·论著·

脂蛋白a水平及超声心动图钙化评分预测冠心病主要心血管不良事件的临床价值

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【摘要】**目的** 探究脂蛋白a水平及超声心动图钙化评分预测冠心病主要心血管不良事件的临床价值。**方法** 选取2020年1月至2021年6月本院收治冠心病患者62例。根据随访期间是否出现主要心血管不良事件(MACE)，将患者分为MACE组(n=27)和非MACE组(n=35)。比较两组患者的临床资料、脂蛋白a水平(Lpa)和超声心动图钙化评分(eCS)，并用采用受试者工作特征曲线评价Lpa和eCS对MACE的预测价值。**结果** MACE组有糖尿病、高血压和冠心病家族史的患者数量显著高于非MACE组(*P*<0.05)。MACE组Lpa水平及eCS评分显著高于非MACE组(*P*<0.05)。ROC曲线对血清Lpa、eCS及联合检测预测MACE效能进行分析，Lpa、eCS检测AUC分别为0.765、0.740，联合检测AUC为0.827，高于其他2种单独检测的AUC值。**结论** 联合检测Lpa和eCS对冠心病患者MACE的特异性和敏感性均高于单独检测，值得临床应用。

【关键词】脂蛋白a水平；超声心动图钙化评分；冠心病；主要心血管不良事件；临床价值
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Clinical Value of Lipoprotein a Level and Echocardiography Calcification Score in Predicting Major Cardiovascular Adverse Events in Coronary Heart Disease

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Abstract: ***Objective*** To explore the clinical value of lipoprotein a level and echocardiography calcification score in predicting major cardiovascular adverse events in coronary heart disease. ***Methods*** 62 patients with coronary heart disease admitted to our hospital from January 2020 to June 2021 were selected. Patients were divided into MACE group (n=27) and non-MACE group (n=35) according to whether major adverse cardiovascular events (MACE) occurred during the follow-up period. The clinical data, lipoprotein a level (Lpa) and echocardiography calcification score (eCS) of the two groups were compared, and the predictive value of Lpa and eCS on MACE was evaluated using the receiver operating characteristic curve.***Results*** The number of patients with family history of diabetes, hypertension and coronary heart disease in MACE group was significantly higher than that in non-MACE group (P<0.05). Lpa level and eCS score in MACE group were significantly higher than those in non-MACE group (P<0.05). ROC curve was used to analyze the prediction of MACE efficacy by serum Lpa, eCS and joint detection. The AUCs of Lpa and eCS were 0.765 and 0.740, respectively, and the AUC of joint detection was 0.827, which was higher than that of the other two separate detections. ***Conclusion*** The specificity and sensitivity of combined detection of Lpa and eCS for MACE in patients with coronary heart disease were higher than those of separate detection, which was worthy of clinical application.

Keywords: Lipoprotein a Level ; Echocardiography Calcification Score ; Coronary Heart Disease; Major Adverse Cardiovascular Events; Clinical Value

冠心病(coronary heart disease，CHD)的病理特征是动脉粥样硬化，是一种与炎症密切相关的慢性病理过程[1]。尽管 CHD 的管理(包括药物治疗，如他汀类药物和非药物治疗，如冠状动脉旁路移植术)和对危险因素(如吸烟、糖尿病并发症或高血压)的识别已经得到了确定，2017年冠心病死亡病例达890万例，仍居首位，预后仍差强人意[2-3]。冠状动脉中的钙化斑块是动脉粥样硬化斑块负荷的标志物，这反过来又高度预测未来的心血管事件和死亡率[4-5]。欧洲心血管疾病预防指南支持在中度心血管风险的无症状成人中使用冠状动脉钙化评分[6]。多项研究已经确定，通过超声心动图检测到的主动脉瓣硬化/钙化 (AVC)和二尖瓣环钙化(MAC)可独立预测心血管疾病的发病率和死亡率[7]。使用超声心动图半定量钙化评分（eCS），它综合评估了主动脉瓣和二尖瓣、乳头肌和升主动脉的钙化程度——范围从无、可见钙化到严重和弥散性钙沉积[8]。升高的脂蛋白(a)(Lpa)是心血管疾病(CVD)的一个非常普遍的遗传风险因素[9]。本研究探究了Lpa及eCS预测冠心病主要心血管不良事件的临床价值。现报告如下。

1 资料与方法

1.1 研究对象 选取2020年1月至2021年6月本院收治冠心病患者62例，年龄28~79岁。

纳入标准：符合《现代冠心病》中关于冠心病的诊断标准[10]；年龄超过 18 岁；无严重的感染、炎症或自身免疫性疾病；无血液系统恶性肿瘤或实体瘤。排除标准：合并先天性心脏病、心肌病或血管痉挛性心绞痛病史；3个月内接受免疫抑制治疗；孕妇或哺乳期妇女。

1.2 方法 根据随访期间是否发生心脏死亡、心肌梗死、支架血栓形成、靶病变血运重建和靶血管血运重建等不良心血管事件，将患者分为两组。在此期间发生了27例MACE事件，其中有1例死亡，5例心肌梗死，7例支架血栓形成，9例靶病变血运重建，5例靶血管血运重建。

1.3 血清Lpa水平检测 所有入组患者抽取静脉血5mL，离心分离血清，采用血清脂蛋白a试剂盒(购自上海申峰生物试剂有限公司)，采用免疫透射比浊法检测血清Lpa水平。

1.4 超声心动图 采用Philips IE33/EPIQ5超声仪器，S5-1探头，频率1MHz~5MHz，检测主动脉根部、主动脉瓣、二尖瓣环、乳头肌和室间隔钙化情况。判断标准：主动脉根部：主动脉窦部以上2cm发现钙化时呈阳性；主动脉瓣：瓣膜回声增强且厚度≥1mm时呈阳性；二尖瓣环、乳头肌和室间隔：回声高于周围相

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邻组织回声即呈阳性。根据以上eCS评分标准(0~5分)，由两名具有5年以上工作经验的心脏超声医师进行独立评估，在上述部位每检测到一处钙化即记录为1分。

1.5 统计学分析 使用SPSS 21.0对收集到的实验数据进行分析，符合正态分布的计量资料采用($\bar{x}\pm s$)表示，两组之间的比较用独立样本t检验，计数资料以例数或率表示，两组比较采用χ^2检验，预测价值分析采用受试者工作特征曲线(ROC)进行评价，以P<0.05为差异具有统计学意义。

2 结 果

2.1 2组临床资料比较 MACE组有糖尿病、高血压和冠心病家族史的患者数量显著高于非MACE组(P<0.05)，见表1。

表1 2组患者一般资料比较

临床病理参数		MACE组(n=27)	非MACE组(n=35)	χ^2	P
糖尿病史	是	21	3	30.771	<0.001
	否	6	32		
高血压病史	是	20	4	25.211	<0.001
	否	7	31		
冠心病家族史	是	23	3	36.741	<0.001
	否	4	32		

2.2 2组患者Lpa及eCS情况比较分析 MACE组Lpa水平及eCS评分显著高于非MACE组(P<0.05)，见表2。

表2 2组患者Lpa及eCS情况对比

指标	MACE组(n=27)	非MACE组(n=35)	t/χ^2	P
Lpa(mg/L)	352.21±20.64	207.57±19.65	28.115	<0.001
eCS(例)				
0~2分	15	10	4.6121	0.032
3~5分	12	25		

2.3 Lpa、eCS联合检测对MACE预测价值 ROC曲线对血清Lpa、eCS及联合检测预测MACE效能进行分析，Lpa、eCS检测AUC分别为0.765、0.740，联合检测AUC为0.827，高于其他2种单独检测的AUC值，见表3和图1。

表3 Lpa、eCS联合检测对MACE预测效能评价

指标	曲线下面积(AUC)	灵敏度(%)	特异度(%)	95%CI	P值
Lpa	0.765	75.54	73.54	0.621~0.874	0.003
eCS	0.740	73.65	71.54	0.604~0.851	0.004
联合检测	0.827	80.32	79.54	0.696~1.054	<0.001

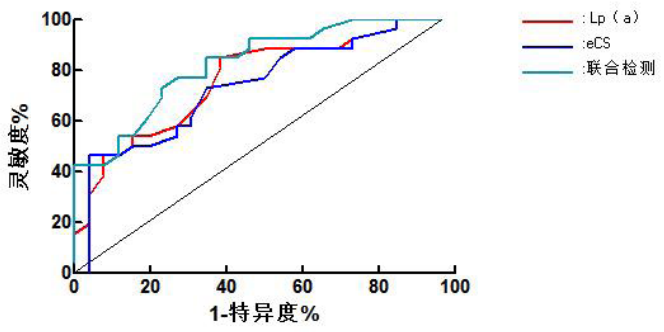

图1 Lpa、eCS联合检测预测MACE的ROC曲线图

3 讨 论

CHD仍然是全球发病率和死亡率的主要原因，考虑到肥胖症的流行和生活方式的改变，冠心病的死亡率在过去几十年中有所上升[11]。根据全球流行病学数据，估计约有 9300 万人患有冠心病，最终导致 810 万人死亡[12]。病理上，冠心病被认为是由动脉粥样硬化引起的动脉狭窄引起的，最近研究表明炎症在动脉粥样硬化斑块的形成中也起重要作用，进一步导致动脉狭窄[13-14]。目前的临床研究，包括动脉血运重建(如经皮冠状动脉介入治疗和冠状动脉旁路移植术)和药物治疗(如阿司匹林)，代表治疗方案的巨大进步；然而，仍有部分患者因冠状动脉事件复发而预后不佳[15-16]。最常见的根本原因是动脉粥样硬化，这是一种疾病过程，其中斑块(一种复杂而多样的成分，包括脂质、炎症细胞、平滑肌细胞和结缔组织)在动脉壁上堆积，斑块形成可导致冠状动脉部分或完全阻塞[17-18]。

最近研究表明，主动脉瓣钙化 (AVC)和二尖瓣环钙化(MAC)都是活跃且高度调节的过程，其组织学与动脉粥样硬化相似[19-20]。研究显示，在发生冠状动脉粥样硬化的患者中，在二尖瓣后叶的心室表面和每个主动脉瓣尖的主动脉方面都有泡沫细胞聚集，代表早期的动脉粥样硬化病变[21-22]。此外，研究证明了 AVC、MAC 和动脉粥样硬化的危险因素有相似之处，包括年龄、高血压、高脂血症和糖尿病[23-24]。研究表明主动脉瓣或二尖瓣环的钙化可能代表一种动脉粥样硬化，这些瓣膜钙化与普通人群心血管疾病和死亡的风险增加密切相关[25-26]。作为胸主动脉钙化的一部分，主动脉根部钙化(ARC)的存在与 CVD 死亡风险的增加独立相关[27]。Lpa是一种血浆脂蛋白，由富含胆固醇的低密度脂蛋白颗粒和一个载脂蛋白B100分子和一个通过二硫键连接的附加蛋白载脂蛋白(a)组成[28-29]。升高的Lpa水平可能会增加 CVD 的风险 ，通过促血栓形成、抗纤溶作用[30]。遗传、流行病学和病理生理学研究表明，Lpa 是冠状动脉疾病(CAD) 、心肌梗塞 (MI)、中风、外周动脉疾病 (PAD)、CAVD 和心力衰竭的致病因素[31-33]。本研究中MACE组有糖尿病、高血压和冠心病家族史的患者数量显著高于非MACE组(P<0.05)。MACE组Lpa水平及eCS评分显著高于非MACE组(P<0.05)，与目前的研究结果一致。本研究发现Lpa、eCS检测AUC分别为0.765、0.740，联合检测AUC为0.827，高于其他2种单独检测的AUC值。说明Lpa和eCS联合检测可以弥补各种指标检测的不足，从而提高对MACE的预测效果。

综上所述，联合检测Lpa和eCS对冠心病患者MACE的特异性和敏感性均高于单独检测，值得临床应用。但是本研究存在局限性，样本量少以及选取中心单一会对结果产生偏移，因此未来需要更具前瞻性的全面研究来证实此结果。

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3 讨 论

国家癌症中心发布的《2015年恶性肿瘤发病率与死亡率报告》[7]：乳腺癌占恶性肿瘤发病率的第5位(女性恶性肿瘤的首位)，占恶性肿瘤死亡率的第6位。发病率呈年轻化趋势逐年增加，以北上广一线城市的女性发病率最高。triple-negative乳腺癌是一种在分子分型、病理及临床特征均较特殊的一类，具有高侵袭性、高复发性、预后极差的特点。临床治疗中对蒽环类药物敏感度不高，且因自身特性限制了内分泌及靶向治疗，临床治疗难度很大，可用药物更是少之又少。因此，寻找有针对性的有效的化疗药物对triple-negative乳腺癌的治疗具有重要意义。triple-negative乳腺癌BRCA1基因存在突变，且BRCA1基因与DNA断裂、修复有关系，因此对抑制DNA修复的化疗药物敏感。铂类药物因与患者体内DNA结合，抑制了DNA的复制与转录，提高患者临床疗效。Hill等[8]报道，顺铂单药治疗晚期triple-negative乳腺癌的总有效率为20%~50%。吉西他滨主要抑制DNA修复，还通过抑制核糖核酸还原酶，使三磷酸脱氧核苷产生量减少，尤其是脱氧三磷酸胞苷减少，最终导致细胞凋亡。Wang等[9]报道，单纯使用吉西他滨治疗晚期triple-negative乳腺癌的总有效率为25%~38%。二者具有协同作用。Wang等[10]报道，顺铂+吉西他滨在治疗晚期triple-negative乳腺癌的总有效率为22%~63%。

本研究结果显示：观察组总缓解率67.8%，中位肿瘤进展时间9个月。解国清等[11]报道，顺铂+吉西他滨治疗晚期triple-negative乳腺癌的总缓解率为65.8%，中位肿瘤进展时间5个月，与本研究结果相差不大。观察组CA125、CA153、CEA、TPS水平均比对照组低，这提示了顺铂与吉西他滨对乳腺癌的肿瘤生长起到抑制作用。观察组癌因性疲乏与对照组相比明显较低，这提示顺铂与吉西他滨改善了该类患者的生活质量，患者疲乏程度减轻。与黎胤谋等[12]报道相一致。

综上所述，吉西他滨联合顺铂对于初治的晚期triple-negative乳腺癌患者疗效显著，可以降低CA125、CA153、CEA、TPS的含量，有效减轻癌因性疲乏。本研究由于样本量小，来源单一，且癌因性疲乏评分主要通过患者的主观感受进行描述，导致本研究不能完全的真实的反映实验结果，日后需进一步进行多中心大样本研究，为临床治疗提供依据。

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