

血脂水平对高脂血症性急性胰腺炎严重性的影响

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【摘要】 目的 分析高脂血症性重症急性胰腺炎(HLSAP)的临床特点,为改善患者的预后提供依据。**方法** 选择2008年1月至2017年12月北京大学第三医院危重医学科及急诊重症加强治疗病房(EICU)收治的27例HLSAP患者,参照美国内分泌协会极严重高脂血症〔甘油三酯(TG) ≥ 22.4 mmol/L〕定义,将患者按入院时血TG水平分为TG增高组(TG < 22.4 mmol/L, 21例)和TG极重度增高组(TG ≥ 22.4 mmol/L, 6例),按改良CT严重度指数(MCTSI)评分分为MCTSI增高组(MCTSI = 4分, 15例)和MCTSI严重增高组(MCTSI > 4 分, 12例)。观察TG、MCTSI水平对疾病严重程度的影响,严重程度指标包括序贯器官衰竭评分(SOFA)、MCTSI和器官功能衰竭情况、多器官功能障碍综合征(MODS)发生比例、住院时间,并分析TG、MCTSI与疾病严重程度指标的相关性。**结果** 与TG增高组比较,TG极重度增高组MCTSI评分显著升高(分: 7.33 ± 2.07 比 5.05 ± 1.63 , $P < 0.05$),而MODS发生率〔33.3% (2/6) 比 14.3% (3/21)〕、最大SOFA评分(分: 2.17 ± 2.86 比 2.00 ± 1.55)以及住院时间(d: 19.17 ± 13.00 比 15.43 ± 10.97)比较差异均无统计学意义(均 $P > 0.05$)。与MCTSI增高组比较,MCTSI严重增高组MODS〔41.7% (5/12) 比 0〕、呼吸衰竭〔66.7% (8/12) 比 26.7% (4/15)〕发生比例明显升高(均 $P < 0.05$),住院时间明显延长(d: 21.58 ± 14.79 比 12.00 ± 4.63 , $P < 0.05$),而两组最大SOFA评分比较差异无统计学意义(分: 2.50 ± 2.43 比 1.67 ± 1.18 , $P > 0.05$)。相关性分析显示,血TG与MCTSI呈正相关($r = 0.413$, $P = 0.032$),与MODS发生比例($r = 0.257$, $P = 0.195$)、住院时间($r = 0.161$, $P = 0.422$)、SOFA($r = 0.017$, $P = 0.931$)无显著相关性。MCTSI与MODS发生比例($r = 0.517$, $P = 0.006$)及住院时间($r = 0.405$, $P = 0.036$)均呈正相关,与SOFA评分($r = 0.165$, $P = 0.411$)无显著相关性。**结论** 血TG与MCTSI均是判断HLSAP预后的良好指标。HLSAP早期应积极控制血脂水平,动态监测胰腺形态学改变,及早进行干预,可改善患者预后。

【关键词】 高脂血症; 胰腺炎,急性; 严重程度

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【Abstract】 Objective To analyze the clinical features of hyperlipidemic severe acute pancreatitis (HLSAP) and provide evidence for improving the patients' prognosis. **Methods** Twenty-seven patients with HLSAP admitted to the Department of Critical Care Medicine and the Emergency Intensive Care Unit (EICU) of Peking University Third Hospital from January 2008 to December 2017 were collected, according to the definition of very severe hypertriglyceridemia [triglyceride (TG) ≥ 22.4 mmol/L] ascertained by the American Endocrine Association and the blood TG level on admission, the 27 patients with HLSAP were divided into TG-increased group (TG < 22.4 mmol/L, 21 cases) and TG-very severely increased group (TG ≥ 22.4 mmol/L, 6 cases), and according to the modified CT severity index (MCTSI) scores, the patients were divided into MCTSI increased group (MCTSI = 4 points, 15 cases) and MCTSI severely increased group (MCTSI > 4 points, 12 cases). The effects of TG and MCTSI levels on disease severity were observed. The severity indicators included sequential organ failure assessment (SOFA), MCTSI, organ failure situation, multiple organ dysfunction syndrome (MODS) incidence, and length of hospital stay. The correlations between TG, MCTSI and disease severity indicators were analyzed. **Results** Compared with the TG-increased group, the MCTSI score was significantly increased in the TG-very severely increased group (7.33 ± 2.07 vs. 5.05 ± 1.63 , $P < 0.05$), while the MODS incidence [33.3% (2/6) vs. 14.3% (3/21)], the maximum SOFA score (2.17 ± 2.86 vs. 2.00 ± 1.55) and hospitalization time (days: 19.17 ± 13.00 vs. 15.43 ± 10.97) were not statistically significant in the comparisons between the above two groups (all $P > 0.05$). Compared with the MCTSI-increased group, the proportions of MODS [41.7% (5/12) vs. 0] and respiratory failure [66.7% (8/12) vs. 26.7% (4/15)] were significantly increased (both $P < 0.05$), and the hospitalization time was significantly prolonged (days: 21.58 ± 14.79 vs. 12.00 ± 4.63 , $P < 0.05$) in the very severely increased MCTSI group, whereas there was no statistical significant difference in the maximum SOFA score between the above two groups (2.50 ± 2.43 vs. 1.67 ± 1.18 , $P > 0.05$). The correlation analyses showed: the blood TG was positively correlated with MCTSI ($r = 0.413$, $P = 0.032$), but the blood TG was not correlated with following indicators: ratio of MODS onset ($r = 0.257$, $P = 0.195$), hospitalization time ($r = 0.161$, $P = 0.422$) and SOFA score ($r = 0.017$, $P = 0.931$). The correlations between MCTSI and the following indicators: ratio of MODS ($r = 0.517$, $P = 0.006$) and the time of hospitalization ($r = 0.405$, $P = 0.036$) were all positively correlated, and the SOFA score ($r = 0.165$, $P = 0.411$) was of

no significant correlation. **Conclusions** Both blood TG and MCTSI are good indicators for the prognosis of HLSAP. Blood lipid levels should be actively controlled in the early stage of patients with HLSAP, the pancreatic morphological changes should be dynamically monitored, and in time early intervention can improve the patients' prognosis.

[Key words] Hyperlipidemia; Acute pancreatitis; Severity degree

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随着生活水平的提高,高脂血症已经成为继胆源性及酒精性之后急性胰腺炎(AP)的又一个独立危险因素^[1-2],同时也是复发性胰腺炎的高危因素^[3],由高脂血症引发的AP患者呈现持续增多趋势,有统计发现高脂血症性急性胰腺炎(HLAP)占所有AP的6.17%^[4],并且更易出现重症急性胰腺炎(SAP)的表现^[5]。本研究通过分析HLAP的临床特征,旨在提高临床医生对该病的认识。

1 资料和方法

1.1 研究对象的选择:选择2008年1月1日至2017年12月30日北京大学第三医院危重医学科及急诊重症加强治疗病房(EICU)收治的27例HLAP患者,其中男性8例,女性19例;年龄 (33.38 ± 8.02) 岁;合并糖尿病10例;既往有高脂血症病史2例,未规律服用降脂药物;既往有胰腺炎病史1例。患者入院后给予单纯口服降脂药物或联合血浆置换治疗。

1.2 纳入标准和排除标准

1.2.1 纳入标准:①AP的诊断从症状体征、实验室检查指标及影像学3个方面进行判断,均符合《中国急性胰腺炎诊治指南(2013年,上海)》^[6];②所有患者均有完整的病历资料;③HLAP的诊断标准为:满足甘油三酯(TG) >11.3 mmol/L或TG $5.65 \sim 11.3$ mmol/L,血清呈乳糜状。

1.2.2 排除标准:胆源性、酒精性、自身免疫性、妊娠、药物性、肿瘤、外伤等其他原因引起的AP。

1.3 伦理学:本研究符合医学伦理学标准,并经本院医学伦理委员会批准立项。

1.4 资料收集:参照美国内分泌协会极严重高脂血症(TG ≥ 22.4 mmol/L)定义^[7],依据入院时血TG浓度,将27例HLAP分为TG增高组(TG < 22.4 mmol/L, 21例)和TG极重度增高组(TG ≥ 22.4 mmol/L, 6例);依据住院期间改良CT严重度指数(MCTSI),将患者分为MCTSI增高组(MCTSI=4分, 15例)和MCTSI严重增高组(MCTSI > 4 分, 12例);对比分析TG、MCTSI水平对疾病严重程度的影响。严重程度指标包括入院48 h内血TG浓度、住院期间MCTSI最大值、序贯器官衰竭评分(SOFA)最大值、住院时间、器官功能衰竭情况、多器官功能

障碍综合征(MODS)。器官功能衰竭定义为单一器官评分 ≥ 2 分^[8]。

1.5 统计学处理:使用SPSS 17.0统计软件分析数据。符合正态分布的计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 t 检验;非正态分布的计量资料以中位数(四分位数) $[M(Q_L, Q_U)]$ 表示,应用秩和检验;计数资料以例(率)描述,采用 χ^2 检验。各指标与疾病严重性的相关性分析采用等级相关分析方法,正态分布的采用Pearson方法,非正态分布的采用Spearman方法。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 MCTSI及血TG浓度分布(表1):所有患者血TG为 $14.28(12.00, 19.48)$ mmol/L。美国内分泌协会规定血脂分级为正常TG < 1.7 mmol/L,轻度高脂血症 $1.7 \sim 2.3$ mmol/L,中度高脂血症 $2.4 \sim 11.2$ mmol/L,重度高脂血症 $11.3 \sim 22.3$ mmol/L,极重度高脂血症 ≥ 22.4 mmol/L。本研究患者血脂水平以重度高脂血症为主,共17例(占63.0%),另有1例患者TG高达116.24 mmol/L。MCTSI评分为 (5.31 ± 2.09) 分。

表1 HLAP患者MCTSI及血TG分布

MCTSI评分(分)		血脂分级	
例(%)		例(%)	
4	15(51.7)	中度	4(14.8)
6	4(13.8)	重度	17(63.0)
8	7(24.1)	极重度	6(22.2)
10	1(3.4)		

2.2 临床结局:住院时间为 $12.00(11.00, 19.50)$ d, SOFA评分为 $2.00(1.00, 2.50)$ 分,发生MODS 5例,器官功能衰竭患者数由多到少依次为:呼吸衰竭(呼衰)14例,急性肾损伤4例(2例需要长期接受肾脏替代治疗),休克3例,凝血功能障碍2例。另外出现腹腔继发感染8例,胰腺假性囊肿2例(存在囊内出血和腹腔出血)。行血浆置换7例,腹腔穿刺引流4例,1例因腹腔内出血接受血管造影动脉栓塞治疗。无死亡病例。

2.3 不同TG水平组患者疾病严重程度指标比较以及TG与疾病严重程度指标的相关性分析(表2~3):TG极重度增高组MCTSI显著高于TG增高组。而两组MODS比例、SOFA评分、呼衰比例、住院时间比较差异均无统计学意义(均 $P > 0.05$;

表 2)。相关性分析显示, TG 与 MCTSI 呈正相关, 与 MODS 比例、住院时间、SOFA 评分无明显相关性 ($P>0.05$; 表 3)。

表 2 HLAP 不同 TG 疾病严重程度指标比较

组别	例数 (例)	MCTSI (分, $\bar{x} \pm s$)	SOFA 评分 (分, $\bar{x} \pm s$)	MODS 发生率 [% (例)]
TG 增高组	21	5.05 $\pm$ 1.63	2.00 $\pm$ 1.55	14.3 (3)
TG 极重度增高组	6	7.33 $\pm$ 2.07 ^a	2.17 $\pm$ 2.86	33.3 (2)
组别	例数 (例)	呼吸衰竭 [例 (%)]	住院时间 (d, $\bar{x} \pm s$)	
TG 增高组	21	10 (47.6)	15.43 $\pm$ 10.97	
TG 极重度增高组	6	2 (33.3)	19.17 $\pm$ 13.00	

注: 与 TG 增高组比较, ^a $P<0.05$

表 3 HLAP 患者 TG、MCTSI 与疾病严重程度指标的相关性分析

项目	TG		MCTSI	
	r 值	P 值	r 值	P 值
MCTSI	0.413	0.032	无此项	无此项
MODS 比例	0.257	0.195	0.517	0.006
住院时间	0.161	0.422	0.405	0.036
SOFA 评分	0.017	0.931	0.165	0.411

2.4 不同 MCTSI 水平组患者疾病严重程度指标比较及 MCTSI 与疾病严重程度指标的相关性分析 (表 3~4): MCTSI 严重增高组发生 MODS 和呼吸衰竭均明显高于 MCTSI 增高组, 且住院时间较 MCTSI 增高组明显延长 (均 $P<0.05$)。相关性分析显示, MCTSI 与 MODS 比例、住院时间呈正相关 (均 $P<0.05$), 与 SOFA 评分无相关性 ($P>0.05$)。

表 4 HLAP 不同 MCTSI 疾病严重程度指标比较

组别	例数 (例)	SOFA 评分 (分, $\bar{x} \pm s$)	MODS 发生率 [例 (%)]
MCTSI 增高组	15	1.67 $\pm$ 1.18	0 (0)
MCTSI 严重增高组	12	2.50 $\pm$ 2.43	5 (41.7) ^a
组别	例数 (例)	呼吸衰竭 [例 (%)]	住院时间 (d, $\bar{x} \pm s$)
MCTSI 增高组	15	4 (26.7)	12.00 $\pm$ 4.63
MCTSI 严重增高组	12	8 (66.7)	21.58 $\pm$ 14.79 ^a

注: 与 MCTSI 增高组比较, ^a $P<0.05$

3 讨论

急性胰腺炎协作组 2006 年发布的我国 AP 的病因依次为胆源性 (54.4%)、特发性 (19.7%)、高脂血症性 (12.6%)、酒精性 (8.0%), 高脂血症已成为公认的 AP 第三大病因^[9], 引起了广大医师的关注, 及早评估 HLAP 的严重程度一直是临床医生工作的首要目标。

目前评估疾病严重程度的指标日趋多样化,

血脂水平是否与胰腺炎严重程度相关目前尚无定论。Balachandra 等^[10]认为血脂水平与胰腺炎局部并发症、入院时急性生理学与慢性健康状况评分系统 II (APACHE II) 评分、最终临床结局无关; Zhang 等^[11]认为血脂水平与疾病的严重性 (综合存在以下任意之一: 局部并发症, Ranson 评分 ≥ 3 分, APACHE II ≥ 8 分, 器官衰竭) 是相关的, 高脂血症中重度胰腺炎比例、病死率明显增高^[12]。Yang 等^[13]认为血脂升高可增加 CT 评分, 而郑丹等^[14]认为血 TG 水平增加并未显著提高 MCTSI 评分, 但与多器官功能衰竭、肾衰竭及 SOFA 评分有显著相关性, 高脂血症是 SAP 的独立危险因素, 即血脂水平与局部并发症及胰腺形态学改变相关性报道存在较大差异, 分析可能与胰腺 CT 检查距发病时间、研究入组血脂水平不同有关。本研究 MCTSI 评分选择患者住院期间最高值, 结果表明 TG 与 MCTSI 有相关性, 因此本研究较客观地反映了血脂水平和胰腺炎局部并发症的关系。研究表明, TG 水平与器官功能衰竭有关^[15-17]。本研究显示, TG 极重度增高组 MODS 比例高于 TG 增高组, 但差异无统计学意义, 可能与研究入组患者 TG 较高, 而缺乏 TG 偏低的比较组有关。

本研究患者 MCTSI 评分较高, 与研究人群分布于 ICU 有关。MCTSI 评分与患者住院时间、MODS 比例呈正相关。但有研究表明, MCTSI 评分与器官功能衰竭的严重程度并不是直接成正比的^[18]。对于出现胰腺坏死继发感染的病例即使未合并器官功能衰竭也需要临床医生高度重视, 因为继发感染本身就是死亡的独立危险因素^[19-21], 因此有学者呼吁将坏死继发感染扩展为严重分级的第 4 级^[22]。

目前关于 HLAP 的治疗除常规抑制胰酶分泌外, 一般采用口服降脂药物和 (或) 联合血浆置换治疗。研究显示, 血液净化联合血液灌流能显著降低 HLAP 血脂水平, 改善氧合指数, 缓解胰腺炎临床症状并降低病死率, 改善器官功能^[23]。血液灌流联合血液透析滤过治疗 HLAP 患者, 能降低血脂水平, 改善临床症状^[24]。也有报道肝素联合胰岛素可显著降低患者 TG 水平, 减轻患者胰腺炎症状^[25]。但也有研究表明, 即使尽快降低血脂水平, 但仍有患者病情进展较快^[26], 这与高脂血症启动胰腺炎发病机制密切相关, 目前关于 HLAP 的发病机制主要有以下几个学说^[27-28]: 游离脂肪酸、钙超载与内质网应激、微循环障碍、炎症介质-细胞因子损伤。只有对关键点进行干预才能改善患者预后。

TG 与 MCTSI 密切相关,二者均是判断 HLAP 预后的良好指标,尽早降低血脂是治疗 HLAP 的早期目标,动态监测胰腺形态学改变,及早进行干预,可改善患者预后。尽管高脂血症被广大临床医师所认识,但目前的临床研究多限于单中心,且每个研究病例数相对较少,多为回顾性,疾病严重程度定义不一,病例信息采集时间点差异较大,均会影响临床结论。因此需要进行大样本量的前瞻性研究或流行病学调查,以进一步证实和阐述 HLAP 的发病机制及临床预后。

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