

乳酸改良的快速序贯器官衰竭评估预测脓毒血症预后的系统评价和 meta 分析

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摘要 目的:评价快速序贯器官衰竭评估(qSOFA)系统与乳酸改良的快速序贯器官衰竭评估(LqSOFA)系统对脓毒血症预后进行早期预测的效能。方法:计算机检索 PubMed、EMBase、Medline、Cochrane 图书馆、维普中文科技期刊数据库、万方数据库,检索时限为建库至 2022 年 5 月,收集采用 qSOFA 和 LqSOFA 两项评分预测脓毒血症预后的研究,进行筛选和质量评价,采用 Stata 15.1 统计软件进行数据分析,使用双变量 meta 分析模型评价两项评估量表在预测高死亡率方面的效能。采用双变量随机效应回归模型对研究的灵敏度、特异性、诊断优势比(DOR)、阳性似然比(PLR)、阴性似然比(NLR)进行综合分析。构建汇总受试者工作特征(ROC)曲线以评估诊断准确性。结果:共纳入 7 项研究、26 937 例患者。qSOFA 与 LqSOFA 均与脓毒血症患者较高死亡风险相关,采用随机效应模型,合并风险比(RR)分别为 1.46(95% CI:1.23 ~ 1.74)和 1.21(95% CI:1.08 ~ 1.35),均有统计学差异(P 均 < 0.0001)。在预测死亡方面,LqSOFA 具有更高的灵敏度 0.82(95% CI:0.71 ~ 0.90),qSOFA 具有更高的特异性 0.74(95% CI:0.59 ~ 0.85)。结论:qSOFA 和 LqSOFA 对脓毒血症患者的高死亡风险均有一定的预测效能,LqSOFA 灵敏度更高,对早期预后预测更有价值。

关键词 脓毒血症; 乳酸; 快速序贯器官衰竭评估; 预后; Meta 分析

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A systematic review and meta-analysis of qSOFA and LqSOFA in predicting the prognosis of sepsis YANG Wei¹, LI Chen-xi², ZHOU Yue-chen¹, ZHANG Shu-juan¹. ¹Department of Emergency and Traumatic Surgery; ²Oncological Department of Oral and Maxillofacial Surgery, the First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, China
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Abstract Objective: To systematically review the efficacy of quick sequential organ failure assessment (qSOFA) score and lactate-modified quick sequential organ failure assessment (LqSOFA) score in early prediction of the prognosis of sepsis to provide evidence-based reference for clinical practice. Methods: Available publications were searched from PubMed, EMBase, Medline, the Cochrane Library, VIP and Wanfang database. The retrieval time was from the establishment of the database to May 2022. We collected studies with two scales for prognostic prediction of sepsis and evaluated the quality of studies that met the inclusion criteria. Stata 15.1 statistical software was applied for meta-analysis. We used a bivariate meta-analysis model to determine the prognostic value in predicting mortality. The bivariate random-effects regression model was used to pool the individual sensitivity, specificity, diagnostic odds ratio (DOR), positive likelihood ratio (PLR), and negative likelihood ratio (NLR). The summary receiver operating characteristic curve (SROC) was constructed to assess the overall diagnostic accuracy. Results: A total of 7 studies with a total of 26 937 patients were included. Both qSOFA and LqSOFA scoring scales were associated with a higher risk of death in patients with sepsis. The combined hazard ratios (RR) calculated with a random-effects model were 1.46 (95% CI: 1.23, 1.74) and 1.21 (95% CI: 1.08, 1.35) respectively, with a statistical difference ($P < 0.0001$). Compared the performance of qSOFA and LqSOFA in predicting mortality, LqSOFA had better sensitivity of 0.82 (95% CI: 0.71, 0.90) while qSOFA had better specificity of 0.74 (95% CI: 0.59, 0.85). Conclusion: Both qSOFA and LqSOFA scores were strongly related to the mortality in sepsis. By contrast with qSOFA, LqSOFA was more sensitive and valuable in predicting the prognosis of sepsis in the early stage.

Key words Sepsis; Lactate; qSOFA; Prognosis; Meta-analysis

脓毒血症是急诊危重病人严重的并发症之一,死亡率高达 20% ~ 40%^[1~3]。早期评估并及时治疗至关重要,学者们相继提出了多种快速简单的急诊评价方法^[4],其中快速序贯器官衰竭评估(quick Sequential Organ Failure Assessment, qSOFA)具有方便、快捷等优点^[5]。研究表明,乳酸改良的快速序贯器官衰竭评估(lactate-modified qSOFA, LqSOFA)评分量表结合床边乳酸和 qSOFA,能快速预测脓毒血症患者死亡率^[6]。本研究比较 qSOFA 和 LqSOFA 预测脓毒血症预后的价值,为临床决策提供循证参考。

资料与方法

1. 检索策略:计算机检索 PubMed、EMBase、Medline、Cochrane 图书馆、维普中文科技期刊数据库、万方数据库,检索时限为建库至 2022 年 5 月。此外,追溯纳入文献的参考文献,以补充获取相关文献。检索采取主题词和自由词相结合的方式。英文检索词包括“sepsis”“septicopyemia”“emergency medicine”“emergency department”“quick sequential organ failure assessment”“qSOFA”“lactate”“modified qSOFA”“lactate-modified quick sequential organ failure assessment”“LqSOFA”“prognosis”“prediction”“all-cause mortality”“death rate”“fatality rate”;中文检索词包括“脓毒血症”“脓毒败血症”“急救医学”“急诊科”“qSOFA”“LqSOFA”“乳酸”“改良 qSOFA”“预测”“死亡率”“预后”。

2. 数据提取及文献质量评估:资料提取由 2 名研究员分别独立进行文献筛选、评价和整理数据,对结果进行核对,通过阅读题目和摘要剔除明显不符合纳入标准的文献,进一步阅读全文后筛选出符合的研究,采用讨论的方法使意见达成一致,意见不一致时由第三方参与讨论并决定。如果相关文献数据缺失或不清楚,尽可能与文献通信作者联系以获取准确数据,无法获取数据或信息不全的文献予以排除。

纳入标准:①qSOFA 和 LqSOFA 量表应用于脓毒血症预后判断;②研究人群为确诊或疑似脓毒血症的患者,其种族、国籍、病程不限;③预测指标 qSOFA ≥ 1 分和 LqSOFA ≥ 2 分;④评判 qSOFA 和 LqSOFA 预测价值的指标:灵敏度、特异性、阳性似然比(positive likelihood ratio, PLR)、阴性似然比(negative likelihood ratio, NLR)、诊断比数比(diagnostic odds ratio, DOR)、汇总受试者工作特征曲线(summary receiver operating characteristic curve, SROC)的曲线下面积(area under curve, AUC)。排

除标准:①综述文章;②信函、会议摘要;③无法获得真阳性值(true positive value, TP)、假阴性值(false negative value, FN)、假阳性值(false positive value, FP)和真阴性值(true negative value, TN)等相关数据,无法建立 2 $\times$ 2 列表进行统计分析的文献;④专家意见;⑤非中英文报道。

3. 定义:qSOFA 指标包括 3 项^[7]:①呼吸频率 ≥ 22 次/min;②收缩压 ≤ 100 mmHg (1 mmHg = 0.133 kPa);③格拉斯哥昏迷评分 ≤ 13 分;满足上述 1 项记为 1 分,最高 3 分;LqSOFA 评价标准是以 qSOFA 为基础,满足血清乳酸水平 ≥ 2 mmol/L,加 1 分^[8]。

4. 统计学分析:使用 Stata 15.1 软件的 MIDAS 模块进行统计分析。根据 qSOFA (≥ 1 分)或 LqSOFA (≥ 2 分)对全因死亡率的影响,确定 TP、FN、FP 和 TN。采用相对风险比(RR)评估 qSOFA 和 LqSOFA 的预测价值,将随机效应或固定效应模型合并。计算 I^2 统计量以评估统计异质性,当 $I^2 > 50\%$,则选择随机效应模型,否则使用固定效果模型。采用双变量随机效应回归模型计算灵敏度、特异性、DOR、PLR 和 NLR 的集合。生成 SROC 以评估总体诊断准确性。发表偏倚采用 Deek's 漏斗图进行分析。

结果

1. 文献检索结果:共检索出相关论文 713 篇,其中 PubMed 316 篇、EMBase 183 篇、The Cochrane Library 1 篇、Medline 166 篇、维普 19 篇、万方 28 篇。阅读标题和摘要后,初步排除 102 篇,初步阅读全文,删除不同数据库中存在的重复文献、实验研究、系统综述共 580 篇,共获得 31 篇文献,再经过详细评估,排除 24 篇,最终纳入 7 项研究^[6, 8~13],共 26 937 例患者。

2. 纳入研究基本特征及方法学质量评价:使用纽卡斯尔-渥太华量表(Newcastle-Ottawa Scale, NOS)^[14]从 3 个方面评价 7 篇入选文献的研究方法:研究小组的选择(0 ~ 4 分)、小组的可比性(0 ~ 2 分)、结果确定的质量(0 ~ 3 分)。总分为 0 ~ 9 分, > 5 分为可接受的方法设计。纳入的 7 篇研究的基本特征及评估情况见表 1。

3. Meta 分析结果:纳入 7 篇研究^[6, 8~13]显示, qSOFA ≥ 1 分和 LqSOFA ≥ 2 分均与脓毒血症死亡率高度相关。采用随机效应模型(全部文献的异质性检验 I^2 分别为 83.6% 和 65.2%),合并风险比 RR = 1.46、1.21 (P 均 < 0.0001),见图 1、2。

表 1 纳入 7 篇研究的基本特征及 NOS 评分

作者/ 年份	研究类型	地区	年龄 (岁, $\bar{x} \pm s$)	样本量 (例)	男性 (例)	不良预后 [例(%)]	结局	诊断标准 (分)	NOS 评分 (分)
Aksu 2019 ^[6]	前瞻性 单中心	土耳其	76.2 $\pm$ 7.7	799	422	228(28.5)	院内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 3	8
Liu 2020 ^[8]	回顾性 单中心	中国	58.3 $\pm$ 17.1	821	528	173(21.1)	院内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	6
Machado 2020 ^[9]	前瞻性 多中心	巴西	64(41 ~ 80)	5460	2519	766(14)	院内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	9
Daga 2021 ^[10]	前瞻性 单中心	印度	48.46 $\pm$ 15.28	150	87	73(48.67)	7d 内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	8
Baumann 2019 ^[11]	回顾性 多中心	美国	60(46 ~ 73)	2584	1341	465(18)	院内死亡 + 重症率	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	7
Hu 2022 ^[12]	回顾性 单中心	中国	幸存者 (50.13 $\pm$ 18.32) 非幸存者 (58.91 $\pm$ 20.92)	936	509	101(10.8)	院内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	6
Toker 2021 ^[13]	回顾性 单中心	土耳其	72.5 $\pm$ 13.7	976	462	191(19.6)	院内死亡	qSOFA $\geq$ 1、 LqSOFA $\geq$ 2	6

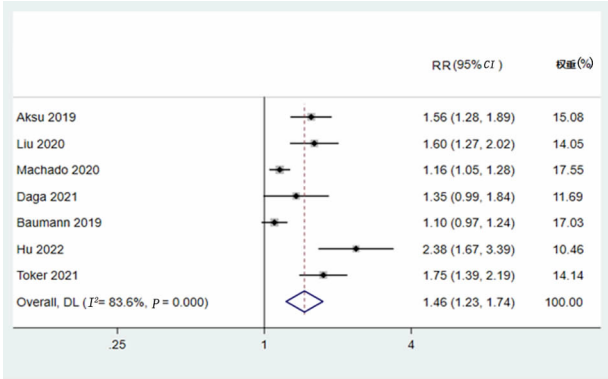


图 1 SOFA $\geq$ 1 分预测脓毒血症死亡率的森林图

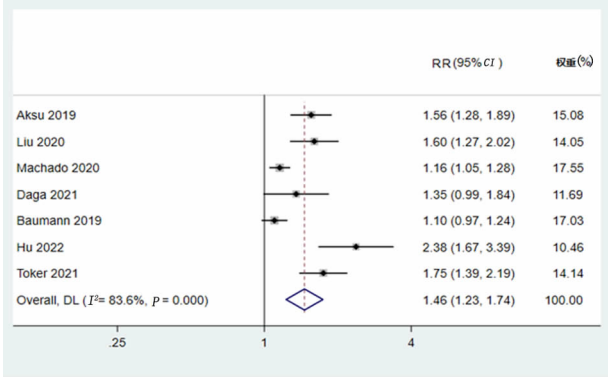


图 2 LqSOFA $\geq$ 2 分预测脓毒血症死亡率的森林图

双变量随机效应回归模型分析显示,qSOFA 的合并灵敏度为 0.67,特异性为 0.74;LqSOFA 的合并灵敏度为 0.82,特异性为 0.57。二者的 SROC 合并 AUC 面积比较,无明显统计学差异($P>0.05$),见表 2,图 3、4。

4. 发表偏倚检测结果:Deek's 漏斗图所示,各研究分布基本对称,2 组数据不存在发表偏倚($P>0.05$),见图 5、6。

讨论

研究表明,结合床边乳酸 qSOFA 的改良 LqSOFA 是一种更有价值的快速预测脓毒血症患者死亡率的工具^[15~19]。Shetty 等^[18,19]的研究纳入了 12 555 例脓毒血症患者,发现添加乳酸 ≥ 2 mmol/L 附加条件或 LqSOFA 评分 ≥ 2 ,可将识别不良预后的灵敏度提高到 65.5%。Liu 等^[20]比较了血清乳酸、qSOFA 评分和 SOFA 评分预测成人脓毒血症死亡率的准确性,但作者并没有同期评估 LqSOFA 的诊断效能。

本研究分析发现 qSOFA ≥ 1 分与 LqSOFA ≥ 2 分的阳性结果均与脓毒血症的死亡率相关(P 均 <0.05),对于早期判断脓毒血症的预后,两者均有良好的应用价值。双随机变量模型合并显示两者的总体诊断价值差异并不明显,但 LqSOFA 在预测脓毒血症预后方面的灵敏度高于 qSOFA,故对于早期预测不良预后方面 LqSOFA 更具有优势。

Askim 等^[21]对 1535 例成人患者进行的一项前瞻性研究发现,qSOFA 在预测急诊科出现住院死亡率方面的灵敏度和特异性分别为 16% 和 96%。根据其他研究的汇总,qSOFA 预测死亡率的灵敏度为 13% ~ 90%,特异性为 86% ~ 96%^[22~24],可见 qSOFA 虽然有较高的特异性,但灵敏度跨度较大,在

表 2 预测脓毒血症不良预后的 qSOFA 和 LqSOFA 标准的混合性能特征

评分系统	灵敏度 (95% CI)	特异性 (95% CI)	PLR (95% CI)	NLR(95% CI)	DOR(95% CI)	AUC (95% CI)
qSOFA	0.67(0.51 ~ 0.79)	0.74(0.59 ~ 0.85)	2.6(1.8 ~ 3.7)	0.45 (0.34 ~ 0.61)	6(4 ~ 9)	0.76(0.72 ~ 0.8)
LqSOFA	0.85(0.71 ~ 0.9)	0.57(0.46 ~ 0.67)	1.9(1.6 ~ 2.2)	0.31 (0.21 ~ 0.46)	6(4 ~ 9)	0.74(0.7 ~ 0.78)

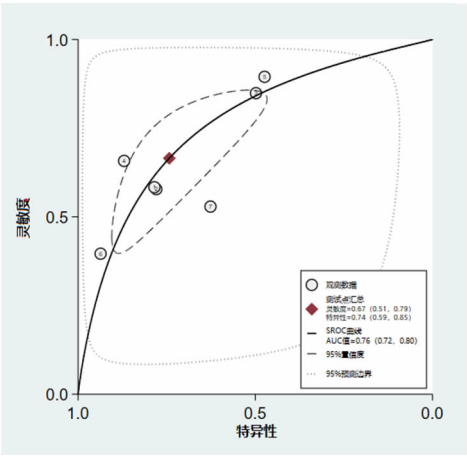


图 3 qSOFA≥1 分预测脓毒血症预后的 SROC 曲线

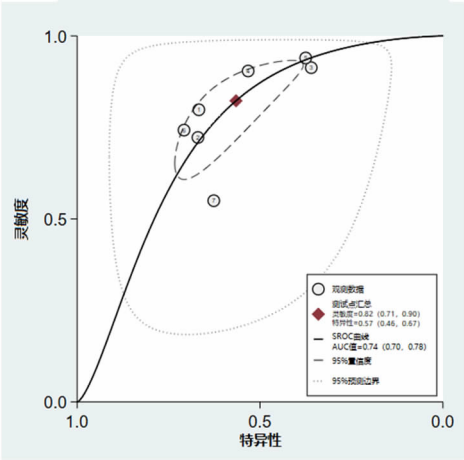


图 4 LqSOFA≥2 分预测脓毒血症预后的 SROC 曲线

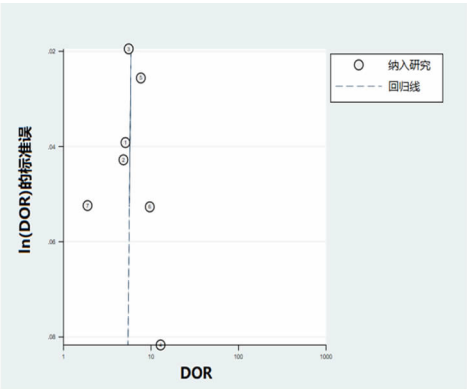


图 5 qSOFA≥1 分的发表偏倚 Deek's 漏斗图(P=0.92)

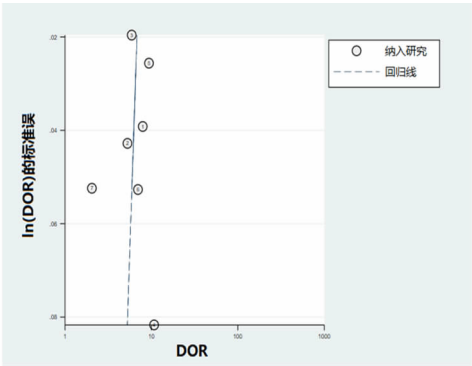


图 6 LqSOFA≥2 分的发表偏倚 Deek's 漏斗图(P=0.73)

早期判断脓毒血症的不良预后表现不佳,与本研究结论相似。

Liu 等^[8]在一项 821 例患者的回顾性研究中引入床边血清乳酸并提出 LqSOFA,结果显示 LqSOFA 优于 qSOFA。本研究结果纳入了该研究的数据,合并之后的数据显示 LqSOFA 较 qSOFA 具有优势。此外,已有研究表明乳酸作为脓毒血症死亡率的预测因子是有效的^[25~27],乳酸有望提高 qSOFA 预测脓毒血症死亡率的有效性^[12,28]。在 qSOFA 的基础上进行综合评分,可以帮助急诊医师将 2 个指标结合起来进行临床决策。

综上所述,qSOFA 和 LqSOFA 的阳性结果均与脓毒血症的死亡率密切相关。LqSOFA 比 qSOFA 灵敏度更高,对早期预测脓毒血症的预后更有价值。需要开展多中心大样本量的前瞻性研究进一步验证。本研究为回顾性研究,受客观条件限制,可能一定程度影响研究质量;meta 分析本身存在较大异质性;需要扩大样本量。

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