

心脏与非心脏术后乳酸水平对重症患者预后影响的比较：附 549 例病例分析

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【摘要】目的 比较心脏术后与非心脏术后患者乳酸平均值和乳酸变异度对预后的影响,并探讨入重症医学科(ICU)乳酸首值和首个24 h乳酸最高值对预后的预测价值。**方法** 采用回顾性研究方法,选择2014年9月至2016年9月郑州大学第一附属医院ICU收治的心脏术后和非心脏术后患者(术后立即转入ICU、年龄 ≥ 18 岁、ICU住院时间 ≥ 1 d)。根据乳酸平均值将两组患者再分为正常乳酸组(0~2 mmol/L)、相对高乳酸组(2~4 mmol/L)、绝对高乳酸血症(>4 mmol/L),分析乳酸平均值与患者预后的关系。根据乳酸变异度四分位数将两组患者再分为4组,采用多因素回归模型评估不同乳酸变异度3组的死亡风险。根据入ICU乳酸首值、首个24 h乳酸最高值绘制受试者工作特征曲线(ROC),评价两项指标对预后的预测价值。**结果** 纳入268例心脏术后和281例非心脏术后患者,两组患者基线资料均衡。① 乳酸平均值与ICU病死率:在正常乳酸水平(0~2 mmol/L)时,心脏术后和非心脏术后患者病死率差异无统计学意义[7.9%(14/177)比6.5%(14/217),优势比(*OR*)=1.245, *P*=0.694];在相对高乳酸水平(2~4 mmol/L)时,两组差异也无统计学意义[33.3%(12/36)比23.7%(9/38), *OR*=1.611, *P*=0.442];在绝对高乳酸水平(>4 mmol/L)时,非心脏术后患者病死率明显高于心脏术后患者[69.2%(18/26)比43.6%(24/55), *OR*=0.344, *P*=0.036]。② 乳酸变异度($\text{mmol} \cdot \text{L}^{-1} \cdot \text{d}^{-1}$)四分位数与ICU死亡风险:非心脏术后组乳酸变异度与ICU病死率呈线性关系, <0.50 (参照), $0.50 \sim 0.85$ (*OR*=1.17, *P*=0.87), $0.85 \sim 1.44$ (*OR*=4.86, *P*=0.04), >1.44 (*OR*=22.66, *P* <0.01),且在较高变异度(0.85~1.44和 >1.44)两组差异有统计学意义;心脏术后组死亡风险呈逐渐升高的趋势,为 <0.55 (参照), $0.55 \sim 1.25$ (*OR*=0.61, *P*=0.61), $1.25 \sim 2.43$ (*OR*=3.46, *P*=0.10), >2.43 (*OR*=12.14, *P* <0.01),死亡风险只在最高变异度(>2.43)组出现差异。③ ROC曲线分析显示:两组患者入ICU首个24 h乳酸最高值预测预后的ROC曲线下面积(AUC)均大于入ICU乳酸首值,对预后评价的敏感度及特异度也较高。心脏术后和非心脏术后患者首个24 h乳酸最高值预测预后的AUC分别为0.877、0.875,截断值分别为5.35 mmol/L、5.65 mmol/L,敏感度为81.6%、67.9%,特异度为93.8%、96.1%。**结论** 非心脏术后患者应更积极控制高乳酸血症和乳酸波动。用24 h乳酸最高值评价术后患者预后的预测价值更大。

【关键词】 24 h乳酸最高值; 乳酸平均值; 乳酸变异度; 心脏术后; 非心脏术后; 预后
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Effect of lactic acid levels on the prognosis of critically ill patients after cardiac and non-cardiac surgery: an analysis of 549 cases Sun Rongqing, Chao Ke, Yang Hongfu

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【Abstract】Objective To compare the impact of mean lactate concentration and lactate variability on postoperative outcome after cardiac surgery and non-cardiac surgery in critical patients, and to explore the prognostic value of the first lactate and the highest lactate during the first 24 hours in intensive care unit (ICU). **Methods** A retrospective study was conducted. The postoperative patients of cardiac surgery and non-cardiac surgery who were transferred to ICU immediately, and who were at least 18 years old and whose ICU lengths of stay were at least 1 day, and who were admitted to ICU of the First Affiliated Hospital of Zhengzhou University from September 2014 to September 2016 were enrolled. According to the mean lactate concentration, the patients were divided into normal lactate group (0-2 mmol/L), relatively high lactate group (2-4 mmol/L), and absolute high lactate group (>4 mmol/L), and the relationship between the mean lactate concentration and the prognosis of patients was analyzed. According to the degree of lactate variability, the patients were divided into four groups, and multivariate regression models were used to assess the risk of death in three different lactate variability groups. The value of the first lactate value and the highest lactate value during the first 24 hours in ICU were evaluated to predict the prognosis by the receiver operating characteristic (ROC) curve. **Results** 268 postoperative patients of cardiac surgery and 281 cases of non-cardiac surgery were selected, and the characteristic of the baseline data in the two groups was balanced. ① Mean lactate concentration and mortality in ICU: in the normal lactate group (0-2 mmol/L), there was no significant difference

in mortality between the post-cardiac operative group and post-non-cardiac operative group [7.9% (14/177) vs. 6.5% (14/217), odds ratio (OR) = 1.245, $P = 0.694$]. In the relatively high lactate group (2–4 mmol/L), there was no significant difference between the two groups, either [33.3% (12/36) vs. 23.7% (9/38), OR = 1.611, $P = 0.442$]. In the absolute high lactate group (> 4 mmol/L), ICU mortality in post-non-cardiac operative group was obviously higher than that of post-cardiac operative group [69.2% (18/26) vs. 43.6% (24/55), OR = 0.344, $P = 0.036$]. ② The ranges of lactate variability per quartile ($\text{mmol} \cdot \text{L}^{-1} \cdot \text{d}^{-1}$) and ICU mortality risk: there was a linear relationship between lactate variability and ICU mortality in post-non-cardiac operative group, < 0.50 (reference), 0.50–0.85 (OR = 1.17, $P = 0.87$), 0.85–1.44 (OR = 4.86, $P = 0.04$), > 1.44 (OR = 22.66, $P < 0.01$), and there was a significant difference between the two groups in the high degree of variability (0.85–1.44 and > 1.44). The risk of death after cardiac surgery tended to increase, < 0.55 (reference), 0.55–1.25 (OR = 0.61, $P = 0.61$), 1.25–2.43 (OR = 3.46, $P = 0.10$), > 2.43 (OR = 12.14, $P < 0.01$), and the risk of death only showed difference in the highest degree of variation (> 2.43). ③ ROC curve showed that the area under ROC curves (AUC) of the highest lactate in 24 hours were larger than that of the first lactate in both groups, with higher sensitivity and specificity. In the post-cardiac operative group and post-non-cardiac operative group, the AUC of the highest lactate in the first 24 hours were 0.877 and 0.875, the cut-off values were 5.35 mmol/L and 5.65 mmol/L, the sensitivity were 81.4% and 67.9%, and the specificity were 93.8% and 96.1%, respectively. **Conclusions** Patients with post-non-cardiac operation should be more active in controlling hyperlactatemia and lactate variability. The highest lactate in the first 24 hours maybe one of the indicator for the assessment of the prognosis of the postoperative patients.

【Key words】 24-hour maximum lactate; Mean lactate concentration; Lactate variability; Post-cardiac surgery; Post-non-cardiac surgery; Prognosis

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乳酸作为无氧代谢产物,是组织低灌注和缺氧的生物标志物及代谢指标^[1-2]。高乳酸血症在重症患者中最为常见,并且与患者的病死率相关,危重患者的血乳酸值常高于 2 mmol/L^[3]。导致高乳酸血症的原因包括乳酸产生过多(包括导致氧分压降低的肺部疾病、心源性休克、脓毒性休克、低血红蛋白血症致氧气携带能力下降、氰化物中毒和恶性肿瘤等)以及乳酸清除不足[包括肝脏疾病、糖异生抑制、丙酮酸脱氢酶(硫胺素)缺乏和氧化磷酸化解耦联等]^[3-6]。研究表明,成人和儿童心脏术后高血清乳酸水平与死亡风险增高和不良预后有关^[7-9];胃肠道术后、胰腺术后、创伤术后高乳酸血症也与预后不良有关^[10-12]。本研究通过比较心脏术后与非心脏术后患者乳酸水平的变化,探讨其对预后的预测价值。

1 资料与方法

1.1 研究对象的选择:采用回顾性研究方法,分析 2014 年 9 月至 2016 年 9 月本院重症医学科(ICU)收治的术后患者的临床资料。

1.1.1 纳入标准:术后立即转入 ICU;年龄 ≥ 18 岁;ICU 住院时间 ≥ 1 d。

1.1.2 排除标准:术前循环功能不稳定,出现高乳酸血症者;术前肝肾功能衰竭者;正在服用二甲双胍降糖药物的糖尿病患者;临床资料缺失者。

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(审批号:2014-LW-93),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:① 收集患者的一般资

料,如性别、年龄、体重指数(BMI)、手术部位、手术时机;入 ICU 第 1 个 24 h 的急性生理学与慢性健康状况评分系统 II (APACHE II)评分;机械通气(MV)时间、ICU 住院时间、总住院时间、结局。根据手术部位将患者分为心脏术后组和非心脏术后组。② 取动脉血测得乳酸,记录患者 ICU 期间的乳酸首值、首个 24 h 乳酸最高值、乳酸平均值和乳酸变异度。乳酸变异度反映的是患者在 ICU 每天血乳酸的波动值,这种方法改良自 Hermanides 等^[13],最先应用于反映血糖波动与 ICU 预后的影响。另外,根据乳酸变异度的四分位数将患者分为 4 组;根据乳酸平均值分为正常乳酸组(0~2 mmol/L)、相对高乳酸组(2~4 mmol/L)、绝对高乳酸组(> 4 mmol/L)。

1.3 统计学分析:使用 SPSS 21.0 软件对数据进行统计分析。符合正态分布的计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验。计数资料组间比较采用 χ^2 检验。使用多自变量回归模型分析乳酸变异度与 ICU 死亡风险之间的关联。以正常乳酸组作为参考,根据人口统计学(年龄、性别)、BMI、疾病严重程度(APACHE II 评分)、手术部位、手术时机进行校正。以乳酸首值、24 h 乳酸最高值绘制受试者工作特征曲线(ROC),计算 ROC 曲线下面积(AUC)。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 不同手术部位两组患者基线资料比较(表 1):两组患者间性别、年龄、24 h APACHE II 评分、BMI、手术时机构成差异均无统计学意义(均 $P > 0.05$),说明两组基线资料均衡,具有可比性;两组 MV 时

间、ICU住院时间、总住院时间差异也无统计学意义(均 $P > 0.05$),说明两组疾病严重程度相当。

表1 基线资料及住院时间在不同手术部位两组患者间的比较

指标	心脏术后组 (n = 268)	非心脏术后组 (n = 281)	χ^2/t 值	P 值
性别[例(%)]			1.157	0.316
男性	187(69.8)	184(65.5)		
女性	81(30.2)	97(34.5)		
年龄(岁, $\bar{x} \pm s$)	56.71 ± 12.48	56.81 ± 17.07	0.069	0.945
BMI(kg/m ² , $\bar{x} \pm s$)	24.23 ± 2.35	24.63 ± 2.66	0.655	0.561
手术部位[例(%)]				
冠脉/普外	115(42.9)	92(32.7)		
大动脉/骨外	70(26.1)	84(29.9)		
瓣膜/神外	70(26.1)	64(22.8)		
其他	13(4.9)	41(14.6)		
手术时机[例(%)]			2.342	0.123
择期	207(77.2)	201(71.5)		
急诊	61(22.8)	80(28.5)		
APACHE II(分, $\bar{x} \pm s$)	18.46 ± 6.03	18.87 ± 6.54	0.730	0.466
MV时间(d, $\bar{x} \pm s$)	5.92 ± 0.37	4.87 ± 0.39	1.934	0.053
ICU住院时间(d, $\bar{x} \pm s$)	9.98 ± 5.99	9.12 ± 8.17	1.349	0.178
总住院时间(d, $\bar{x} \pm s$)	33.48 ± 20.47	30.75 ± 19.96	1.520	0.129

注: BMI 为体重指数, APACHE II 为急性生理学与慢性健康状况评分系统 II, MV 为机械通气, ICU 为重症医学科

2.2 乳酸平均值、乳酸变异度与术后患者 ICU 病死率的关系

2.2.1 乳酸平均值与病死率的关系(表2):随着乳酸水平升高,不同手术部位两组患者 ICU 病死率逐渐升高。根据乳酸平均值分组显示,正常乳酸组、相对高乳酸组非心脏术后患者 ICU 病死率与心脏术后患者相比差异无统计学意义(均 $P > 0.05$);但绝对高乳酸组非心脏术后患者 ICU 病死率明显高于心脏术后患者($P < 0.05$)。

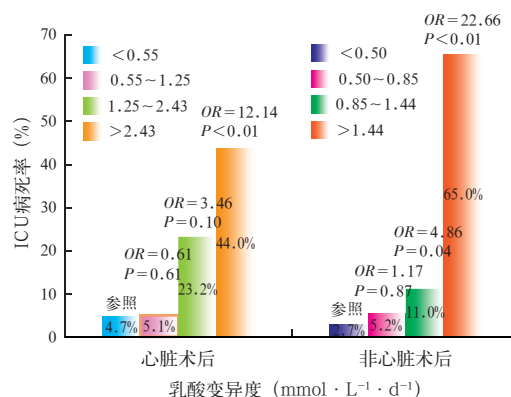
2.2.2 乳酸变异度与病死率的关系(图1):根据两组患者乳酸变异度($\text{mmol} \cdot \text{L}^{-1} \cdot \text{d}^{-1}$)的四分位数分组,心脏术后患者分为 < 0.55 (参照)、 $0.55 \sim 1.25$ 、 $1.25 \sim 2.43$ 和 > 2.43 组;非心脏术后患者分为 < 0.50 (参照)、 $0.50 \sim 0.85$ 、 $0.85 \sim 1.44$ 和 > 1.44 组。结果显示,心脏术后患者的死亡风险随血糖变异度增加呈逐渐增高趋势;在较低变异度(< 0.55 和 $0.55 \sim 1.25$)

表2 不同水平乳酸平均值各组心脏术后与非心脏术后成人患者 ICU 病死率比较

组别	术后患者	例数(例)	病死率[% (例)]	OR 值	95%CI	P 值
正常乳酸组	心脏	177	7.9(14)	1.245	0.577 ~ 2.687	0.694
	非心脏	217	6.5(14)			
相对高乳酸组	心脏	36	33.3(12)	1.611	0.581 ~ 4.466	0.442
	非心脏	38	23.7(9)			
绝对高乳酸组	心脏	55	43.6(24)	0.344	0.128 ~ 0.925	0.036
	非心脏	26	69.2(18)			

注: 正常乳酸组乳酸 $0 \sim 2 \text{ mmol/L}$, 相对高乳酸组乳酸 $2 \sim 4 \text{ mmol/L}$, 绝对高乳酸组乳酸 $> 4 \text{ mmol/L}$; ICU 为重症医学科, OR 为优势比, 95%CI 为 95% 可信区间

两组之间病死率相当, 较高变异度($1.25 \sim 2.43$)组病死率有所升高, 在最高变异度(> 2.43)组死亡风险差异有统计学意义($P < 0.01$)。非心脏术后患者乳酸变异度与 ICU 病死率呈线性关系, 随着乳酸变异度增大, 病死率明显增高; 在 $0.85 \sim 1.44$ 和 > 1.44 两组差异出现统计学意义(均 $P < 0.05$)。心脏术后组乳酸变异度较非心脏术后组大, 但病死率低。



注: ICU 为重症医学科, OR 为优势比

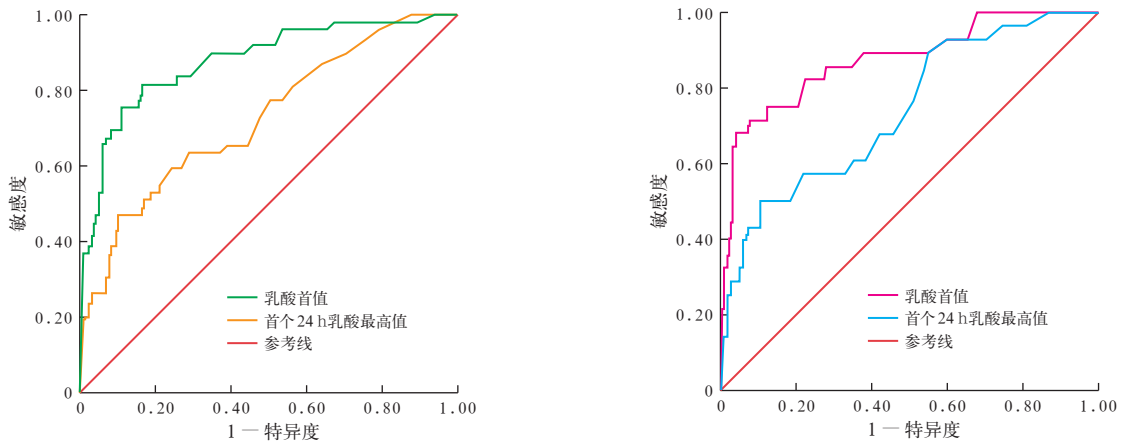
图1 心脏术后和非心脏术后患者乳酸变异度与 ICU 病死率的关系

2.3 入 ICU 乳酸首值、首个 24 h 乳酸最高值对两组术后患者预后的预测价值(表3; 图2):入 ICU 乳酸首值对不同手术部位两组患者预后的预测价值较低。入 ICU 首个 24 h 乳酸最高值对两组术后患者预后的 AUC 均大于乳酸首值的 AUC, 对预后评价的敏感度及特异度也较高。

表3 入 ICU 乳酸首值、首个 24 h 乳酸最高值对不同手术部位成人患者预后的预测价值

指标	组别	AUC	95%CI	P 值	截断值	敏感度(%)	特异度(%)	阳性预测值(%)	阴性预测值(%)	约登指数
乳酸首值	心脏术后组	0.726	0.644 ~ 0.803	0.000	5.00	53.1	89.9	51.2	88.2	0.368
	非心脏术后组	0.740	0.641 ~ 0.835	0.000	3.85	50.0	89.3	35.9	93.7	0.414
24 h 乳酸最高值	心脏术后组	0.877	0.819 ~ 0.935	0.000	5.35	81.6	93.8	52.8	95.4	0.654
	非心脏术后组	0.875	0.799 ~ 0.952	0.000	5.65	67.9	96.1	54.3	96.9	0.668

注: ICU 为重症医学科, AUC 为受试者工作特征曲线下面积, 95%CI 为 95% 可信区间



注：ICU 为重症医学科，ROC 曲线为受试者工作特征曲线

图2 入ICU 乳酸首值、首个24 h 乳酸最高值对心脏术后(左)和非心脏术后(右)患者预后评估的ROC 曲线

3 讨论

有氧糖酵解是为细胞提供能量和产生三磷酸盐的主要途径。然而,当有氧糖酵解受损时,细胞通过厌氧糖酵解增加葡萄糖的利用;通过厌氧糖酵解产生三磷酸酯约为有氧糖酵解效率的6.7%^[14]。厌氧糖酵解还可产生丙酮酸盐,其通过乳酸脱氢酶进行氧化还原耦联相互转化,产生乳酸盐。术后重症患者常出现高血糖及糖代谢障碍,当厌氧糖酵解增多时,乳酸随之增多^[15]。在健康人群中,存在乳酸产生和清除的连续循环,确保血乳酸浓度处于较低水平,当两者平衡被打破时就会造成高乳酸血症^[16]。

1834年Scherer首次报道了血乳酸水平的升高与重症患者的发病率和病死率有关^[17]。目前血乳酸水平的测定被广泛用于评估组织灌注情况,实验研究明确证实了组织缺氧与高乳酸血症之间的关系。传统上,危重患者的高乳酸被认为是氧气供应不足导致的厌氧代谢产物^[18]。有研究表明,心脏术后患者在入ICU即刻及术后6、12h的乳酸水平与术后不良事件有关^[19]。而非心脏术后患者乳酸变化水平是否与心脏术后不良事件一致?两者之间乳酸变化水平对患者的临床治疗是否具有重要指导意义?本研究中我们发现,在血乳酸浓度>2 mmol/L时,心脏术后患者死亡风险明显大于非心脏术后患者;同时我们发现,非心脏术后患者乳酸变异度>1.44 mmol·L⁻¹·d⁻¹时病死率超过50%,而心脏术后患者乳酸变异度>2.43 mmol·L⁻¹·d⁻¹时病死率接近50%。我们在对乳酸变异度的分析中未对ICU住院期间乳酸测量的频率进行校正,然而我们对疾病的严重程度作出了判断,发现其与乳酸测量频率和ICU病死率明显相关。当乳酸以恒定的速度不断变

化时,乳酸变异度与测量次数无关;同样,当乳酸没有变化时,乳酸变异度与测量次数也无关。实际上,乳酸变异度大时,乳酸测量频率增加,获得的变异度可信性也会增加。我们用APACHE II评分对疾病严重程度进行了校正。虽然缺乏使用APACHE II评分来准确预测心脏手术患者病死率的证据,但这种调整是目前最好的方法^[20]。基于上述结果,在ICU患者临床诊治中,对于非心脏术后患者应更加积极改善循环功能,纠正高乳酸血症的病因。

在对重症患者预后的预测中,乳酸清除率是一个很好的预测指标^[21-22]。研究表明,在临床干预后观察乳酸的变化,动态监测的乳酸清除率可以预测预后。本研究为回顾性研究,虽无临床干预措施,但证实了乳酸变异大则预后不良这一临床现象。乳酸清除率是个比值,而乳酸变异度是具体的数值。假如测量3次乳酸,第1次与第3次相同,第2次乳酸下降,这时乳酸清除率则提示为好转、又加重,单凭乳酸清除率无法判断患者病情是恶化还是好转,而乳酸变异度则是明显增大的,根据本研究的结果提示预后不良,说明乳酸变异度对预后的预测可能更加敏感。给予临床干预后,乳酸变异度的变化是否还能预测预后以及与乳酸清除率相比哪个预测价值更高仍需进一步研究证实。

健康者乳酸浓度为(1.0±0.5) mmol/L,严重疾病患者乳酸浓度<2 mmol/L时被认为处于正常水平;此外,2 mmol/L的临界值被认为是一个保守的阈值。Shapiro等^[23]认为乳酸浓度>4 mmol/L可以作为严重组织低灌注的标志,也是预测患者预后的一个重要指标。Pölönen等^[24]的研究表明,对于接受心脏手术的患者,将乳酸浓度标准化作为治疗目

标与病死率和住院时间有关。虽然有研究已经描述了乳酸水平高于 3 mmol/L 与手术危重患者的恶化结果相关,且这一研究讨论了这些患者乳酸值的适当范围,但有关心脏术后和非心脏术后患者严重组织低灌注血乳酸浓度的临界值尚无统一标准^[25]。本研究中我们比较了入 ICU 乳酸首值和首个 24 h 乳酸最高值对心脏术后及非心脏术后严重组织低灌注血乳酸浓度的临界值差异,发现首个 24 h 乳酸最高值可以更好地反映患者严重组织低灌注情况,优于现有报道的临界值^[26]。24 h 乳酸值对评估感染性休克患者预后同样具有较高的应用价值^[27]。

综上所述,与心脏术后患者相比,非心脏术后患者在临床诊疗中应更加密切监测乳酸变化,避免乳酸剧烈波动,及时改善组织灌注,纠正组织缺氧;入 ICU 首个 24 h 乳酸最高值可以更好地反映心脏术后和非心脏术后患者严重的组织低灌注,对临床患者诊治具有良好的指导意义。

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