631)	0.144(-0.317, 0.207)	0.000

评分改善时,复苏后 0-24hPcv-aCO₂/Ca-cvO₂ 变化率的 ROC 曲线下面积最大(AUROC=0.851),最佳界值是 0.307,敏感度是 76.5%,特异度是 92.9%。其余 4 个指标的曲线下面积和复苏后 0-24hPcv-aCO₂/Ca-cvO₂ 变化率的曲线下面积进行 Z 检验无统计学差异($P>0.05$),详见图 1、图 2 和表 3。0h 和 6h 乳酸值、0h、6h 和 24hPcv-aCO₂ 值、0h 和 6hPcv-aCO₂/Ca-cvO₂ 及 6-24h Pcv-aCO₂/Ca-cvO₂ 变化率不能预测 24hSOFA 评分的改善($P>0.05$)。

2.4.2 LCR 与 Pcv-aCO₂/Ca-cvO₂ 0-24h 变化率预测死亡的 ROC

曲线 根据是否院内死亡进一步分成两组,两组患者的一般临床资料无统计学差异($P>0.05$)。用 ROC 曲线评价乳酸、乳酸清除率、Pcv-aCO₂/Ca-cvO₂ 以及 Pcv-aCO₂/Ca-cvO₂ 变化率对高乳酸血症患者院内死亡的预测能力及最佳界值,发现:复苏前(T0h)的乳酸值、复苏后 6h 和 24h 的乳酸值、复苏后 24h 的 Pcv-aCO₂ 值以及复苏后 24hPcv-aCO₂/Ca-cvO₂ 值大于最佳界值时,能有效预测患者院内死亡的发生($P<0.05$);而复苏后 0-24h 乳酸清除率、6-24h 乳酸清除率以及 0-24hPcv-aCO₂/Ca-cvO₂ 值清除率在小于最佳界值时,能有效预测患者院内死亡的发生

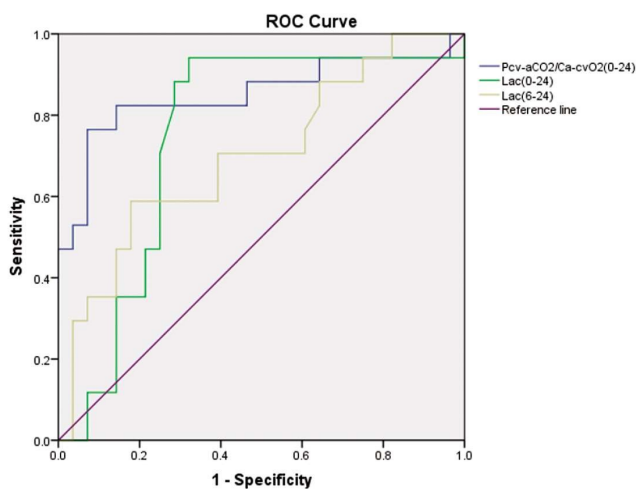


图 1 大于等于最佳界值时预测改良 SOFA 改善的 ROC 曲线

Fig.1 ROC curve for prediction Modified SOFA Score improved when values $\geq$ cut-off

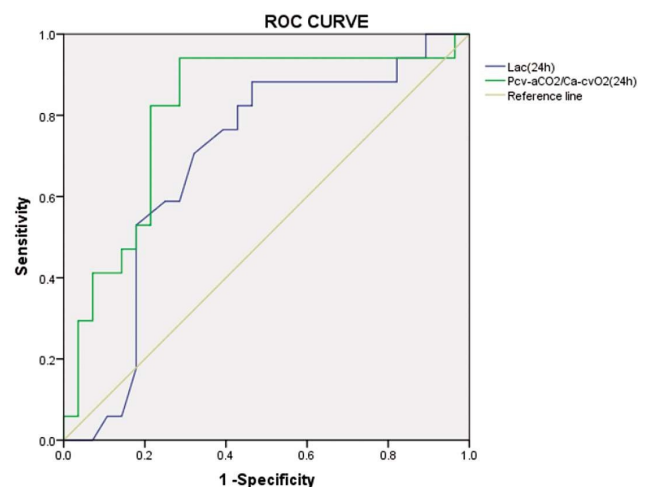


图 2 小于等于最佳界值时预测改良 SOFA 改善的 ROC 曲线

Fig.2 ROC curve for prediction Modified SOFA Score improved when values $\leq$ cut-off

($P < 0.05$)。这 8 个指标预测院内死亡时,复苏后 24h 乳酸值的 ROC 曲线下面积最大(AUROC=0.897),最佳界值是 2.55,敏感度,85%,特异度是 96%。其余 7 个指标的曲线下面积和复苏后 0-24hPcv-aCO₂/Ca-cvO₂ 变化率的曲线下面积进行 Z 检验无统

计学差异($P > 0.05$),见图 3、图 4 和表 4。0h 和 6hPcv-aCO₂ 值、0h 和 6hPcv-aCO₂/Ca-cvO₂ 及 6-24hPcv-aCO₂/Ca-cvO₂ 变化率不能预测院内死亡的发生($P > 0.05$)。

表 3 能有效预测 SOFA 评分改善指标的 AUC 面积的比较

Table 3 Comparison of the areas under the ROC curves for predicting the improvement of SOFA score

Variables	AUC	95%CI	P value*	Cutoff value	Sensitivity/%	Specificity/%	Youden's index	P value **
Pcv-aCO ₂ /Ca-cvO ₂ 0-24h	0.851	0.715-0.986	0.000	0.307	76.500	92.900	0.693	/
Pcv-aCO ₂ /Ca-cvO ₂ 24h	0.811	0.673-0.949	0.001	0.198	94.118	71.429	0.655	0.686
Lac 0-24h	0.748	0.592-0.904	0.006	0.643	94.100	67.900	0.620	0.163
Lac 6-24h	0.699	0.537-0.860	0.027	0.327	58.800	82.100	0.410	0.078
Lac 24h	0.690	0.673-0.949	0.034	2.950	88.235	53.571	0.418	0.135

Note: *P value of ROC curve analysis; **Comparison with the area under the ROC curve of Pcv-aCO₂/Ca-cvO₂ 0-24h.

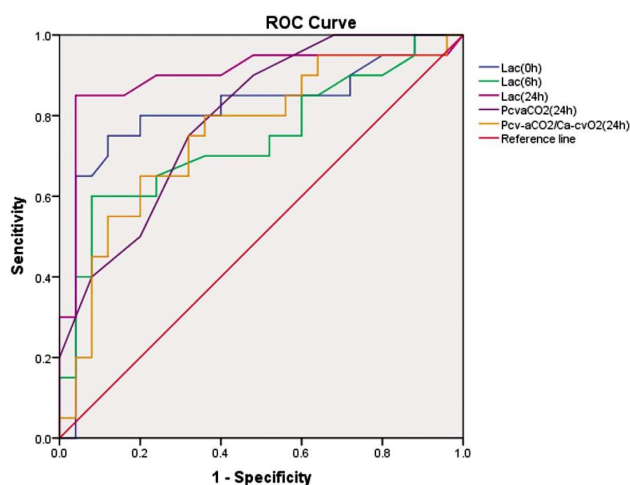


图 3 大于等于最佳界值时预测患者死亡的 ROC 曲线

Fig.3 ROC curves for predicting patient mortality when values $\geq$ cut-off

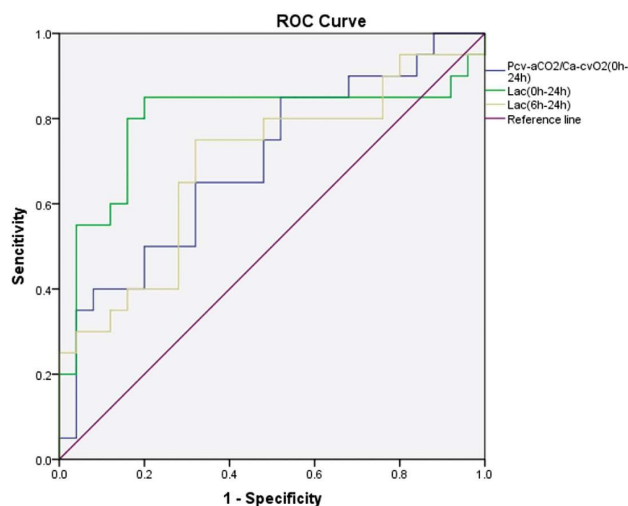


图 4 小于等于最佳界值时预测患者死亡的 ROC 曲线

Fig.4 ROC curves for predicting patient mortality when values $\leq$ cut-off

表 4 能有效预测患者院内死亡指标的 AUC 面积的比较

Table 4 Comparison of the areas under the ROC curves for predicting mortality in the septic patients

Variables	AUC	95%CI	P value*	Cutoff value	Sensitivity/%	Specificity/%	Youden's index	P value**
Lac T24h	0.897	0.786-1.000	0.000	2.550	85.000	96.000	0.810	/
Lac T0h	0.815	0.675-0.955	0.000	7.000	75.000	88.000	0.630	0.180
Pcv-aCO ₂ T24h	0.795	0.668-0.922	0.001	5.500	75.000	68.000	0.430	0.120
Lac 0-24h	0.794	0.639-0.949	0.001	0.656	85.000	80.000	0.650	0.843
Pcv-aCO ₂ /Ca-cvO ₂ T24h	0.754	0.607-0.901	0.004	0.217	65.000	80.000	0.450	0.835
Lac T6h	0.741	0.588-0.894	0.006	3.250	60.000	92.000	0.520	0.482
Pcv-aCO ₂ /Ca-cvO ₂ 0-24h	0.696	0.540-0.852	0.025	0.181	65.000	68.000	0.330	0.266
Lac 6-24h	0.692	0.531-0.853	0.028	0.166	75.000	68.000	0.430	0.257

*P value of ROC curve analysis; **Comparison with the area under the ROC curve of Lac24h.

3 讨论

乳酸是重要的代谢指标,无氧酵解可产生乳酸,乳酸增高是一个明确的组织缺氧的标志。有研究表明脓毒血症患者存在

组织的灌注不足,从而导致细胞的无氧代谢增加,血乳酸水平继而升高,而且高乳酸血症与老年患者的病死率紧密相关^[10],用血乳酸水平反映复苏效果的敏感和可靠性较高^[11]。重症患者在多种因素的影响下,乳酸水平可升高,并一定程度上能反映疾病严重程度^[12],有研究已经证实乳酸的值和乳酸清除率能预测的患者复苏效果和预后^[13,14],动态监测动脉血乳酸清除率比乳酸值有更高的价值^[15]。本研究结果也提示复苏后 0-24h 乳酸清除率有预测 24hSOFA 改善的价值。

正常生理情况下,CO₂是氧代谢的最终产物,正常范围在 2~5 mmHg。生理组织代谢产生的 CO₂通过弥散进入血液,以 HCO₃⁻为主要形式运输。中心静脉-动脉血中的二氧化碳分压差(Pcv-aCO₂)是指 PvCO₂与 PaCO₂之差,在休克的病理状态下,Pv-aCO₂的值会升高^[16]。Pcv-aCO₂/Ca-cvO₂值作为进一步使用 Ca-vO₂对 Pcv-aCO₂进行校正的结果,可以更有力地作为乏氧代谢的标志物^[17,18]。Pcv-aCO₂/Ca-cvO₂比值能够检测“正在进行的”无氧代谢,并且比乳酸反应更快,可以为复苏早期阶段的乳酸变化提供重要的预后信息^[19]。复苏后的 Pcv-aCO₂/Ca-cvO₂值与患者的 8h 乳酸清除率负相关^[20],复苏后的高 Pcv-aCO₂/Ca-cvO₂值还可以预示着患者后续的乳酸清除能力不佳^[21]。有研究显示脓毒症休克患者 Pcv-aCO₂/Ca-cvO₂的升高对于识别无氧代谢的敏感度和特异度均较高,且与预后不佳相关,Pcv-aCO₂/Ca-cvO₂≥ 1.8 可预测液体反应性^[22,23]。Pcv-aCO₂/Ca-cvO₂值升高表明在 MAP 和 ScvO₂正常的脓毒症休克患者中乳酸清除率减小,以动态监测组织灌注是否改善,有助于在治疗过程中,判断终止复苏的时机,同时 Pcv-aCO₂/Ca-cvO₂值升高与死亡率存在显著相关,而且 Pcv-aCO₂/Ca-cvO₂值的升高提示随后几小时内乳酸清除率有降低的可能性^[21],使其变化率更具有临床应用的价值。研究已证实高乳酸血症患者 24h 内乳酸浓度降低 > 50%的患者比清除率低的患者更容易存活^[24],乳酸清除率与死亡率存在明显相关^[25]。中心静脉血氧饱和度、乳酸的清除率等被推荐用于脓毒症和脓毒症休克的患者,作为反映组织缺氧的标志物和复苏的终点参照^[26]。

本研究结果显示两组患者间复苏后 24h 的 Pcv-aCO₂/Ca-cvO₂的值及其 0-24h 变化率存在统计学差异,且 24h Pcv-aCO₂/Ca-cvO₂变化率与 24h 的乳酸清除率有良好的相关性。因此,我们推测 Pcv-aCO₂/Ca-cvO₂变化率一定程度可提示疾病的进展情况,可能作为预测疾病预后的参考依据。多项研究结果显示 Pcv-aCO₂/Ca-cvO₂的变化以及 Pcv-aCO₂的变化可以提示在无氧代谢中机体微循环组织的氧耗情况,评估在早期复苏时脓毒症患者的微循环情况^[27-30]。本研究 ROC 曲线结果显示 Pcv-aCO₂/Ca-cvO₂(0-24h)变化率既能有效预测高乳酸脓症患者 24hSOFA 的改善,也可以预测患者院内死亡的发生。预测 24hSOFA 改善时,ROC 曲线下面积在所有参数中最大,优于乳酸、乳酸清除率和 Pcv-aCO₂/Ca-cvO₂,虽然不存在统计学上的差异,可能和我们收集的病例数不够多有关。预测患者院内死亡的发生时,ROC 曲线下面积小于各时间点乳酸、乳酸清除率(0-24h)以及 Pcv-aCO₂/Ca-cvO₂(24h)值,但不存在统计学差异。综上,我们推测 Pcv-aCO₂/Ca-cvO₂的值及其变化率在高

乳酸的脓毒症血症患者中除了可以作为评价乏氧代谢及微循环情况的指标,还可以与乳酸的清除率一样,可以更多角度地提供评估患者复苏效果及预后的信息。根据最大约登指数设立的最佳界值,也可能成为治疗终点的指标之一。

通常认为休克患者早期的高乳酸血症多为循环衰竭时的组织缺氧所致,除乳酸生成增多以外,乳酸清除减少也是高乳酸血症的另一个原因。在脓毒症中,乳酸水平升高可能是由于乳酸清除率的降低、乳酸过度地产生或前两者共同的结果,因此高水平的乳酸可能是器官功能障碍的表现,本次研究样本量较小,入组的高乳酸脓症患者中缺少肝功能障碍等其他可能导致乳酸增高的情况,导致本次研究结果可能存在一定程度的偏移。而且,乳酸清除率、Pcv-aCO₂/Ca-cvO₂仅体现了患者全身无氧代谢变化的情况,针对于局部低氧及低灌注情况,本研究缺乏组织灌注的局部监测以及 CO、CI 等有创监测指标,一定程度上局限了本研究的结果。

综上所述,本研究结果表明 Pcv-aCO₂/Ca-cvO₂的值及其变化率可以有效预测高乳酸脓毒症患者的器官功能改善情况,也能有效预测脓症患者院内死亡的发生。可能未来作为脓毒症液体复苏终点参考指标。

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