

LAR联合MHR对急性上消化道出血患者预后的预测价值

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摘要 目的 研究血清乳酸/白蛋白比值(LAR)、单核细胞/高密度脂蛋白胆固醇比值(MHR)早期动态升高对于急性上消化道出血患者预后的预测价值。**方法** 收集2019年1月至2021年10月北部战区总医院急诊医学科就诊的440例急性上消化道出血患者的临床资料。根据是否发生急性上消化道出血主要临床结局事件(因任何原因死亡,再次出现消化道出血,需要急诊外科手术和急诊介入手术)分为有主要临床结局事件组($n=91$)和无主要临床结局事件组($n=349$)。采用logistic回归分析影响患者出现主要临床结局的危险因素。采用受试者操作特征(ROC)曲线、净重新分类指数(NRI)、整体鉴别指数(IDI)、校准曲线分析LAR、MHR及两者联合对急性上消化道出血患者主要临床结局事件的预测效能。**结果** Logistic回归分析结果显示,LAR、MHR升高,年龄增大,血红蛋白及红细胞压积减少等是急性上消化道出血患者出现主要临床结局的独立危险因素(均 $P < 0.05$)。相关性分析显示,HB与MHR呈负相关($r = -0.165, P < 0.01$),HB与LAR呈负相关($r = -0.247, P < 0.01$)。ALT($r = 0.165$)、PT($r = 0.178$)与LAR呈正相关(均 $P < 0.01$),PT与MHR呈正相关($r = 0.142, P < 0.01$);ROC曲线分析结果显示LAR、MHR及二者联合预测患者不良结局的曲线下面积分别为:0.665(95%CI:0.598~0.731)、0.863(95%CI:0.821~0.905)、0.886(95%CI:0.845~0.927),LAR、MHR最佳截断值分别为0.332、0.715。IDI、NRI及校准曲线结果显示,LAR联合MHR对急性上消化道出血是否出现主要临床结局的预测价值优于单独使用LAR及MHR;LAR联合MHR的灵敏度为84.6%,特异度为88.5%。**结论** LAR、MHR早期动态升高对于预测急性上消化道患者主要临床结局事件具有较高的临床价值,且二者联合的预测价值优于LAR及MHR单独使用。

关键词 急性上消化道出血; 乳酸/白蛋白比值; 单核细胞/高密度脂蛋白胆固醇比值; 预后

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Predictive value of LAR plus MHR for prognosis of patients with acute upper gastrointestinal bleeding

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Abstract Objective To study the predictive value of serum lactate/albumin ratio (LAR) and monocyte/high-density lipoprotein cholesterol ratio (MHR) for the prognosis of patients with acute upper gastrointestinal bleeding. **Methods** Clinical data were collected from 440 patients with acute upper gastrointestinal bleeding treated at the Emergency Department of General Hospital Northern Theater Command from January 2019 to October 2021. According to whether the main clinical outcome event of acute upper gastrointestinal bleeding occurred (death for any reason, recurrence of gastrointestinal bleeding, requirement for emergency surgery, interventional surgery), patients were divided into the main clinical outcome event group (group A, $n=91$) and the no-main clinical outcome event group (group B, $n=349$). A logistic regression analysis analyzed the factors influencing the main clinical outcome events. Receiver operating characteristic (ROC) curves, integrated discrimination improvement (IDI), net reclassification index (NRI), and calibration curves were used to analyze the predictive efficacy of an early dynamic elevated LAR alone, MHR alone, and a combination thereof. **Results** The logistic regression analysis showed that elevated LAR and MHR, increased age, and reduced hemoglobin and hematocrit levels were independent risk factors for the occurrence of the main clinical outcomes (all $P < 0.05$). A correlation analysis showed that hemoglobin level was negatively correlated with MHR and LAR ($r = -0.165$ and -0.247 , all $P < 0.01$). Alanine aminotransferase (ALT) and prothrombin time (PT) were positively correlated with LAR ($r = 0.165$ and 0.178 , all $P < 0.01$). PT was positively correlated with MHR ($r = 0.142, P < 0.01$). The ROC curve analysis results showed that the area under the curve of LAR alone, MHR alone, and the combination thereof was 0.665 (95% CI: 0.598–0.731), 0.863 (95% CI: 0.821–0.905), and 0.886 (95% CI: 0.845–0.927), while the cut-off values of LAR and MHR were 0.332 and 0.715, respectively. The IDI, NRI, and calibration curve results showed that the predictive value of LAR plus MHR for the occurrence

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of the main clinical outcome event was better than that of either alone. The sensitivity and specificity of LAR plus MHR were 84.6% and 88.5%, respectively. **Conclusion** Early dynamic elevation of LAR and MHR has high predictive value for the main clinical outcome events in patients with acute upper gastrointestinal bleeding, and the predictive value of LAR plus MHR is better than that of either alone.

Keywords acute upper-gastrointestinal bleeding; lactate /albumin ratio; monocyte/ high-density lipoprotein cholesterol ratio; prognosis

急性上消化道出血是临床常见的危重症,尽管在药物、介入和手术等治疗方法上都取得了进展,但其死亡率仍在14%左右^[1-2]。因此,早期风险分层对于降低急性上消化道出血患者死亡率及改善患者预后至关重要。目前临床上有多种方法评估急性上消化道出血患者病情的严重程度,包括格拉斯哥布拉奇福德评分(Glasgow Blatchford Score, GBS)、罗克韦尔评分(Rockwell Score, RS)、AIMS65评分系统等^[3-4]。由于这些评估方法复杂且需要内镜检查结果、明确诊断结果以及患者潜在疾病等临床资料,故难以在急诊使用。近期已有研究^[5-7]证明,血清乳酸/白蛋白比值(lactate /albumin ratio, LAR)与单核细胞/高密度脂蛋白胆固醇比值(monocyte/ high-density lipoprotein cholesterol ratio, MHR)是新型炎症标志物,而且可以预测急诊急危重症患者的预后情况。另外,早期研究^[8]发现急性上消化道出血患者的不良结局与炎症之间存在关系,血清炎症指标升高可以作为消化道出血患者死亡等不良结局的预测因素($P < 0.001$)。因此,推测LAR、MHR可能与急性上消化道出血病情严重程度及预后有关;而且目前尚未有评分系统将患者LAR、MHR早期动态变化作为评估急性上消化道出血预后的指标。本研究探讨LAR、MHR水平及二者联合对急性上消化道出血患者主要临床结局事件的预测价值。

1 材料与方法

1.1 研究对象及分组

收集2019年1月至2021年10月就诊于北部战区总医院急诊医学科的急性上消化道出血患者的临床资料。纳入标准:(1)患者出现呕血和黑便症状,伴或不伴头晕、心悸、面色苍白、心率增快、血压降低等周围循环衰竭征象并确诊;(2)年龄 ≥ 18 岁;(3)消化道出血部位经手术、血管造影、钡剂造影或内镜检查证实;(4)临床实验室检查数据(血常规、白蛋白、血乳酸及脂蛋白等)完整。排除标准:(1)患有慢

性肾脏病、下消化道出血及血液系统疾病引起的急性上消化道出血;(2)院外转诊患者。急诊内科患者超过1次时,选择首次急诊入院病历资料纳入研究。本研究获得我院伦理委员会批准[伦审Y(2022)218号]。

最终纳入440例患者。根据急诊治疗期间是否出现主要临床结局事件(因为任何原因死亡;再次出现消化道出血;需要急诊外科手术和急诊介入手术)^[9],将患者分为有主要临床结局事件组($n = 91$, A组)和无主要临床结局事件组($n = 349$, B组)。

1.2 方法

通过电子病历系统收集患者一般资料(性别、年龄、心率、血压、呼吸、体温)、就诊后早期(24 h内)实验室检查结果(白细胞、单核细胞绝对值、血红蛋白、红细胞压积、血小板、乳酸、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、总胆固醇、白蛋白、凝血功能指标、总胆红素、直接胆红素、丙氨酸转氨酶、天冬氨酸转氨酶、血尿素氮、血肌酐等)。并进一步计算获得LAR和MHR。

1.3 统计学分析

采用SPSS 25.0软件进行统计学分析,符合正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较采取独立样本 t 检验,非正态分布的计量资料以 $M(P_{25} \sim P_{75})$ 表示,2组间比较采用Mann-Whitney秩和检验或者Kruskal-Wallis秩和检验。计数资料以率(%)表示,组间比较采用 χ^2 检验或Fisher确切概率法。采用Spearman秩相关分析变量间的相关性。危险因素评估采用单因素分析和多因素logistic回归分析。绘制受试者操作特征(receiver operating characteristic, ROC)曲线分析指标的诊断性能,通过ROC曲线下面积(area under curve, AUC)评估LAR、MHR及二者联合对急性上消化道出血患者预后的预测效能,最佳截断值采用约登指数最大值法进行计算,同时计算灵敏度和特异度。采用RStudio2023软件计算净重新分类指数(net reclassification index, NRI)和整体鉴别

指数 (integrated discrimination improvement, IDI), 并绘制校准曲线图。检测水准: $\alpha_{\text{双侧}}=0.05$ 。

2 结果

2.1 2组患者各项临床指标比较

440例患者年龄63(52~70)岁, 男283例, 女157

例。A、B组患者年龄、舒张压、凝血酶原时间、D-二聚体、国际标准化比值、单核细胞、乳酸、血红蛋白、红细胞压积、谷氨酸氨基转移酶、白蛋白、高密度脂蛋白胆固醇比较差异有统计学意义(均 $P < 0.05$), 其他指标比较差异均无统计学意义(均 $P > 0.05$)。见表1。

表1 2组患者临床指标比较
Tab.1 Comparison of clinical indexes between two groups

Item	Total (n = 440)	Group A (n = 91)	Group B (n = 349)	t/Z	P
Age (year)	63 (52-70)	65 (58-70)	62 (50-70)	-2.26	0.02
Male [n (%)]	283 (64.30)	55 (60.40)	228 (65.30)	-0.87	0.39
SBP (mmHg)	123.56 ± 26.62	120.40 ± 23.73	124.38 ± 27.29	1.27	0.20
DBP (mmHg)	74.00 (64.00-81.00)	69.00 (59.00-80.00)	75.00 (65.00-82.00)	-2.37	0.02
Respiration rate (time/min)	17 (16-18)	18 (16-19)	17 (16-18)	-1.07	0.28
Heart rate (beat/min)	88 (78-102)	88 (78-103)	88 (77-102)	-0.88	0.38
Temperature (°C)	36.5 (36.2-36.6)	36.5 (36.2-36.6)	36.5 (36.2-36.6)	-0.69	0.49
White blood cells (×10 ⁹ /L)	8.50 (5.93-11.38)	8.50 (6.40-10.60)	8.50 (5.90-11.40)	-0.32	0.75
Hemoglobin (g/L)	95.00 (68.25-116.00)	60.00 (52.00-84.00)	95.00 (75.00-123.50)	-8.39	<0.01
Hematocrit (L/L)	0.27 (0.21-0.35)	0.20 (0.16-0.25)	0.29 (0.23-0.37)	-8.19	<0.01
Platelet (×10 ⁹ /L)	207.70 ± 101.38	211.01 ± 131.97	206.83 ± 91.97	-0.35	0.18
Blood urea nitrogen (mmol/L)	8.77 (5.87-13.40)	9.47 (6.09-13.23)	8.48 (5.85-13.52)	-0.85	0.40
Creatinine (μmol/L)	68.55 (55.49-88.05)	65.20 (53.70-103.20)	69.00 (55.90-85.70)	-0.48	0.63
Total bilirubin (μmol/L)	9.20 (5.80-15.90)	7.90 (5.30-16.70)	9.30 (6.00-15.55)	-0.95	0.34
Direct bilirubin (μmol/L)	2.90 (1.80-6.28)	2.90 (1.60-5.30)	2.90 (1.90-6.40)	-1.08	0.28
ALT (U/L)	16.61 (11.18-28.70)	13.68 (9.60-28.26)	16.94 (11.73-29.89)	-2.00	0.04
AST (U/L)	20.00 (15.24-32.66)	19.67 (13.56-32.79)	20.04 (15.56-32.50)	-1.08	0.28
Prothrombin time (s)	14.30 (13.50-15.68)	15.10 (14.20-16.60)	14.10 (13.40-15.35)	-4.70	<0.01
INR	1.11 (1.03-1.27)	1.20 (1.07-1.34)	1.09 (1.02-1.23)	-3.80	<0.01
D-dimer (mg/L)	0.62 (0.27-1.53)	0.84 (0.30-2.01)	0.56 (0.26-1.42)	-2.21	0.03
Lactate (mmol/L)	1.30 (0.90-1.90)	1.70 (0.90-2.70)	1.30 (0.90-1.70)	-3.20	<0.01
Albumin (g/L)	34.10 (29.83-38.48)	33.20 (29.00-38.10)	34.20 (30.10-38.55)	-8.82	<0.01
Monocyte (×10 ⁹ /L)	0.43 (0.32-0.61)	0.65 (0.49-0.82)	0.39 (0.29-0.53)	-8.70	<0.01
HDL (mmol/L)	1.35 (1.08-1.60)	0.91 (0.78-1.06)	1.45 (1.26-1.65)	-11.37	<0.01
LDL (mmol/L)	3.21 (2.30-4.21)	3.29 (2.42-4.25)	3.21 (2.25-4.18)	-1.10	0.27
Triglyceride (mmol/L)	1.75 (1.08-2.42)	1.67 (0.84-2.46)	1.78 (1.14-2.41)	-1.16	0.24
MHR	0.28 (0.20-0.38)	0.68 (0.55-0.87)	0.28 (0.20-0.38)	-12.08	<0.01
LAR	0.03 (0.02-0.04)	0.05 (0.03-0.08)	0.03 (0.02-0.04)	-4.64	<0.01

SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

2.2 LAR、MHR与各项临床指标的相关性分析

双变量Pearson检验结果显示, 年龄、舒张压、红细胞压积、谷氨酸氨基转移酶、INR及D-二聚体与患者LAR、MHR值不相关, 血红蛋白与MHR负相关($r = -0.165, P < 0.01$), 凝血酶原时间与MHR正相

关($r = 0.142, P < 0.01$)。血红蛋白与LAR负相关($r = -0.247, P < 0.01$), 凝血酶原时间、谷氨酸氨基转移酶与LAR值呈正相关(均 $P < 0.01$)。见表2。

2.3 影响主要临床结局事件的多因素分析

将单因素分析有统计学意义($P < 0.05$)指标

(LAR、MHR、年龄等)作为自变量,将是否出现主要临床结局事件作为因变量进行二元logistic回归模型分析。结果显示,血清乳酸、单核细胞、LAR、MHR升

高,年龄增大,白蛋白、高密度脂蛋白胆固醇、血红蛋白及红细胞压积减少是患者出现主要临床结局的独立危险因素(均 $P < 0.05$)。见表3。

表2 LAR及MHR与各项临床指标的相关性 (r)
Tab.2 Correlation between LAR or MHR and relevant clinical indicators (r)

Item	Age	Hemoglobin	Diastolic pressure	Hematocrit	Alanine aminotransferase	Prothrombin time	International normalized ratio	D-dimer
MHR	0.016	-0.165 ¹⁾	-0.077	-0.032	-0.002	0.142 ¹⁾	0.040	0.077
LAR	0.046	-0.247 ¹⁾	-0.090	-0.025	0.165 ¹⁾	0.178 ¹⁾	0.083	0.047

1) $P < 0.01$.

表3 急性上消化道出血患者出现主要临床结局危险因素的多因素logistic回归分析

Tab.3 Multi-factor logistic regression analysis of main clinical outcome risk factors in patients with acute upper gastrointestinal bleeding

Variable	OR	95%CI	P
LAR	3.142	1.504-6.560	0.002
MHR	48.728	20.099-118.139	<0.001
Age	1.030	1.005-1.056	0.019
Hemoglobin	0.962	0.948-0.975	0.001
D-dimer	0.965	0.870-1.070	0.753
Diastolic blood pressure	1.000	0.973-1.011	0.400
Hematocrit	0.983	0.000-0.793	0.038
Alanine aminotransferase	1.003	0.994-1.012	0.480
Prothrombin time	1.076	0.943-1.227	0.277
International normalized ratio	0.561	0.211-1.492	0.247
Lactate	1.247	1.038-1.874	0.001
Albumin	0.271	0.699-0.850	<0.001
Monocyte	11.634	3.384-34.715	0.002
High-density lipoprotein cholesterol	0.006	0.000-0.631	0.001
Constant	0.047	-	0.037

2.4 MHR、LAR及二者联合预测患者发生主要临床结局事件的ROC曲线分析

ROC曲线分析如图1所示,LAR、MHR、LAR联合MHR的AUC分别为0.665 (95%CI:0.598~0.731)、0.863 (95%CI:0.821~0.905) 和0.886 (95%CI:0.845~0.927)。LAR最佳截断值为0.332,灵敏度52.7%,特异度80.5%; MHR最佳截断值0.715,灵敏度90.1%,特异度81.4%; LAR联合MHR的灵敏度84.6%,特异度88.5%。NRI和IDI分析显示,LAR联合MHR均优于单独应用LAR或MHR的预测价值。见表4。

校准曲线结果显示,LAR与MHR对急性上消化道出血患者出现主要临床结局的预测近似于实际情况,故效果理想。见图2。

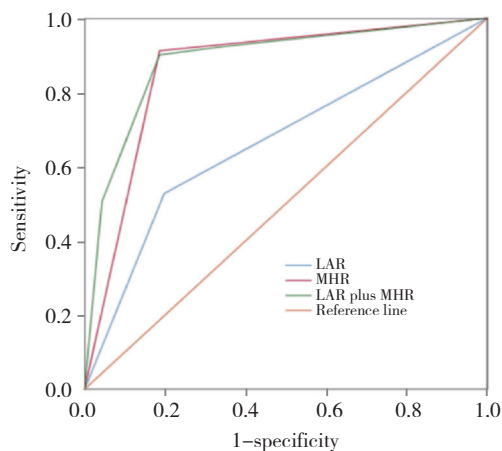


图1 LAR、MHR和二者联合预测患者出现主要临床结局事件的ROC曲线分析

Fig.1 ROC curve of LAR, MHR, and LAR combined with MHR for occurrence of major clinical outcome events

表4 NRI和IDI分析
Tab.4 Analysis of NRI and IDI

Item	NRI	P1	IDI	P2
LAR combined with MHR vs. LAR	0.604	<0.001	0.441	<0.001
LAR combined with MHR vs. MHR	0.043	0.023	0.035	0.020

LAR, lactate/albumin ratio; MHR, monocyte/high-density lipoprotein cholesterol ratio; NRI, net reclassification index; IDI, integrated discrimination improvement.

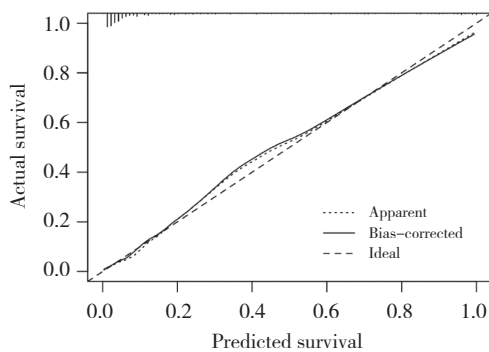


图2 校准曲线
Fig.2 Calibration curve

3 讨论

急性上消化道出血发病急、病情危重,患者会在短时间内因大量失血而出现失血性休克、死亡情况,因此对急性上消化道出血患者早期进行精准病情评估非常必要。目前,患者病情评分系统多且运用复杂,急诊科就诊患者早期使用存在局限性;另外,医生决策存在主观性等因素。因此预测急性上消化道出血患者客观指标显得尤为重要。

研究^[9-10]显示,乳酸是与上消化道出血危重患者死亡率相关的重要因素。血白蛋白水平反映个体营养状况,低白蛋白血症与患者不良预后和死亡率相关^[11-12]。SHADVAR等^[13]研究发现LAR对预测休克患者的预后具有更好的表现,能及时反映患者死亡率及重症监护室住院时间(95%CI:0.918~0.987, $P < 0.001$)。BOU CHEBL等^[6]研究发现急诊监护室脓毒症患者中,LAR比单独使用血乳酸更能预测住院患者死亡率($P < 0.001$)。

单核细胞能直接影响血小板和内皮细胞,从而诱导促炎细胞因子和血栓形成。早期研究发现,浸润性单核细胞是出血后血管痉挛的中心介质,外周血管病和出血性脑血管病表现出早期单核细胞持续增加^[14];另外,单核细胞表达的组织因子与血小

板结合对血栓也产生调节作用^[15]。高密度脂蛋白胆固醇具有抗血栓、抗炎和抗氧化作用^[16]。体外实验研究^[17]发现高密度脂蛋白胆固醇可作为内在和外在凝血级联的调节剂。患者急性消化道出血后出现贫血、心动过速和动脉低血压引起的肝细胞缺血,导致肝功能进一步降低,高密度脂蛋白胆固醇生成减少。高密度脂蛋白胆固醇和单核细胞参与许多炎症反应,近来有研究^[18-19]将MHR作为新的炎症标志物。YI等^[20]研究发现较高的MHR可以预测接受血管介入治疗的动脉瘤性蛛网膜下腔出血患者的不良结局(最佳截断值为1.5, $P < 0.05$)。YOU等^[21]研究发现,急性脑出血患者中,较高的MHR与出院时残疾或死亡风险增加有关。

本研究多因素logistic回归分析结果显示,MHR与LAR每增加1个单位,患者出现主要临床结局的风险增加48.728和3.142倍($P < 0.001$),而且血清乳酸、单核细胞及年龄增大,白蛋白、高密度脂蛋白胆固醇、血红蛋白及红细胞压积减少是患者出现主要临床结局的独立危险因素(均 $P < 0.05$)。相关性分析结果显示,血红蛋白与LAR、MHR均呈负相关(均 $P < 0.01$),血红蛋白水平越低,LAR与MHR越高;而谷氨酸氨基转移酶、凝血酶原时间与LAR值呈正相关,凝血酶原时间与MHR值呈正相关(均 $P < 0.01$)。LAR、MHR及二者联合预测患者不良结局的AUC分别为0.665、0.863、0.886,提示LAR及MHR对急性上消化道出血患者的预测效能均较好;且二者联合的预测价值优于LAR及MHR单独使用。LAR联合MHR预测与单独使用LAR或MHR比较的NRI值分别为0.604、0.043;IDI值分别为0.441、0.035。NRI、IDI及校准曲线分析显示,LAR联合MHR预测效能优于单独使用LAR或MHR(均 $P < 0.05$)。

综上所述,LAR、MHR早期动态升高对于预测急性上消化道患者主要临床结局事件具有较高的

临床价值,且二者联合的预测价值优于LAR及MHR单独使用。本研究属于单中心回顾性研究,临床决策受到医师主观选择、患者经济情况以及治疗意愿等因素影响,部分患者因资料不全剔除而增加了选择偏倚,因此需增大样本量,进行多中心研究进一步论证。

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