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## 心外膜脂肪厚度与冠脉病变严重程度相关性的研究\*

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**摘要 目的:**探讨心外膜脂肪组织(Epicardial adipose tissue, EAT)厚度与冠状动脉病变严重程度的相关性。**方法:**收集 167 名符合纳入标准的患者,根据冠状动脉造影(coronary arteriography, CAG)结果分 2 组:正常冠脉组(65 例)及冠心病冠脉病变组( $\geq 1$  支冠状动脉病变狭窄程度 $\geq 50\%$ )(102 例)。同期经胸超声心动图测量 EAT 厚度,并依据 CAG 图像计算 Gensini 评分、Syntax 评分。**结果:**冠脉正常组和冠心病病变组 EAT 厚度分别为( $3.89 \pm 0.2$  mm)、( $6.19 \pm 1.19$  mm),冠心病病变组显著高于冠脉正常组( $P < 0.001$ )。进一步分析 EAT 的厚度分别为  $< 5$  mm、 $5 - 7$  mm 和  $> 7$  mm 时, Gensini 评分分别为:  $7.21 \pm 7.73$ ,  $37.80 \pm 29.55$  和  $62.77 \pm 27.26$ ; Syntax 评分分别为:  $7.13 \pm 7.70$ ,  $19.71 \pm 7.27$  和  $24.95 \pm 4.31$ 。EAT 的厚度与 Gensini 评分( $r = 0.621$ ;  $P < 0.001$ )、Syntax 评分( $r = 0.689$ ;  $P < 0.001$ )呈正相关。**结论:**心外膜脂肪组织厚度与冠状动脉狭窄的复杂程度评分 Gensini 评分、Syntax 评分呈正相关。

**关键词:**心外膜脂肪组织; Gensini 评分; Syntax 评分; 超声心动图

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## Correlative Analysis of Epicardial Adipose Tissue Thickness with the Severity of Coronary Atherosclerotic Heart Disease\*

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**ABSTRACT Objective:** To investigate the correlation of thickness of epicardial adipose tissue (EAT) with the severity of coronary artery stenosis. **Methods:** 167 cases of patients were selected and allocated into 2 groups according to the coronary angiography (coronary arteriography, the CAG), normal coronary group ( $n=65$  cases) and coronary heart disease lesion group (1 coronary artery lesions in 50% or higher) or higher ( $n=102$  cases). Thoracic echocardiography was used to measure the EAT thickness and review the CAG image Gensini score. **Results:** The thickness of the EAT in the normal coronary group and coronary heart disease lesion group were  $3.89 \pm 0.2$  mm,  $6.19 \pm 1.19$  mm, which was significantly higher in the coronary heart disease group ( $P < 0.001$ ). The mean Gensini score of patients with thickness of EAT  $< 5$ ,  $5 - 7$  and  $> 7$  mm were  $7.21 \pm 7.73$ ,  $37.80 \pm 29.55$  and  $62.77 \pm 27.26$ ; the Syntax score were  $7.13 \pm 7.70$ ,  $19.71 \pm 7.27$  and  $24.95 \pm 4.31$ . The EAT thickness and Gensini score ( $r = 0.621$ ;  $P < 0.001$ ), the Syntax score ( $r = 0.689$ ,  $P < 0.001$ ), and pathological changes of coronary heart disease were associated with the severity of coronary artery stenosis. **Conclusions:** EAT thickness and the complexity of the coronary artery stenosis and Gensini score, Syntax score.

**Key words:** Epicardial adipose tissue (EAT); Gensini score; Syntax score; Ultrasonic cardiogram

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### 前言

冠状动脉粥样硬化作为冠心病的病理生理过程,其发生和发展的具体机制尚未完全明确。肥胖与心血管疾病的发展密切相关,越来越多的证据表明心血管疾病是由肥胖驱动的脂肪组织功能紊乱的"附带损伤",肥胖促进了机体内的慢性炎症状态,常导致亲炎性脂肪激素类和抗炎脂类的下降,从而导致心血管疾病的发病<sup>[1]</sup>。

心外膜脂肪组织(epicardial adipose tissue, EAT)与心肌之间具有独特的解剖位置、代谢功能及内分泌、旁分泌特性、脂肪

浸润,与冠状动脉粥样硬化病理生理过程的关系密切,在冠心病发生、发展中处于极其重要的地位<sup>[2,3]</sup>。目前,针对 EAT 与冠状动脉粥样硬化病理生理相关机制及临床症状的研究逐渐增多,相关研究也基本肯定了 EAT 与冠心病发生及其预后具有相关性,但其与冠状动脉 Gensini 评分、Syntax 评分的是否具有相关性尚未阐明。Gensini 评分、Syntax 评分作为评判术后不良心脑血管事件(major adverse cardiac and cerebrovascular event, MACCE)发生率、冠脉病变复杂程度的重要评分,是决定患者临床治疗方案的最佳临床策略制定工具<sup>[4]</sup>。本研究旨在探讨超声测量心外膜脂肪组织厚度是否与冠状动脉病变 Gensini 评

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分、Syntax 评分相关, 以期为评估冠状动脉狭窄的严重程度提供参考依据。

## 1 对象和方法

### 1.1 对象

回顾性收集新疆维吾尔自治区人民医院心血管内科 2016 年 1 月~2016 年 12 月收治经冠脉造影确诊的冠心病患者并除外既往有 PCI 和(或 CABG)手术史患者共计 102 例(男 78 例、女 42 例), 年龄 36~92(62± 12)岁, 排除标准: 既往有胸廓畸形, 有心包、纵膈手术史, 有心包纵膈占位、积液病史, 有肺气肿、肺部阻塞性肺病, 有肺部占位, 有胸腔积液, 有甲状腺疾病, 有快速性心律失常, 有肝肾功能不全。入选患者均对本研究签署知情同意书。

### 1.2 冠状动脉造影

所有患者均采用选择性冠状动脉造影方式, 评估冠状动脉疾病情况。左冠脉至少在 4 个体位摄影, 右冠脉至少在 2 个体位摄影, 如有部分偏心性病变显示不清时, 可增加其他体位协助显示, 直达冠脉各段能够充分显示后, 由三名从事冠心病介入治疗工作的副主任医师以上职称人员分别根据造影结果对所有患者冠脉疾病严重程度进行评价, 介入医师对 EAT 检查结果单盲。

### 1.3 评价方法

Syntax 评分最初作为一个评分系统, 帮助评估对于冠脉病变既适于 PCI 又适于冠状动脉旁路移植术 (coronary artery bypass grafting, CABG), 同时患者一般状况较好, 能耐受外科手术治疗, 且预期外科手术病死率低的患者, 帮助制定治疗决策<sup>[9]</sup>, 且此评分能很好量化冠脉病变复杂程度<sup>[6]</sup>。Gensini 评分法: 首先根据解剖定位将冠脉分成 14 段, 根据不同病变血管在冠状动脉血液供应、对心肌重要性的不同, 分别将不同病变血管的不同节段制定不同的权重系数。根据冠状动脉血管重构后, 管

腔狭窄程度的不同, 分别给以不同的权重系数, 评分方法为冠状动脉腔狭窄程度权重系数乘以各病变血管的权重系数, 最后总评分为各分支血管评分之和。

### 1.4 超声心动图

所有患者的超声心动图测量都是由同一名超声医师完成, 使用美国通用电气 VIVID E9 彩色多普勒超声诊断仪, 探头为: 2.5 mHz 二维心脏探头, 测量切面选择美国超声心动图学会指定的, EAT 厚度测量标准: 胸骨旁左室长轴切面, 角度为垂直于主动脉瓣环, 于心室收缩末期, 测量右室游离壁与心包脏层之间低无回声区的厚度, 重复测量 3 次后取平均值<sup>[7]</sup>。

### 1.5 统计学分析

使用 SPSS16.0 统计软件进行统计分析, 连续变量表示为均数± 标准差, 样本率的比较使用卡方检验, 符合正态分布的数据进行 Shapiro-Wilk 测试, 不符合正态分布资料, 采用中位数± 四分位数间距进行秩和检验。所有相关性分析采用 Pearson 相关性检验, 以 P<0.05 为差异具有统计学意义。

## 2 结果

在 102 例样本中, 我们排除了其中 7 例因以下原因: 冠状动脉血管痉挛、冠状动脉肌桥、肥厚性心肌病、冠脉慢流、严重瓣膜病、超声心动图图像模糊。剩余的 95 名患者临床表现如下: 不稳定心绞痛 52 人, 非 ST 段抬高性心肌梗死、ST 段抬高性心肌梗死 8 人, 稳定心绞痛 35 人。同时随机纳入经冠脉造影证实冠脉未见狭窄的冠心病患者 65 例作为对照组。

### 2.1 两组患者临床资料比较

冠心病病变组的患者有糖尿病比例较冠脉正常组高。两组之间年龄、性别、有无高血压病史、有无冠心病家族史、院外使用他汀类药物情况、血脂代谢无明显差异性。EAT 厚度: 冠脉正常组 3.89± 0.2 mm, 冠心病病变组 6.19± 1.19 mm, 冠心病病变组显著高于冠脉正常组(P<0.001)。

表 1 两组患者一般临床资料的比较

Table 1 Comparison of the general clinical data between two groups of patients

| Clinical general data   | Normal coronary group<br>(n=65) | Coronary lesion group<br>(n=95) | P      |
|-------------------------|---------------------------------|---------------------------------|--------|
| Age(year)               | 43.70± 9.07                     | 44.84± 11.72                    | 0.768  |
| Sex(male / female)      | (38/27)                         | (63/32)                         | 0.312  |
| BMI(kg/m <sup>2</sup> ) | 24.80± 4.42                     | 25.19± 3.77                     | 0.818  |
| CHD History(yes/no)     | (7/58)                          | (18/77)                         | 0.162  |
| Smoking(yes/no)         | (36/29)                         | (65/30)                         | 0.093  |
| HBP(yes/no)             | (30/35)                         | (58/37)                         | 0.063  |
| T2DM(yes/no)            | (26/39)                         | (47/48)                         | 0.237  |
| CHOL(mmol/L)            | 5.11± 1.02                      | 4.83± 1.19                      | 0.543  |
| LDL-C(mmol/L)           | 3.4± 0.53                       | 3.8± 0.74                       | 0.078  |
| TG(mmol/L)*             | 2.02(1.49,2.75)                 | 1.53(1.25,2.28)                 | 0.073  |
| EAT thickness(mm)       | 3.89± 0.29                      | 6.19± 1.19                      | <0.001 |

\*\*\*non normal distribution data, median± four digit spacing, rank sum test.

## 2.2 不同 EAT 厚度冠脉病变组 Gensini 评分、Syntax 评分的比较

依据超声结果,按 EAT 的厚度分为 <5 毫米组、5-7 毫米组、>7 毫米组,各组 Gensini 评分为:7.21± 7.73,37.80± 29.55

和 62.77± 27.26;Syntax 评分为:7.13± 7.70,19.71± 7.27 和 24.95± 4.31。随着 EAT 厚度的增加,各组 Gensini 评分、Syntax 评分也逐渐增加(P<0.05)。

表 2 不同 EAT 厚度冠脉病变组 Gensini 评分、Syntax 评分的比较

Table 2 Comparison of the Gensini score, Syntax score between patients with different EAT thickness

| Scoring system | < 5 mm     | 5 - 7 mm     | 0> 7 mm      | P                       |
|----------------|------------|--------------|--------------|-------------------------|
| Gensini score  | 7.21± 7.73 | 37.80± 29.55 | 62.77± 27.26 | <0.004 <sup>a,b,c</sup> |
| Syntax score   | 7.13± 7.70 | 19.71± 7.27  | 24.95± 4.31  | <0.003 <sup>a,b,c</sup> |

There was a difference between the a:<5 mm group and the >5-7 mm group; there was a difference between the b:<5 mm group and the > 7 mm group; there was a difference between the c:5 7 mm group and the > 7 mm group (P < 0.05).

## 2.3 EAT 与 Gensini 评分、Syntax 评分的相关性

分(r=0.689,P<0.001)均呈正相关。

EAT 的厚度与 Gensini 评分 (r=0.621,P<0.001)、Syntax 评

表 3 EAT 厚度与 Gensini 评分、Syntax 评分的相关性分析

Table 3 Correlative analysis of the EAT thickness with Gensini score, Syntax score

| Epicardial adipose tissue thickness | Pearson correlation coefficient | P      |
|-------------------------------------|---------------------------------|--------|
| Gensini score                       | 0.621                           | <0.001 |
| Syntax score                        | 0.689                           | <0.001 |

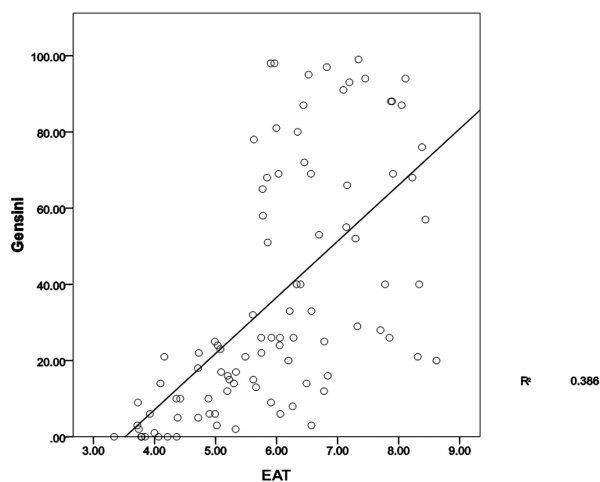


图 1 EAT 厚度与 Gensini 评分的相关性分析散点图

Fig.1 Scatterplot of EAT thickness and Gensini score correlation

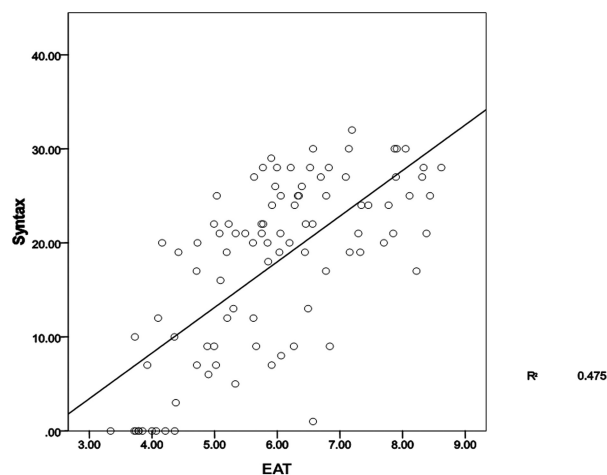


图 2 EAT 厚度与 Syntax 评分相关性分析散点图

Fig.2 Scatterplot of EAT thickness and Syntax score correlation

## 3 讨论

目前研究多表明在特定位置测量 EAT 体积及组织厚度与冠心病发病率、发展过程、预后等方面密切相关。Mazurek T<sup>[8]</sup>等研究发现心外膜脂肪相较于内脏脂肪或其他脂肪组织摄入更多的 18- 氟脱氧葡萄糖,这一结果表明心外膜脂肪可能通过炎症反应参与心脏疾病的发生发展。Alexios s<sup>[9]</sup>等首次人类身上证明 EAT 中脂联素的表达是由心脏释放的氧化产物的旁分泌作用控制的,这些效应构成心脏抗心肌氧化应激的新型防御机制。越来越多的证据表明心外膜脂肪在冠脉粥样硬化的发生发展中发挥重要的作用。Yu Du<sup>[10]</sup>等研究发现与 EAT 直接相关连的 Omentin-1 与冠状动脉疾病直接相关,且在 CAD 人群中,该因子水平较非 CAD 患者中显著降低,换言之,EAT 完全参

与了冠状动脉粥样硬化进程。然而,鲜有直接揭示 EAT 厚度与冠心病病变程度是否具有相关性。

Uchida Y 等在尸解冠状动脉段及冠状动脉外包裹的心外膜脂肪组织(Pericoronary Adipose Tissue,PCAT)进行免疫组化,发现包含氧化低密度脂蛋白的单核细胞同时沉积于与冠状动脉管壁及 PCAT 中,且包含氧化低密度脂蛋白的单核细胞穿越 PCAT 与冠脉血管外膜、冠脉血管外弹性膜及内弹性膜,进而推测单核细胞从 PCAT 运输氧化低密度脂蛋白到冠脉内膜下,参与冠脉粥样硬化的形成<sup>[12,13]</sup>。进一步研究显示炎性介质在心外膜脂肪组织中的局部反应加重损害血管内皮功能,加速动脉粥样硬化进程<sup>[14-16]</sup>。

本研究中,冠脉正常组与冠心病病变组的 EAT 值为:3.89± 0.29 mm 和 6.19± 1.19 mm,,这一结果与国内外多位学

者研究结果相似,提示 EAT 与冠心病形成有关。Gil N. Bachar<sup>[17,18]</sup>等研究发现无症状但冠脉血管明显狭窄(狭窄大于 50%)的患者 EAT 显著高于无冠脉明显狭窄的患者,受试者分析(receiver operating characteristic, ROC)显示 EAT 厚度 $\geq 2.4$  mm 可预测显著的冠状动脉狭窄( $> 50\%$ 的直径值)的存在,且与冠状动脉钙化指数无明显相关性。Bai-Chin Lee<sup>[19]</sup>等人对 846 名无冠心病缺血症状的患者进行冠状动脉 CTA 检查,了解其冠状动脉血管狭窄程度及心外膜脂肪组织百分比(percentage of epicardial adipose tissue, %EAT),经过多变量逻辑回归分析发现%EAT $>0.41\%$ 时提示阻塞性冠状动脉疾病,%EAT  $>0.47\%$ 时提示严重阻塞性冠状动脉疾病,而且其独立于肥胖、冠状动脉钙负担和弗雷明汉风险因素等,可预测冠状动脉疾病的发生风险。

Gensini 评分、Syntax 评分作为评价冠心病 PCI 和 CABG 术中级术后风险的指标,亦可作为评价冠脉病变复杂程度的标准。据超声测得 EAT 厚度并进行分组,统计显示组间 Gensini 评分、Syntax 评分存在显著差异性。Gensini 评分分别为:7.21 $\pm$ 7.73、37.80 $\pm$ 29.55、62.77 $\pm$ 27.26。Syntax 评分分别为:7.13 $\pm$ 7.70、19.71 $\pm$ 7.27、24.95 $\pm$ 4.31。二者随 EAT 厚度的增加逐渐增加,直线相关分析表明 EAT 的厚度与 Gensini 评分( $r=0.621$ )、Syntax 评分( $r=0.689$ )均呈显著正相关,与冠心病病变复杂程度正相关,进一步揭示 EAT 厚度与患者冠脉病变复杂程度呈正相关。

EAT 包绕冠状动脉的部分被定义为 PCAT,其通过直接浸润、旁分泌等途径影响冠脉血管的舒张、收缩和重构功能。伍琼<sup>[20]</sup>等人回顾 143 例冠脉造影提示冠脉血管狭窄小于 50%患者,根据造影结果评价 TIMI 血流分级,同时采取经胸超声的办法,了解心外膜脂肪组织厚度;通过统计学分析多因素 logistic 回归分析发现心外膜脂肪组织厚度可作为危险因素之一预测非阻塞性冠状动脉慢血流的发生。相关性分析还显示二者负相关,应用 ROC 曲线对准确率、特异性进行分析后可知,心外膜脂肪组织厚度的准确率较高,可作为预测非阻塞性冠状动脉慢血流的条件之一,提示心外膜脂肪组织厚度可作为非阻塞性冠状动脉慢血流预测因素。Santosh Kumar Sinha<sup>[21]</sup>等研究显示经胸超声心动图测量的厚度与 CAD 的存在和严重程度密切相关,具有较高的敏感的,且临床操作简便,成本低等优点。对 ACS 可能有助于危险分层,在 ROC 生存曲线分析中,EAT $>4.65$  mm 时,预测冠状动脉狭窄的敏感性为 71.6%,特异性为 73.1%,其结果与本研究相似。

然而,不同冠心病分型,其具体机制不同,对比急性冠脉综合征与稳定性心绞痛,冠脉粥样斑块稳定预后,其中参与机制复杂<sup>[22]</sup>。因此本研究存在一定的局限性,首先纳入样本量偏小,其次,EAT 测量现有较为准确的方法为心肌 MRI,但因其价格昂贵,技术难度大,临床可操作性较小,故本研究采用超声心动图检查,临床简便易行,为了尽可能减少干扰因素,研究设计时要求使用同一台超声仪器、同一名超声医师重复多次测量,尽可能减少测量误差。为增加说服力,随着研究的深入,今后增加样本量,条件许可可选用心肌 MRI 作为测量 EAT 的“金指标”。

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