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· 论著 ·

血清脂蛋白相关磷脂酶 A2 联合同型半胱氨酸对老年冠心病患者下肢动脉粥样硬化疾病的诊断价值研究

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【摘要】 背景 目前, 联合检测脂蛋白相关磷脂酶 A2 (Lp-PLA2)、同型半胱氨酸 (Hcy) 常用于心血管疾病的诊断, 但二者联合对下肢动脉粥样硬化疾病 (LEAD) 的诊断价值尚不清楚。目的 分析血清 Lp-PLA2 联合 Hcy 对老年冠心病患者 LEAD 的诊断价值, 以期为该类患者的临床诊断、治疗提供理论依据。方法 选取 2018 年 1 月—2019 年 6 月在长江大学附属仙桃市第一人民医院就诊的 92 例老年冠心病合并 LEAD 患者为 LEAD 组, 另选取同期本院收治的 80 例老年冠心病未合并 LEAD 患者作为对照组。比较两组患者临床资料及实验室检查指标, 老年冠心病合并 LEAD 患者血清 Lp-PLA2 与 Hcy 的相关性分析采用 Pearson 相关分析; 老年冠心病患者合并 LEAD 的影响因素分析采用多因素 Logistic 回归分析; 绘制受试者工作特征 (ROC) 曲线以评估血清 Lp-PLA2、Hcy 及二者联合对老年冠心病患者合并 LEAD 的诊断价值。结果 LEAD 组患者体质指数 (BMI) 大于对照组, 冠心病病程长于对照组, 吸烟率、高血压发生率、Friesinger (FS) 评分、低密度脂蛋白胆固醇 (LDL-C)、空腹血糖 (FPG)、超敏 C 反应蛋白 (hs-CRP)、Lp-PLA2 及 Hcy 均高于对照组 ($P < 0.05$)。Pearson 相关分析结果显示, 老年冠心病合并 LEAD 患者血清 Lp-PLA2 与 Hcy 无直线相关关系 ($r=1.241$, $P > 0.05$)。多因素 Logistic 回归分析结果显示, 冠心病病程 [$OR=4.618$, 95%CI (1.523, 14.004)]、吸烟 [$OR=4.351$, 95%CI (1.362, 13.902)]、高血压 [$OR=3.653$, 95%CI (1.200, 11.123)]、LDL-C [$OR=3.542$, 95%CI (1.152, 10.890)]、FPG [$OR=3.657$, 95%CI (1.129, 11.845)]、hs-CRP [$OR=5.063$, 95%CI (1.635, 15.677)]、Lp-PLA2 [$OR=4.641$, 95%CI (1.459, 14.764)] 及 Hcy [$OR=17.013$, 95%CI (4.206, 66.820)] 是老年冠心病患者合并 LEAD 的独立影响因素 ($P < 0.05$)。ROC 曲线分析结果显示, 血清 Lp-PLA2、Hcy 诊断老年冠心病患者合并 LEAD 的曲线下面积 (AUC) 分别为 0.696、0.707, 最佳截断值分别为 179.79 $\mu\text{g/L}$ 、11.51 $\mu\text{mol/L}$, Youden 指数分别为 0.285、0.344。Lp-PLA2+Hcy (并联) 诊断老年冠心病患者合并 LEAD 的灵敏度为 88.04%, 特异度为 62.50%, Youden 指数为 0.505; Lp-PLA2+Hcy (串联) 诊断老年冠心病患者合并 LEAD 的灵敏度为 56.96%, 特异度为 95.00%, Youden 指数为 0.520。结论 血清 Lp-PLA2、Hcy 升高是老年冠心病患者合并 LEAD 的独立危险因素, 临床上联合检测血清 Lp-PLA2 和 Hcy 可以提高对老年冠心病患者 LEAD 的诊断效能。

【关键词】 冠心病; 下肢; 动脉粥样硬化; 脂蛋白相关磷脂酶 A2; 同型半胱氨酸; 诊断

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Diagnostic Value of Serum Lp-PLA2 Combined with Hcy on Lower Extremity Atherosclerosis in Elderly Patients with Coronary Heart Disease

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【Abstract】 **Background** Combined testing of lipoprotein associated phospholipase A2 (Lp-PLA2) and homocysteine (Hcy) is commonly used in the diagnosis of cardiovascular diseases, but its value in specifically diagnosing the lower extremity atherosclerotic disease (LEAD) is still unclear. **Objective** To evaluate the diagnostic value of serum Lp-PLA2 combined with Hcy on LEAD in elderly patients with coronary heart disease, which forms the theoretical basis for the clinical diagnosis and treatment of LEAD in this group of patients. **Methods** A total of 92 elderly patients with coronary heart disease combined with

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LEAD who were admitted to the Xiantao First People's Hospital Affiliated to Yangtze University from January 2018 to June 2019 were selected as the LEAD group, and 80 elderly patients who had coronary heart disease but without LEAD, admitted to this hospital during the same period, were selected as the control group. The clinical data and laboratory examination indexes of the two groups were compared. Pearson correlation analysis was conducted to analyze the correlation between the serum Lp-PLA2 and the Hcy of elderly patients with coronary heart disease combined with LEAD. Multivariate Logistic regression analysis was applied to examine the influencing factors of LEAD in elderly patients with coronary heart disease. Receiver operating characteristic (ROC) curves were drawn to evaluate the diagnostic value of the serum Lp-PLA2 alone, the Hcy alone, and the combination of both, on LEAD in elderly patients with coronary heart disease. **Results** Compared with the control group, the LEAD group showed higher body mass index (BMI) and longer course of the coronary heart disease, besides elevated smoking rate, incidence of hypertension, Friesinger (FS) score, low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), high-sensitivity C-reactive protein (hs-CRP), Lp-PLA2 and Hcy ($P < 0.05$). Pearson correlation analysis showed that there was no linear correlation between the serum Lp-PLA2 and the Hcy of elderly patients with coronary heart disease combined with LEAD ($r=1.241$, $P > 0.05$). Multivariate Logistic regression analysis indicated that the course of the coronary heart disease [$OR=4.618$, 95%CI (1.523, 14.004)], smoking [$OR=4.351$, 95%CI (1.362, 13.902)], hypertension [$OR=3.653$, 95%CI (1.200, 11.123)], LDL-C [$OR=3.542$, 95%CI (1.152, 10.890)], FPG [$OR=3.657$, 95%CI (1.129, 11.845)], hs-CRP [$OR=5.063$, 95%CI (1.635, 15.677)], Lp-PLA2 [$OR=4.641$, 95%CI (1.459, 14.764)] and Hcy [$OR=17.013$, 95%CI (4.206, 66.820)] were independent influencing factors of LEAD in elderly patients with coronary heart disease ($P < 0.05$). ROC curve analysis suggested that in diagnosing the LEAD of elderly patients with coronary heart disease, the areas under the curve (AUC) were 0.696 for serum Lp-PLA2 and 0.707 for Hcy; the best cut-off values were 179.79 $\mu\text{g/L}$ for serum Lp-PLA2 and 11.51 $\mu\text{mol/L}$ for Hcy; and the Youden index values were 0.285 for serum Lp-PLA2 and 0.344 for Hcy. The sensitivity, the specificity and the Youden index values were 88.04%, 62.50%, and 0.505 respectively for Lp-PLA2+Hcy (in parallel connection), and were 56.96%, 95.00% and 0.520 for Lp-PLA2+Hcy (in series connection). **Conclusion** Elevated serum Lp-PLA2 and Hcy are independent risk factors for LEAD in elderly patients with coronary heart disease. Combined testing of serum Lp-PLA2 and Hcy helps to improve the diagnostic efficacy of LEAD in elderly patients with coronary heart disease.

【Key words】 Coronary heart disease; Lower extremity; Atherosclerosis; Lipoprotein-related phospholipase A2; Homocysteine; Diagnosis

下肢动脉粥样硬化疾病(lower extremity atherosclerosis disease, LEAD)指下肢动脉节段性狭窄甚至闭塞的一类疾病^[1],其早期症状为缺血、疼痛等,晚期可造成下肢溃疡、坏疽甚至截肢^[2]。LEAD是冠心病等心脑血管疾病最常见的并发症,尤其在老年患者中最为常见,因此需要引起临床更多重视^[3]。脂蛋白相关磷脂酶A2(lipoprotein-associated phospholipase A2, Lp-PLA2)是一种炎性递质,可参与血管炎性病变的过程^[4]。此外,同型半胱氨酸(homocysteine, Hcy)也被证实与血脂代谢异常、动脉粥样硬化密切相关^[5-6]。目前联合检测Lp-PLA2、Hcy常用于心血管疾病的诊断,但二者联合对LEAD的诊断价值尚不清楚。本研究旨在探讨血清Lp-PLA2联合Hcy对老年冠心病患者LEAD的诊断价值,以为临床诊断、治疗提供理论依据。

1 资料与方法

1.1 一般资料 选取2018年1月—2019年6月在长江大学附属仙桃市第一人民医院就诊的92例老年冠心病合并LEAD患者为LEAD组,均符合冠心病^[7]及

LEAD的诊断标准^[8]。LEAD的诊断标准:静息踝肱指数(ankle brachial index, ABI) < 0.9 或运动后ABI下降20%或趾肱指数(toe brachial index, TBI) < 0.6 ;多普勒超声检查或其他影像学检查显示下肢动脉粥样硬化狭窄或闭塞。纳入标准:年龄 ≥ 65 岁。排除标准:(1)多发性大动脉炎、急性动脉栓塞及血管闭塞性脉管炎等者;(2)合并自身免疫系统疾病、白血病及恶性肿瘤者。另选取同期在长江大学附属仙桃市第一人民医院就诊的80例老年冠心病未合并LEAD患者作为对照组。本研究经长江大学附属仙桃市第一人民医院伦理委员会审核通过,所有患者签署知情同意书。

1.2 观察指标 收集所有患者临床资料及实验室检查指标,临床资料包括年龄、性别、体质指数(body mass index, BMI)、冠心病病程、吸烟情况(吸烟定义:累计吸烟 ≥ 100 支,戒烟 ≥ 1 年者除外)、饮酒情况(饮酒定义:乙醇摄入量 $\geq 30\text{ g/周}$,戒酒 ≥ 1 年者除外)^[9]、高血压发生情况、糖尿病发生情况及冠状动脉病变严重程度。采用Friesinger(FS)评分评估冠状动脉病变严重程度^[10],具体如下:采用CT血管造影

(CT angiography, CTA) 评估患者左前降支、左回旋支及右冠状动脉狭窄程度, 按照狭窄程度从无到重度分别记为 0~4 分, 上述 3 支冠状动脉评分之和为 FS 评分。实验室检查指标及其检测方法/仪器如下: 采用全自动生化分析仪测定血清三酰甘油 (triglyceride, TG)、总胆固醇 (total cholesterol, TC)、高密度脂蛋白胆固醇 (high-density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇 (low-density lipoprotein cholesterol, LDL-C)、空腹血糖 (fasting plasma glucose, FPG) 及 Hcy 水平; 采用免疫比浊法测定血清超敏 C 反应蛋白 (high-sensitivity C-reactive protein, hs-CRP) 水平; 采用双抗体夹心酶联免疫吸附试验测定血清 Lp-PLA2 水平。

1.3 统计学方法 采用 SPSS 19.0 统计学软件进行数据分析。符合正态分布的计量资料以 $(\bar{x} \pm s)$ 表示, 组间比较采用两独立样本 t 检验; 计数资料以相对数表示, 组间比较采用 χ^2 检验; 老年冠心病合并 LEAD 患者血清 Lp-PLA2 与 Hcy 的相关性分析采用 Pearson 相关分析; 老年冠心病患者合并 LEAD 的影响因素分析采用多因素 Logistic 回归分析; 绘制受试者工作特征 (receiver operating characteristics, ROC) 曲线以评估血清 Lp-PLA2、Hcy 及二者联合对老年冠心病患者合并 LEAD 的诊断价值。以 $P < 0.05$ 为差异有统计学意义。

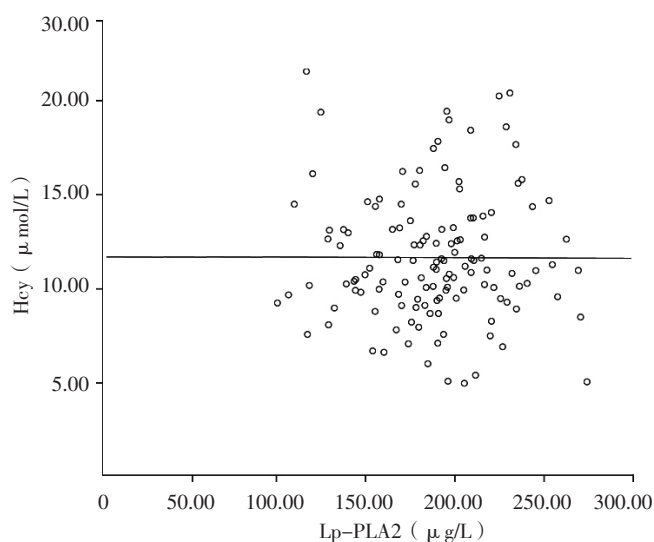
2 结果

2.1 两组患者临床资料及实验室检查指标比较 两组患者年龄、性别、饮酒率、糖尿病发生率、TG、TC、HDL-C 比较, 差异无统计学意义 ($P > 0.05$); LEAD 组患者 BMI 大于对照组, 冠心病病程长于对照组, 吸烟率、高血压发生率、FS 评分、LDL-C、FPG、hs-CRP、Lp-PLA2 及 Hcy 均高于对照组, 差异有统计学意义 ($P < 0.05$), 见表 1。

2.2 相关性分析 Pearson 相关分析结果显示, 老年冠

心病合并 LEAD 患者血清 Lp-PLA2 与 Hcy 无直线相关关系 ($r=1.241$, $P > 0.05$), 见图 1。

2.3 多因素 Logistic 回归分析 以老年冠心病患者 LEAD 为因变量 (赋值: 未合并=0, 合并=1), 以 BMI (赋值: $< 25.4 \text{ kg/m}^2=0$, $\geq 25.4 \text{ kg/m}^2=1$)、冠心病病程 (赋值: $< 7.0 \text{ 年}=0$, $\geq 7.0 \text{ 年}=1$)、吸烟 (赋值: 否=0, 是=1)、高血压 (赋值: 无=0, 有=1)、FS 评分 (赋值: $< 6.0 \text{ 分}=0$, $\geq 6.0 \text{ 分}=1$)、LDL-C (赋值: $< 2.84 \text{ mmol/L}=0$, $\geq 2.84 \text{ mmol/L}=1$)、FPG (赋值: $< 5.92 \text{ mmol/L}=0$, $\geq 5.92 \text{ mmol/L}=1$)、hs-CRP (赋值: $< 3.48 \text{ mg/L}=0$, $\geq 3.48 \text{ mg/L}=1$)、Lp-PLA2 (赋值: $< 182.40 \text{ mmol/L}=0$, $\geq 182.40 \text{ mmol/L}=1$) 及 Hcy (赋值: $< 11.08 \text{ } \mu\text{mol/L}=0$, $\geq 11.08 \text{ } \mu\text{mol/L}=1$), 进行多因素 Logistic



注: Lp-PLA2= 脂蛋白相关磷脂酶 A2, Hcy= 同型半胱氨酸

图 1 老年冠心病合并 LEAD 患者血清 Lp-PLA2 与 Hcy 相关性的散点图

Figure 1 Scatter plot of correlation between serum Lp-PLA2 and Hcy of elderly patients with coronary heart disease combined with LEAD

表 1 两组患者临床资料及实验室检查指标比较

Table 1 Comparison of clinical data and laboratory examination indexes between the two groups

组别	例数	年龄 ($\bar{x} \pm s$, 岁)	性别 (男 / 女)	BMI ($\bar{x} \pm s$, kg/m ²)	冠心病病程 ($\bar{x} \pm s$, 年)	吸烟 [n (%)]	饮酒 [n (%)]	高血压 [n (%)]	糖尿病 [n (%)]	FS 评分 ($\bar{x} \pm s$, 分)
对照组	80	69.9 $\pm$ 5.1	56/24	24.9 $\pm$ 2.3	6.4 $\pm$ 3.1	30 (37.5)	32 (40.0)	32 (40.0)	20 (25.0)	4.9 $\pm$ 2.4
LEAD 组	92	70.5 $\pm$ 4.8	70/22	25.8 $\pm$ 2.4	7.6 $\pm$ 3.2	52 (56.5)	50 (54.3)	56 (60.9)	30 (32.6)	6.0 $\pm$ 2.4
t (χ^2) 值		0.737	0.809 ^a	2.210	2.424	6.207 ^a	3.531 ^a	7.459 ^a	1.201 ^a	3.165
P 值		0.462	0.368	0.029	0.016	0.013	0.060	0.006	0.273	0.002

组别	TG ($\bar{x} \pm s$, mmol/L)	TC ($\bar{x} \pm s$, mmol/L)	HDL-C ($\bar{x} \pm s$, mmol/L)	LDL-C ($\bar{x} \pm s$, mmol/L)	FPG ($\bar{x} \pm s$, mmol/L)	hs-CRP ($\bar{x} \pm s$, mg/L)	Lp-PLA2 ($\bar{x} \pm s$, μ g/L)	Hcy ($\bar{x} \pm s$, μ mol/L)
对照组	2.18 $\pm$ 0.60	4.67 $\pm$ 0.67	1.30 $\pm$ 0.14	2.78 $\pm$ 0.42	5.60 $\pm$ 1.48	3.33 $\pm$ 0.44	169.36 $\pm$ 34.04	9.98 $\pm$ 2.50
LEAD 组	2.40 $\pm$ 0.64	4.92 $\pm$ 0.78	1.25 $\pm$ 1.58	3.07 $\pm$ 0.74	6.31 $\pm$ 1.20	3.67 $\pm$ 0.53	196.16 $\pm$ 35.25	12.39 $\pm$ 3.45
t (χ^2) 值	1.908	1.791	1.761	2.296	2.905	3.526	4.056	3.978
P 值	0.059	0.076	0.081	0.023	0.004	0.001	< 0.001	< 0.001

注: BMI= 体质指数, FS=Friesinger, TG= 三酰甘油, TC= 总胆固醇, HDL-C= 高密度脂蛋白胆固醇, LDL-C= 低密度脂蛋白胆固醇, FPG= 空腹血糖, hs-CRP= 超敏 C 反应蛋白, Lp-PLA2= 脂蛋白相关磷脂酶 A2, Hcy= 同型半胱氨酸, LEAD= 下肢动脉粥样硬化性疾病; ^a 为 χ^2 值

回归分析, 回归方法为“条件-向前”, 结果显示, 冠心病病程、吸烟、高血压、LDL-C、FPG、hs-CRP、Lp-PLA2 及 Hcy 是老年冠心病患者合并 LEAD 的独立影响因素 ($P < 0.05$), 见表 2。

2.4 诊断价值 ROC 曲线分析结果显示, 血清 Lp-PLA2、Hcy 诊断老年冠心病患者合并 LEAD 的曲线下面积 (AUC) 分别为 0.696、0.707, 最佳截断值分别为 179.79 $\mu\text{g/L}$ 、11.51 $\mu\text{mol/L}$, Youden 指数分别为 0.285、0.344, 见图 2、表 3。将血清 Lp-PLA2 和 Hcy 分别采用并联 (血清 Lp-PLA2 或 Hcy 高于最佳截断值诊断为 LEAD) 和串联 (血清 Lp-PLA2 和 Hcy 均高于最佳截断值诊断为 LEAD) 的方式诊断 LEAD, 结果显示, Lp-PLA2+Hcy (并联) 诊断老年冠心病患者合并 LEAD 的灵敏度为 88.04%, 特异度为 62.50%, Youden 指数为 0.505; Lp-PLA2+Hcy (串联) 诊断老年冠心病患者

合并 LEAD 的灵敏度为 56.96%, 特异度为 95.00%, Youden 指数为 0.520。

表 3 血清 Lp-PLA2 和 Hcy 诊断老年冠心病患者合并 LEAD 的 ROC 曲线分析结果

Table 3 ROC curve analysis results of serum Lp-PLA2 and Hcy in predicting LEAD in elderly patients with coronary heart disease

指标	AUC	95%CI	最佳截断值	灵敏度 (%)	特异度 (%)	Youden 指数
Lp-PLA2	0.696	(0.610, 0.773)	179.79 $\mu\text{g/L}$	70.6	57.5	0.281
Hcy	0.707	(0.622, 0.783)	11.51 $\mu\text{mol/L}$	54.4	80.0	0.344

注: AUC= 曲线下面积

3 讨论

随着我国老龄化进程加剧, 下肢动脉粥样硬化已成为老年人常见的外周动脉疾病, 其中 LEAD 较为常见, 可严重影响患者的生活质量^[11]。目前研究表明, 合并冠心病、糖尿病等内科疾病的老年人易发生 LEAD^[12], 且冠心病患者更易并发复杂的外周动脉血管疾病^[13]。LEAD 发病早期无特异性临床表现, 且多数老年患者感知觉较迟缓, 常会将早期症状或体征误认为是衰老或其他疾病的表现, 进而导致就诊时病情较为严重甚至错失最佳干预时机^[14]。因此, 早期预测、及时干预对 LEAD 患者预后改善具有重要的临床意义。

动脉粥样硬化被认为是一种慢性炎症过程^[15]。Lp-PLA2 是炎症标志物之一, 主要由成熟的巨噬细胞、淋巴细胞等合成、分泌, 其在低密度脂蛋白的氧化、动脉粥样硬化及脑卒中的发生等方面发挥着重要作用^[16-17]。研究发现, Lp-PLA2 主要与低密度脂蛋白结合, 能水解低密度脂蛋白中的氧化卵磷脂, 从而生成溶血卵磷脂和氧化型游离脂肪酸, 促进炎症因子和黏附分子表达, 加重血管内炎性反应, 最终导致动脉粥样硬化进展^[18-19]。Hcy 是由蛋氨酸去甲基代谢生成的一种含硫氨基酸, 具有多种代谢生物学效应。研究发现, Hcy 可促进氧化作用及平滑肌细胞增殖、迁移、聚集, 导致动脉管壁增厚, 引起管腔狭窄、闭塞, 同时还能促进动脉管壁胶原合成, 管壁弹性减退, 最终促发动脉粥样硬化^[20-21]。此外, Hcy 还能影响基质金属蛋白酶的表达, 有效降解基底膜, 促进平滑肌细胞迁移及动脉粥样硬化的发生和发展^[22-23]。本研究结果显示, LEAD 组患者血清 Lp-PLA2、Hcy 高于对照组, 多因素 Logistic 回归分析结果显示, 血清 Lp-PLA2、Hcy 升高是老年冠心病患者合并 LEAD 的独立危险因素, 提示临床应早期预防血清 Lp-PLA2、Hcy 升高的老年冠心病患者发生 LEAD。

Lp-PLA2、Hcy 分别作为炎症和代谢异常的生物标志物之一, 常联合用于疾病的诊断。裴东旭等^[24]研究结果显示, Hcy、Lp-PLA2 和胱抑素 C 联合检测

表 2 老年冠心病患者合并 LEAD 影响因素的多因素 Logistic 回归分析
Table 2 Multivariate Logistic regression analysis on influencing factors of LEAD in elderly patients with coronary heart disease

变量	β	SE	Wald χ^2 值	P 值	OR 值	95%CI
冠心病病程	1.530	0.566	7.307	0.007	4.618	(1.523, 14.004)
吸烟	1.470	0.592	6.156	0.013	4.351	(1.362, 13.902)
高血压	1.296	0.568	5.200	0.023	3.653	(1.200, 11.123)
LDL-C	1.256	0.569	4.870	0.027	3.542	(1.152, 10.890)
FPG	1.297	0.600	4.675	0.031	3.657	(1.129, 11.845)
hs-CRP	1.622	0.577	7.909	0.005	5.063	(1.635, 15.677)
Lp-PLA2	1.533	0.590	6.758	0.009	4.641	(1.459, 14.764)
Hcy	2.834	0.713	15.797	< 0.001	17.013	(4.206, 66.820)

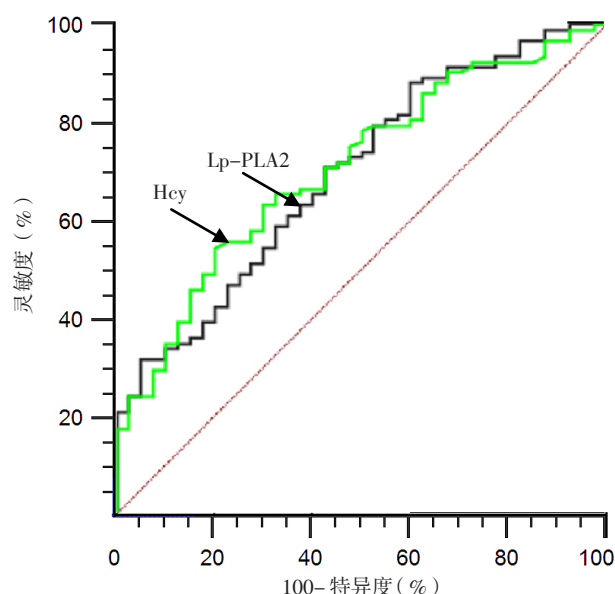


图 2 血清 Lp-PLA2 和 Hcy 诊断老年冠心病患者合并 LEAD 的 ROC 曲线

Figure 2 ROC curve of serum Lp-PLA2 and Hcy in predicting LEAD in elderly patients with coronary heart disease

对老年脑卒中的诊断效能优于单一指标;刘柳等^[25]研究结果显示,Hcy、Lp-PLA2与氧化低密度脂蛋白(ox-LDL)联合检测诊断脑梗死的灵敏度、特异度分别为93%、100%。本研究ROC曲线分析结果显示,血清Lp-PLA2、Hcy诊断老年冠心病患者合并LEAD的最佳截断值分别为179.79 $\mu\text{g/L}$ 、11.51 $\mu\text{mol/L}$, Youden指数分别为0.285、0.344; Lp-PLA2+Hcy(并联)、Lp-PLA2+Hcy(串联)诊断老年冠心病患者合并LEAD的Youden指数分别为0.505、0.520,提示血清Lp-PLA2、Hcy联合检测对老年冠心病患者合并LEAD的诊断效能高于单一指标,且Lp-PLA2+Hcy(串联)的诊断效能高于Lp-PLA2+Hcy(并联),提示临床诊断老年冠心病合并LEAD时应同时检测血清Lp-PLA2、Hcy水平,以提高诊断准确率。

综上所述,血清Lp-PLA2、Hcy升高是老年冠心病患者合并LEAD的独立危险因素,临床上联合检测血清Lp-PLA2和Hcy可以提高对老年冠心病患者LEAD的诊断效能。

作者贡献:郭根心进行文章的构思与设计,数据收集、整理、分析,结果分析与解释,撰写论文,并负责文章的质量控制及审校;成宏兵进行研究的实施与可行性分析、论文的修订,并对文章整体负责、监督管理。

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