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消化系统疾病专题·论著

外周血 RLP-C、RC/HDL-C 表达与高脂血症性急性胰腺炎患者病情严重程度及复发的关系*

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摘要: 目的 探讨血清残粒脂蛋白胆固醇(RLP-C)、残余胆固醇/高密度脂蛋白胆固醇(RC/HDL-C)与高脂血症性急性胰腺炎(HLAP)病情严重程度及复发的关系。**方法** 回顾性分析2018年1月—2021年1月西安高新医院收治的92例HLAP患者的病历资料,分析不同严重程度HLAP患者的RC/HDL-C、RLP-C水平。根据2年内的复发情况分为复发组和非复发组,分析HLAP患者复发的影响因素,评估RC/HDL-C、RLP-C对HLAP患者复发的预测效能。**结果** 92例HLAP患者轻度26例(28.26%)、中度54例(58.70%)、重度12例(13.04%)。轻度组RC/HDL-C和RLP-C水平均低于中度组和重度组($P < 0.05$),中度组RC/HDL-C和RLP-C水平均低于重度组($P < 0.05$)。RC/HDL-C、RLP-C与HLAP严重程度呈正相关($r_s = 0.472$ 和 0.459 ,均 $P = 0.000$)。92例HLAP患者中复发38例(41.30%)。复发组HDL-C低于非复发组($P < 0.05$),RC/HDL-C、RLP-C高于非复发组($P < 0.05$)。多因素逐步Logistic回归分析结果显示:RC/HDL-C水平高[OR=3.899(95% CI:1.344,11.319)],RLP-C水平高[OR=4.491(95% CI:1.547,13.033)]是HLAP复发的危险因素($P < 0.05$);HDL-C水平低[OR=0.229(95% CI:0.079,0.665)]是HLAP复发的保护因素($P < 0.05$)。RC/HDL-C、RLP-C单一及联合预测HLAP复发的敏感性分别为72.15%(95% CI:0.635,0.804)、81.73%(95% CI:0.729,0.916)、87.09%(95% CI:0.764,0.931),特异性分别为71.29%(95% CI:0.628,0.815)、78.04%(95% CI:0.712,0.841)、92.31%(95% CI:0.835,0.981)。**结论** RC/HDL-C、RLP-C水平与HLAP患者的病情严重程度呈正相关,可用于预测HLAP患者的复发风险,且预测效能良好。

关键词: 高脂血症性急性胰腺炎; 残粒脂蛋白胆固醇; 残余胆固醇/高密度脂蛋白胆固醇; 严重程度; 复发
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Associations of peripheral blood RLP-C and RC/HDL-C levels with disease severity and recurrence in patients with hyperlipidemic acute pancreatitis*

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Abstract: Objective To explore the associations of serum remnant lipoprotein cholesterol (RLP-C) and remnant cholesterol/high-density lipoprotein cholesterol (RC/HDL-C) levels with the disease severity and recurrence of hyperlipidemic acute pancreatitis (HLAP). **Methods** A retrospective analysis was conducted on the medical records of 92 HLAP patients admitted to Xi'an High-tech Hospital from January 2018 to January 2021, and the levels of RC/HDL-C and RLP-C in patients with varying degrees of disease severity were analyzed. According to the recurrence outcomes within 2 years, the patients were divided into a recurrence group and a non-recurrence group. The factors affecting the HLAP recurrence were analyzed, and the predictive efficacy of RC/HDL-C and RLP-C

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levels for HLAP recurrence was evaluated. **Results** Among the 92 patients with HLAP, 26 cases (28.26%) were classified as mild, 54 cases (58.70%) as moderate, and 12 cases (13.04%) as severe. The RC/HDL-C and RLP-C levels in the mild group were lower than those in the moderate and severe groups ($P < 0.05$), and the RC/HDL-C and RLP-C levels in the moderate group were lower than those in the severe group ($P < 0.05$). The RC/HDL-C and RLP-C levels were positively correlated with the severity of HLAP ($r_s = 0.472$ and 0.459 , both $P = 0.000$). Among the 92 HLAP patients, 38 (41.30%) experienced disease recurrence. The HDL-C level in the recurrence group was lower than that in the non-recurrence group, while the RC/HDL-C and RLP-C levels were higher in the recurrence group than in the non-recurrence group ($P < 0.05$). Multivariable Logistic regression analysis revealed that high RC/HDL-C levels [$\hat{OR} = 3.899$ (95% CI: 1.344, 11.319)] and high RLP-C levels [$\hat{OR} = 4.491$ (95% CI: 1.547, 13.033)] were risk factors for HLAP recurrence ($P < 0.05$), and that low HDL-C levels [$\hat{OR} = 0.229$ (95% CI: 0.079, 0.665)] were found to be a protective factor ($P < 0.05$). The sensitivities of RC/HDL-C, RLP-C, and their combination in predicting HLAP recurrence were 72.15% (95% CI: 0.635, 0.804), 81.73% (95% CI: 0.729, 0.916), and 87.09% (95% CI: 0.764, 0.931), respectively. The specificities were 71.29% (95% CI: 0.628, 0.815), 78.04% (95% CI: 0.712, 0.841), and 92.31% (95% CI: 0.835, 0.981), respectively. **Conclusion** RC/HDL-C and RLP-C levels are positively associated with the severity of HLAP and demonstrate good predictive performance for assessing the risk of disease recurrence.

Keywords: hyperlipidemic acute pancreatitis; remnant lipoprotein cholesterol; remnant cholesterol/high-density lipoprotein cholesterol; severity; recurrence

高脂血症性急性胰腺炎(hyperlipidemic acute pancreatitis, HLAP)是以脂代谢异常为病理特点的急性胰腺炎,其发病、进展与血清高脂质水平密切相关^[1-2]。血清残粒脂蛋白胆固醇(remnant lipoprotein cholesterol, RLP-C)、残余胆固醇/高密度脂蛋白胆固醇(remnant cholesterol/ high-density lipoprotein cholesterol, RC/HDL-C)可灵敏地反映人体脂代谢异常^[3-4]。RLP-C是由极低密度脂蛋白、中间密度脂蛋白代谢产生的颗粒,其携带的胆固醇水平能够反映机体对脂质的清除能力^[5]。研究表明,RC与胰腺内脂肪沉积有关,是独立于HDL-C、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C),评价潜在脂质代谢异常的指标,能够揭示极低密度脂蛋白、乳糜微粒等脂蛋白的异常代谢状态^[6]。HDL-C能够促进脂肪转运,调节脂质水平^[7]。研究发现,急性胰腺炎患者肥胖加重是早期急性胃肠损伤和肠屏障功能障碍的危险因素^[8-9]。目前,血清RLP-C、RC/HDL-C与HLAP患者病情及预后的报道有限,本研究旨在探讨血清RLP-C、RC/HDL-C与HLAP患者病情严重程度关系,为HLAP的预后评估提供参考。

1 资料与方法

1.1 研究对象

回顾性分析2018年1月—2021年1月西安高新医院收治的92例HLAP患者的病历资料,年龄30~

56岁,平均(39.18 ± 4.25)岁;男性72例,女性20例。本研究获得医院医学伦理委员会审批(No: LMF1202302015)。

1.2 诊断、纳入及排除标准

1.2.1 诊断标准 符合《中国急性胰腺炎诊治指南(2013年,上海)》^[10]中HLAP的诊断:①出现与急性胰腺炎相符的急性、持续性、剧烈上腹痛,多向背部放射;②甘油三酯(Triglycerides, TG) ≥ 11.30 mmol/L或TG 5.56~11.30 mmol/L,但血样呈乳糜状;③排除胆源性胰腺炎、酒精性胰腺炎或其他明确病因胰腺炎。

1.2.2 纳入标准 ①符合上述诊断;②首次胰腺发病;③发病后72 h内入院接受治疗;④年龄 > 18 岁;⑤临床资料完整。

1.2.3 排除标准 ①入组前1个月内服用影响胰腺代谢的药物;②自身免疫性疾病;③消化道活动性出血;④慢性胰腺炎;⑤腹部开放性外伤;⑥妊娠或哺乳期女性;⑦精神病;⑧恶性肿瘤;⑨心脑血管疾病;⑩病毒性或药物相关性肝肾损伤;⑪未遵医嘱定期入院复查或中途失访。

1.3 病历资料收集

于患者入院24 h内,收集患者的性别、年龄、体质质量指数(body mass index, BMI)、糖尿病、高血压、血清TG、总胆固醇(total cholesterol, TC)、HDL-C、LDL-C、胰腺CT严重程度指数(computed tomography

severity index, CTSI)、并发症(胰腺坏死、腹腔积液、全身炎症反应综合征)。计算 RC, $RC=TC-HDL-C- LDL-C$ 。RC 为 TC 中除 HDL 和 LDL 以外的胆固醇部分, 主要包括极低密度脂蛋白、中间密度脂蛋白及脂蛋白(a)等残余颗粒中的胆固醇; 血清 RLP-C 采用免疫分离法检测, 试剂盒购自日本 Immunoreserch Laboratories 公司。

1.4 严重程度分级

参考急性胰腺炎亚特兰大分类标准^[11], 轻度: 无局部并发症或全身并发症、不伴有器官功能障碍、病程具有自限性、可早期治愈、病死率低; 中度: 伴有局部并发症和/或全身并发症、无持续性器官功能障碍, 或出现短暂的器官功能障碍后 48 h 内恢复, 病死率低; 重度: 出现持续 > 48 h 器官功能障碍, 病死率高。根据严重程度, 分为轻度 26 例, 中度 54 例, 重度 12 例。

1.5 治疗及复发

所有患者依据《中国急性胰腺炎诊治指南(2013 年, 上海)》^[10]及实际病情予以对症治疗, 包括禁食、补液支持、解痉止痛、抑酸、抑酶、抗感染、器官

保护等, 对胰腺局部并发症出现感染、压迫(胆道梗阻、消化道梗阻、胰瘘等)等症状者可联合手术治疗。患者首次治疗出院后, 指导患者定期入院复查, 根据门诊病历记录随访 2 年, 将患者再次确诊 HLAP 判定为复发, 分为复发组 38 例和非复发组 54 例。

1.6 统计学方法

数据分析采用 SPSS 24.0 统计软件。计量资料以均数 ± 标准差($\bar{x} \pm s$)表示, 比较用方差分析, 两两比较用 SNK-*q* 检验; 计数资料以构成比或率(%)表示, 比较用 χ^2 检验; 相关性分析用 Spearman 法; 影响因素的分析用多因素逐步 Logistic 回归模型; 绘制受试者工作特征(receiver operating characteristic, ROC)曲线。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 不同严重程度患者一般资料比较

轻度组、中度组和重度组性别构成、年龄、BMI 构成、糖尿病患病率和高血压患病率比较, 经 χ^2 检验或方差分析, 差异均无统计学意义 ($P > 0.05$)。见表 1。

表 1 不同严重程度患者的一般资料比较

组别	<i>n</i>	男/女/例	年龄/(岁, $\bar{x} \pm s$)	BMI/例		糖尿病/例	高血压/例
				>24 kg/m ²	≤24 kg/m ²		
轻度组	26	20/6	40.12 ± 3.06	22	4	8	4
中度组	54	43/11	38.97 ± 4.15	48	6	13	7
重度组	12	9/3	39.64 ± 4.23	10	2	3	3
χ^2/F 值		0.162	0.799	0.442		0.416	1.103
<i>P</i> 值		0.922	0.453	0.802		0.812	0.576

2.2 不同严重程度患者 RC/HDL-C、RLP-C 水平比较

轻度组、中度组和重度组 RC/HDL-C 和 RLP-C 水平比较, 经方差分析, 差异均有统计学意义 ($P < 0.05$); 轻度组 RC/HDL-C 和 RLP-C 水平均低于中度组和重度组 ($P < 0.05$), 中度组 RC/HDL-C 和 RLP-C 水平均低于重度组 ($P < 0.05$)。见表 2。

2.3 RC/HDL-C、RLP-C 与 HLAP 严重程度的相关性分析

Spearman 相关性分析得出, RC/HDL-C、RLP-C 与 HLAP 严重程度均呈正相关($r_s = 0.472$ 和 0.459 , 均 $P = 0.000$)。

表 2 不同严重程度患者的 RC/HDL-C、RLP-C 比较 ($\bar{x} \pm s$)

组别	<i>n</i>	RC/HDL-C	RLP-C/(mmol/L)
轻度组	26	2.11 ± 0.32	0.47 ± 0.08
中度组	54	2.27 ± 0.34 ^①	0.52 ± 0.11
重度组	12	2.52 ± 0.41 ^{①②}	0.63 ± 0.15 ^{①②}
<i>F</i> 值		5.917	8.918
<i>P</i> 值		0.004	0.001

注: ①与轻度组比较, $P < 0.05$; ②与中度组比较, $P < 0.05$ 。

2.4 影响 HLAP 复发的单因素分析

92 例 HLAP 患者中复发 38 例 (41.30%)。复发

组和非复发组性别构成、年龄、BMI、饮酒、糖尿病、高血压、TG、TC、LDL-C、CTSI、胰腺坏死、腹腔积液、全身炎症反应综合征比较,经 χ^2/t 检验,差异均无统计学意义($P>0.05$)。复发组和非复发组 HDL-

C、RC/HDL-C、RLP-C 比较,经 t 检验,差异均有统计学意义($P<0.05$);复发组 HDL-C 低于非复发组,RC/HDL-C、RLP-C 高于非复发组($P<0.05$)。见表 3。

表 3 影响HLAP复发的单因素分析 ($\bar{x} \pm s$)

组别	n	男/女/ 例	年龄(岁, $\bar{x} \pm s$)	BMI 例(%)		饮酒 例(%)	糖尿病 例(%)	高血压 例(%)	TG/(mmol/L, $\bar{x} \pm s$)	TC/(mmol/L, $\bar{x} \pm s$)
				> 24 kg/m ²	≤ 24 kg/m ²					
复发组	38	29/9	40.15 ± 4.09	34(89.47)	4(10.53)	23(60.53)	12(31.58)	5(13.16)	16.41 ± 2.01	8.53 ± 1.71
非复发组	54	43/11	38.86 ± 3.75	46(85.19)	8(14.81)	39(72.22)	12(22.22)	9(16.67)	15.99 ± 1.86	8.29 ± 1.53
χ^2/t 值		0.144	0.983	0.362		1.388	1.013	1.013	0.213	1.031
P 值		0.704	0.383	0.548		0.239	0.314	0.314	0.645	0.305

组别	HDL-C/(mmol/L, $\bar{x} \pm s$)	LDL-C/(mmol/L, $\bar{x} \pm s$)	CTSI/(分, $\bar{x} \pm s$)	RC/HDL-C ($\bar{x} \pm s$)	RLP-C/(mmol/L, $\bar{x} \pm s$)	胰腺坏死 例(%)	腹腔积液 例(%)	全身炎症反应综 合征 例(%)
复发组	1.76 ± 0.42	2.28 ± 0.73	3.59 ± 0.41	2.51 ± 0.46	0.59 ± 0.16	6(15.79)	6(15.79)	26(68.42)
非复发组	1.93 ± 0.34	2.15 ± 0.67	3.52 ± 0.39	2.08 ± 0.41	0.47 ± 0.12	7(12.96)	5(9.26)	27(50.00)
χ^2/t 值	2.141	0.884	0.830	4.709	4.112	0.147	0.904	3.099
P 值	0.035	0.379	0.409	0.001	0.001	0.702	0.342	0.078

2.5 影响HLAP复发的多因素分析

以 HLAP 是否复发(否=0,是=1)为因变量,将差异有统计学意义的 HDL-C(实测值)、RC/HDL-C(实测值)和 RLP-C(实测值)为自变量,进行多因素逐步 Logistic 回归分析(引入水准为 0.05,排除水准为 0.10),结果显示:RC/HDL-C 水平高[$\hat{OR} = 3.899$

(95% CI: 1.344, 11.319)]、RLP-C 水平高[$\hat{OR} = 4.491$ (95% CI: 1.547, 13.033)]是 HLAP 复发的危险因素($P<0.05$); HDL-C 水平低[$\hat{OR} = 0.229$ (95% CI: 0.079, 0.665)]是 HLAP 复发的保护因素($P<0.05$)。见表 4。

表 4 影响HLAP复发的多因素逐步 Logistic 回归分析参数

因素	b	S _b	Wald χ^2 值	P 值	$\hat{OR}$ 值	95% CI	
						下限	上限
RC/HDL-C	1.361	0.589	5.339	0.014	3.899	1.344	11.319
RLP-C	1.502	0.627	5.739	0.013	4.491	1.547	13.033
HDL-C	-1.472	0.631	5.442	0.014	0.229	0.079	0.665

2.6 RC/HDL-C、RLP-C 对 HLAP 复发的预测效能

ROC 曲线分析得出,RC/HDL-C、RLP-C 单一及联合预测 HLAP 复发的敏感性分别为 72.15%

(95% CI: 0.635, 0.804)、81.73%(95% CI: 0.729, 0.916)、87.09%(95% CI: 0.764, 0.931),特异性分别为 71.29%(95% CI: 0.628, 0.815)、78.04%(95% CI: 0.712, 0.841)、92.31%(95% CI: 0.835, 0.981)。见表 5 和图 1。

表 5 RC/HDL-C、RLP-C 预测HLAP复发的效能分析

指标	截断值	曲线下面积	95% CI		敏感性/%	95% CI		特异性/%	95% CI	
			下限	上限		下限	上限		下限	上限
RC/HDL-C	2.29	0.739	0.635	0.837	72.15	0.635	0.804	71.29	0.628	0.815
RLP-C	0.53 mmol/L	0.782	0.685	0.884	81.73	0.729	0.916	78.04	0.712	0.841
联合		0.887	0.809	0.959	87.09	0.764	0.931	92.31	0.835	0.981

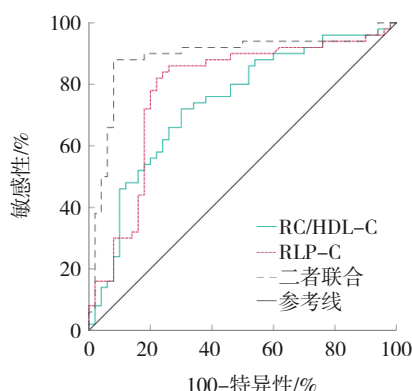


图 1 RC/HDL-C、RLP-C 预测 HLAP 复发的 ROC 曲线

3 讨论

HLAP 是高脂血症引起的急腹症,病情进展与脂质代谢紊乱有关^[12-13]。研究报道,HLAP 的发病具有年轻化,脂肪肝、糖尿病等并发症多,反复发作等特点^[14-15]。研究认为,胰腺毛细血管内的脂质沉积、胰液分泌受阻及胰腺缺血等因素可导致急性胰腺炎的病理性加重^[16-17]。目前,针对 HLAP 的治疗尚无特效治愈方案,临床上仍以对症治疗、预防感染、控制病因及预防并发症的综合治疗为主,但病死率仍较高^[18-19]。因此,寻找高敏性生物学标志物辅助评估 HLAP 疾病进展风险及预后,有助于提供新的分子生物学治疗依据及靶点,逆转预后。

本研究中,轻、中、重度组 HLAP 患者 RC/HDL-C、RLP-C 水平逐渐升高;相关性分析得出,RC/HDL-C、RLP-C 水平与 HLAP 患者的病情严重程度均呈正相关,提示 RC/HDL-C、RLP-C 升高与 HLAP 的病情严重程度密切相关。本研究中,与非复发组比较,复发组 HLAP 患者的 HDL-C 更低,RC/HDL-C、RLP-C 更高,提示 HLAP 患者的复发可能与 HDL-C 降低及 RC/HDL-C、RLP-C 升高有关。本研究中多因素逐步 Logistic 回归分析得出,RC/HDL-C、RLP-C 是 HLAP 复发的危险因素, HDL-C 是 HLAP 复发的保护因素,表明 RC/HDL-C、RLP-C、HDL-C 表达异常与 HLAP 复发相关。HDL-C 能够促进脂质转运、代谢,是维护血管健康的生物因子^[20-21]。RC/HDL-C 和 RLP-C 是反映脂质代谢紊乱的重要指标。RC/HDL-C 表示残余胆固醇与 HDL-C 的比值,反映胆固醇逆转运的障碍程度^[22]。RLP-C 是残粒脂蛋白中的胆固醇含量,既往研究中常作为动脉粥样硬化等心血管疾病的高敏性生物学标志因子^[23]。研究表明, HDL-C 降

低、RC/HDL-C 升高及 RLP-C 升高可导致脂质代谢紊乱加剧^[24]。胰脂肪酶水解脂质为游离脂肪酸 (free fatty acid, FFA) 与白蛋白结合,而过量的 FFA 超过白蛋白的代谢负荷时,能够对毛细血管内皮细胞、胰腺腺泡细胞等细胞产生细胞毒性^[25]。且胰腺仅有一条供血动脉,无侧支循环,高脂质导致血液黏滞度增加,脂质颗粒聚集堵塞可引起胰腺血供不足,损伤胰腺^[25]。脂质水平升高后胰蛋白酶原引起胰腺细胞自身消化,同样可导致 HLAP 发病^[26-28]。本研究中 ROC 曲线分析得出,RC/HDL-C、RLP-C 单一及联合预测 HLAP 复发的敏感性、特异性及曲线下面积值均较高,表明 RC/HDL-C、RLP-C 对 HLAP 复发的预测具有较好的效能。本研究结果可见,血脂代谢紊乱在 HLAP 的疾病进展与复发中起着关键作用, HDL-C、RC/HDL-C、RLP-C 等指标有助于评估 HLAP 患者的病情严重程度及预后。

本研究虽然在一定程度上揭示了 RC/HDL-C、RLP-C 及 HDL-C 与 HLAP 复发的关系,但仍存在一些局限性。首先,本研究为回顾性研究,可能存在病例选择偏倚和信息收集不全等问题,其次本研究复发的随访时间较长,其间可能掺杂混淆因素,后续将陆续完善大样本前瞻性研究,完善高危指标的定期监测变化趋势并结合多种生物学标志物进行综合评估,以更加准确地预测 HLAP 复发的风险。

综上所述,RC/HDL-C、RLP-C 水平与 HLAP 患者的病情严重程度呈正相关,可用于预测 HLAP 患者的复发风险,且预测效能良好。

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