

doi: 10.13241/j.cnki.pmb.2014.19.017

血清网膜素 -1 与绝经后女性冠心病的相关性

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摘要 目的:网膜素是最近发现的脂肪因子,肥胖或 2 型糖尿病(diabetes mellitus, DM)患者血清网膜素 -1 较正常者明显降低。本研究主要为观察绝经后女性血清网膜素 -1 水平与冠心病的相关性。**方法:**选取我院心内科住院有心绞痛症状,并行冠脉造影的 105 例绝经后女性患者。依据冠脉造影结果分为冠心病组(67 例)和对照组例(3),常规收集临床资料,包括年龄、体重指数(body mass index, BMI)、吸烟史、高血压病史、糖尿病史及血液生化和血脂指标;酶联免疫吸附剂测定(enzyme linked immunosorbent assay, ELISA)法检测血清网膜素 -1 浓度。**结果:**冠心病组血清网膜素 -1 水平显著低于对照组(205.62 ± 73.31 vs 401.64 ± 146.79 , $P < 0.001$)。单因素 logistic 回归分析示吸烟、高血压病史、糖尿病史、高脂血症史、网膜素 -1 水平降低是冠心病组的独立危险因素($P < 0.05$)。多因素 logistic 回归分析示血清网膜素 -1 水平降低是冠心病组的独立危险因素($P < 0.001$)。**结论:**绝经后女性血清网膜素 -1 水平下降是冠心病的独立危险因素,可能可成为绝经后女性冠心病的预测指标。

关键词: 冠心病;绝经后女性;网膜素 -1

中图分类号: R541.4 **文献标识码:** A **文章编号:** 1673-6273(2014)19-3669-03

Omentin-1 Is Associated with Coronary Artery Disease in Postmenopausal Women

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ABSTRACT Objective: Omentin-1 is a newly identified adipokine expressed mainly in visceral adipose tissue, with reportedly lower levels in patients with overweight or patients with obesity and in those with type 2 diabetes mellitus. We investigated whether serum omentin-1 levels were associated with coronary artery disease (CAD) among postmenopausal women. **Methods:** We enrolled 105 postmenopausal women who had undergone coronary angiography for suspected angina, and they were divided into 2 groups based on the results of coronary angiography (CAD group and control group). The age, body mass index, the history of hypertension, diabetes mellitus, hyperlipidemia, smoking and blood biochemical indicators were recorded. Omentin-1 levels were measured using ELISA methods. **Results:** Serum omentin levels decreased significantly in the CAD patients (205.62 ± 73.31 vs 401.64 ± 146.79 , $P < 0.001$). Several parameters were found to be significant in the univariate analysis, including the history of hypertension, diabetes mellitus, hyperlipidemia, smoking and omentin 1 level. After Multivariate Analyses for CAD, a decreased omentin-1 level was found to be an independent predictor of CAD. **Conclusions:** Our article indicates that a decreased omentin -1 level is associated with CAD among postmenopausal women.

Key words: Coronary artery disease; Postmenopausal women; Omentin-1

Chinese Library Classification(CLC): R541.4 **Document code:** A

Article ID: 1673-6273(2014)19-3669-03

前言

冠心病(Coronary artery disease, CAD)是健康的主要威胁,随着饮食结构的改变,心脑血管病在发展中国家的发病率逐渐增加,成为人类死亡的主要原因^[1]。绝经后女性 CAD 发病率增高与雌激素降低及一般的心血管疾病危险因素如衰老,高血压

,DM,肥胖,血脂异常等有关^[2]。脂肪组织分泌多种称为脂肪因子的生物活性分子,直接促进肥胖,DM 等代谢性疾病发生动脉粥样硬化。网膜素是最近发现的脂肪因子,主要由内脏脂肪组织表达。许多慢性炎症性疾病网膜素表达下降。其中血清中主要为网膜素 -1,肥胖或 2 型 DM 患者血清网膜素 -1 较正常者明显降低^[3,4],有报道显示血清网膜素 -1 与炎症因子白介素 -6 有关^[5]。肥胖,炎症,胰岛素抵抗(insulin resistance, IR)和 2 型 DM 均为 CAD 的风险因素已成定论,因此,我们假设网膜素 -1 参与 CAD 的发病。

研究显示 CAD 男性患者和颈动脉粥样硬化患者血清网膜素 -1 水平下降^[5-7]。然而,女性 CAD 患者的血清网膜素 -1 水平

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(收稿日期:2014-02-23 接受日期:2014-03-25)

的研究国内尚无相关研究,因此,本次研究的目的是观察绝经后女性血清网膜素 -1 水平与 CAD 及其严重程度之间的关系。

1 资料与方法

1.1 临床资料

选择 2009 年 5 月 ~ 2013 年 11 月在我院心内科住院的有心绞痛症状,并行冠脉造影的 105 例绝经后女性患者。排除标准:(1)恶性肿瘤患者;(2)严重肝肾功能不全患者;(3)系统性炎症或免疫疾病患者;(4)先天性心脏病、心肌病、瓣膜性心脏病、肺源性心脏病等器质性心脏病患者;(5)既往行冠脉搭桥术或经皮冠脉介入治疗患者;(6)近 6 个月重大外伤或手术患者。

依据冠脉造影结果分为 CAD 组和对照组,上述 105 例患者有 67 例冠脉造影示冠状动脉一支以上狭窄 $\geq 50\%$, 作为 CAD 组;其余 38 例经冠脉造影证实冠状动脉正常作为对照组。

1.2 研究方法

1.2.1 常规临床资料收集 患者年龄、BMI、吸烟史、高血压病史、糖尿病史及血液生化指标(包括血糖、血清总胆固醇、甘油三酯、低密度脂蛋白胆固醇、高密度脂蛋白胆固醇)。

1.2.2 血清学指标 所有受试者均于入院后第二天清晨空腹采

静脉血 5 mL,1500 转 / 分 $\times$ 7 分钟后,收集血清置于 -80°C 冰箱保存。网膜素 -1 ELISA 检测试剂盒购于 abcam (货号: ab136953),严格按照说明书检测患者血清网膜素 -1 浓度。检测下限为 0.5 ng/ml。

1.3 统计学分析

使用 SPSS 21 统计学软件对所得数据进行处理,定量资料进行正态性检验。定量资料用均数 $\pm$ 标准差表示。两组间正态分布、方差齐的计量资料比较采用独立样本的 t 检验;正态分布、方差不齐的计量资料则采用 t 检验;定性资料采用 χ^2 检验。多因素 logistic 回归分析用于确定 CAD 的独立预测因子,结果以相对风险和 95%置信区间 (confidence interval, CI)表示。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 CAD 组与对照组临床资料的比较

由表 1 可见:CAD 组与对照组相比,年龄、BMI、血脂水平、空腹血糖水平统计学上无显著差异($P > 0.05$)。而吸烟史、糖尿病史、高血压史、高脂血症史,CAD 组显著高于对照组($P < 0.05$)。

表 1 CAD 组与对照组临床资料

Table 1 Baseline Characteristics of CAD group and control group

	Control group(n=38)	CAD group(n=67)	Statistical value	P
Age	61.42 $\pm$ 3.96	62.42 $\pm$ 3.02	$t = -1.449$	0.15
Glucose	5.36 $\pm$ 1.59	5.80 $\pm$ 1.03	$t = -1.523$	0.09
Total cholesterol	4.59 $\pm$ 1.38	4.69 $\pm$ 1.52	$t = -0.33$	0.742
Triglycerides	1.42 $\pm$ 0.60	1.62 $\pm$ 0.31	$t = -1.913$	0.062
LDL-C	3.10 $\pm$ 1.21	3.03 $\pm$ 0.99	$t = 0.343$	0.733
HDL-C	0.98 $\pm$ 0.37	1.01 $\pm$ 0.43	$t = -0.361$	0.719
BMI	24.34 $\pm$ 3.33	24.65 $\pm$ 2.16	$t = -0.576$	0.566
Smoking	3/35	17/50	$\chi^2 = 4.804$	0.038
History of hypertension (presence/not)	11/27	35/32	$\chi^2 = 5.344$	0.025
History of DM (presence/not)	1/37	15/52	$\chi^2 = 7.328$	0.009
History of hyperlipidemia (presence/not)	4/34	19/48	$\chi^2 = 4.507$	0.048

Note: LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol

2.2 CAD 组与对照组血清网膜素 -1 水平。

CAD 组血清网膜素 -1 水平明显较对照组低,差异具有统

计学意义($P < 0.05$)(表 2)。

表 2 CAD 组与对照组血清网膜素 -1 水平

Table 2 Serum Omentin 1 levels of CAD group and control group

	Control group(n=38)	CAD group(n=67)	Statistical value	P
Omentin 1 (ng/ml)	401.64 $\pm$ 146.79	205.62 $\pm$ 73.31	$t = 9.109$	0.000

2.3 CAD 单因素与多因素 logistic 回归分析

单因素 logistic 回归分析显示:吸烟史、糖尿病史、高血压史、高脂血症史及网膜素 -1 水平分别与 CAD 相关($P < 0.05$)。对

这些因素行多因素 logistic 回归分析示:网膜素 -1 水平与 CAD 独立相关($P < 0.05$)。

表 3 CAD 单因素与多因素 logistic 回归分析
Table 3 Predictors of CAD in univariate and multivariate logistic regression analysis

	Exp (B)	95% CI	P
Univariate logistic regression analysis			
Smoking	3.967	1.080-14.572	0.038
History of hypertension	2.685	1.148-6.277	0.023
History of DM	10.673	1.350-84.385	0.025
History of hyperlipidemia	3.365	1.050-10.779	0.041
Omentin 1	7.375	2.783-19.543	0.000
multivariate logistic regression analysis			
Omentin 1	5.802	2.053-16.398	0.000

3 讨论

CAD 是绝经后女性的主要死亡原因之一。降低绝经后女性 CAD 的风险因素和早期干预很大程度上依赖于提高对 CAD 的认识,发现可反应 CAD 病理生理分子机制的可靠生物标记物。除了 CAD 传统的危险因素,反应炎症,内皮功能和氧化应激状态的新生物标记物受到越来越来的重视。

近年来,脂肪组织作为内分泌器官分泌脂肪特异性激素参与炎症和糖代谢得到大量关注^[8,9]。肥胖者脂肪组织含有活化的巨噬细胞,同脂肪细胞一起产生多种细胞因子。这包括炎症相关脂肪因子如瘦素、脂联素、肿瘤坏死因子- α 、IL-1 和 IL-6;促凝物质如纤维蛋白溶酶原激活物抑制-1;血管活性分子如血管紧张素和内皮素;可能促成 IR 的抵抗素^[10]。人类肺、肠和心脏组织中均已发现网膜素。网膜素-1 可能是一种抗炎因子,被认为可经旁分泌和自分泌作用改善 IR^[3,4,11]。研究显示血清网膜素-1 水平与腰围、BMI 和 IR 负相关^[3,6,11,12],此外,网膜素-1 水平降低与内皮功能障碍、动脉粥样硬化和心血管疾病有关^[6,7,12]。网膜素可降低 IR、抗炎和抗动脉粥样硬化的特性预示其是一个有希望的治疗靶点^[13]。绝经后女性网膜素-1 水平与 CAD 的特异性关系目前国内尚无报道。本研究表明,CAD 组血清网膜素-1 水平显著低于对照组,且网膜素-1 水平降低增加绝经后女性 CAD 的风险。此外,多因素 logistic 回归分析示血清网膜素-1 水平是绝经后女性 CAD 的独立预测因子。这与最近发表的一些研究相一致^[14-16]。这些提示网膜素-1 在 CAD 发病过程中起着重要作用。

网膜素-1 和 CAD 相关的病理生理机制可能多重的。首先,重组网膜素增加体外脂肪细胞摄取葡萄糖的能力,增强胰岛素诱导的蛋白激酶 B 磷酸化,提示网膜素参与调节胰岛素抵抗^[17]。其次,研究表明慢性炎症性疾病网膜素-1 表达降低^[18,19]。第三,Yamawaki 等的研究显示网膜素-1 作用于分离的血细胞有促进血管舒张的作用,提示网膜素-1 可能可调节血管功能^[20]。最后,网膜素可抑制细胞因子刺激的内皮细胞表达粘附分子。综上,网膜素-1 可能通过内皮依赖性冠脉舒张、IR 和炎症反应参与 CAD 的发生发展。

综上所述,我们的研究显示绝经后女性 CAD 患者血清网

膜素-1 水平降低。血清网膜素-1 水平降低是绝经后女性 CAD 的独立预测因子。然而,我们的研究也有不足之处。由于样本量较少,我们无法确定预测 CAD 的血清网膜素-1 水平的最佳截断值。因此,绝经后女性 CAD 血清网膜素-1 水平仍需进一步大样本量的研究,以期临床预测及治疗 CAD 带来新的曙光。

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(上接第 3671 页)

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