

## • 临床研究 •

## 冠状动脉重构的血管内超声研究

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**【摘要】 目的** 应用血管内超声探讨冠状动脉重构的病变特征及其与临床表现的关系。**方法** 39例急性冠脉综合征患者与45例稳定性心绞痛患者进行冠脉造影及血管内超声检查,对病变进行定性和定量测定。包括外弹力膜血管面积(EEMA)、最小血管内腔面积、斑块面积、斑块体积及斑块的性状和重构指数,根据血管内超声斑块的性状分为软斑块和硬斑块(包括纤维斑块、钙化斑块和混合斑块)。重构指数(RI) = 病变处 EEMA/平均参考血管处 EEMA。若  $RI > 1.0$  为阳性重构,  $RI < 1.0$  为阴性重构。**结果** 阳性重构及阴性重构两组年龄、性别及冠心病危险因素等无明显差别,急性冠状动脉综合征的患者更多的表现为阳性重构(61.4% vs 30.0%,  $P < 0.01$ )。稳定性心绞痛的患者更多的表现为阴性重构(70.0% vs 38.6%,  $P < 0.01$ )。与阴性重构相比,阳性重构一般狭窄程度较轻,但病变部位的血管面积及斑块面积较大[(17.8±7.0) vs (13.6±4.9) mm<sup>2</sup>, (12.2±5.5) vs (9.5±4.8) mm<sup>2</sup>,  $P < 0.01$ ],同时阳性重构多为偏心性软斑块,发生钙化的较少。**结论** 阳性重构及阴性重构的病理特征不同,阳性重构病变以软斑块及偏心性斑块多见,冠状动脉重构与临床表现及斑块特征有关。

**【关键词】** 冠状动脉疾病;超声检查,介入性

## Investigation of coronary arterial remodeling by intravascular ultrasound

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**【Abstract】 Objective** To investigate the lesion characteristics of coronary remodeling by intravascular ultrasound(IVUS) and to evaluate the relation between coronary remodeling pattern and clinical presentation of coronary heart disease. **Methods** Eighty-four selected patients who underwent coronary angiography and pre-intervention IVUS were analyzed. 39 cases of acute myocardial infarction and unstable angina pectoris were categorized as acute coronary syndrome (ACS), and 45 cases of stable angina pectoris (SAP) as stable coronary artery disease (CAD). IVUS was used to measure the external elastic membrane area(EEMA), minimal luminal area, plaque area(PA), plaque volume, plaque character and arterial remodeling index. The lesions were classified into soft plaque and hard plaque(including fibrous plaque, calcified plaque and mixed plaque) according to different ultrasound patterns of tissue reflection. The remodeling index(RI) was defined as the ratio of vessel cross sectional area(EEMA) of lesion segment to the mean reference EEMA. Positive remodeling was defined as  $RI > 1.0$  and negative remodeling as  $RI < 1.0$ . Coronary remodeling patterns and plaque morphology of the culprit lesion obtained by IVUS were analyzed in terms of their relation with clinical presentation or angiographic morphology. **Results** The age, sex and risk factors for coronary heart disease (hypertension, diabetes, smoking, hyperlipemia) had no significant differences between negative remodeling and positive remodeling groups( $P > 0.05$ ). In ACS group, positive remodeling was observed more frequently than in SAP group (61.4% vs 30.0%,  $P < 0.01$ ), whereas in SAP group negative remodeling was more frequently observed than in ACS group (70.0% vs 38.6%,  $P < 0.01$ ). Positive remodeling was usually based on mild stenosis ( $\leq 50\%$ ), but the EEMA and the PA were significantly larger in positive remodeling lesion than those in negative remodeling lesion[(17.8±7.0) mm<sup>2</sup> vs (13.6±4.9) mm<sup>2</sup>, (12.2±5.5) mm<sup>2</sup> vs (9.5±4.8) mm<sup>2</sup>,  $P < 0.01$ ]. In patients with positive remodeling, soft plaque, eccentric plaque with little calcification was most frequent (63.6%,

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65.9% respectively). **Conclusion** The plaque morphology of the culprit lesion are different between the two kinds of coronary remodeling patterns. The lesion feature in positive remodeling is apparently soft eccentric plaque. These results may reflect the impact of remodeling types and its culprit lesion characteristics of CAD on clinical presentation.

**【Key words】** coronary artery disease; ultrasound; interventional

冠状动脉(冠脉)重构是血管对斑块的代偿性反应,血管的代偿性扩张称为正性重构(positive remodeling),反之称为负性重构(negative remodeling)。血管重构在冠心病病理生理方面起重要作用<sup>[1]</sup>。冠脉造影只能评价血管内腔的大小而无法对重构及其性质做出判断。血管内超声检查(intravascular ultrasound, IVUS)不仅能够反映血管内腔的变化,同时也能反映含斑块在内的血管横断面结构以及斑块的性状等<sup>[2]</sup>,因此 IVUS 在冠心病的诊断上发挥重要的作用<sup>[3,4]</sup>。笔者对冠心病罪犯血管进行了 IVUS 研究,试图探讨血管重构的病理特征及临床特点。

## 1 对象和方法

**1.1 对象** 2002年6月至2003年10月,84例冠心病患者接受冠脉造影及 IVUS,选择罪犯血管进行比较。其中男 51 例,女 33 例,年龄 42~78 (60.4±8.3)岁。84 例患者中急性冠脉综合征 39 例(不稳定性心绞痛 30 例、心肌梗死 9 例)、稳定性心绞痛 45 例。

**1.2 方法** 通过计算机辅助的心血管造影分析系统对造影资料进行分析,测量病变前后参照血管径(reference vessels diameter, RD)、最小血管径(minimum lumen diameter, MLD)、直径狭窄率[diameter stenosis, DS,  $DS = (RD - MLD) \div RD \times 100\%$ ]及病变长度。

血管内超声仪为 Boston Scientific 公司生产的 Clearview 型超声仪,采用 3F 30MHz 单轨机械探头,所有超声图像通过一自动回辙系统获得,回辙速度为 1mm/s,所有数据记录在录像带上,然后通过计算机软件进行分析,对冠脉病变进行定量定性诊

断,包括:血管外弹力膜面积(the external elastic membrane cross sectional area, EEMA)代表血管的总面积、最小血管内膜腔截面积(minimal luminal cross-sectional areas, MLA)、斑块面积[plaque cross-sectional areas, PA,  $PA = \text{血管面积}(\text{vessel area, VA}) - \text{MLA}$ ]及斑块的性状,包括钙化斑块、纤维斑块、软斑块、混合斑块以及斑块的偏心程度等。钙化斑块为斑块的回声比血管管壁外膜回声强并伴有声影,其范围 $>90^\circ$ ;硬斑块为斑块的回声与血管管壁外膜回声大致相同,但后方无声影;软斑块为斑块的回声比血管管壁外膜回声弱。钙化斑块、纤维斑块及混合斑块统称为硬斑块。血管重构指数(remodeling index, RI) = 病变处 EEMA/ 参照血管平均 EEMA。RI $>1$  为正性重构,RI $<1$  为负性重构。斑块体积测量方法:通过软件将图像逐帧回放,对血管面积进行连续测量后自动生成血管体积(vessel volume, SV)及血管腔体积(luminal volume, LV),然后计算出斑块体积(plaque volume, PV), $PV = SV - LV$ 。

**1.3 统计学处理** 所测数据采用 SPSS10.0 软件进行统计学分析,计量数据以  $\bar{x} \pm s$  表示,组间均数比较用  $t$  检验。计数资料组间比较采用  $\chi^2$  检验,  $P < 0.05$  认为差异有统计学意义。

## 2 结果

**2.1 重构与患者临床背景及临床表现的关系** 84 例患者中正性重构 44 例,负性重构 40 例,正性重构及负性重构两组患者的病史情况等无统计学意义差异(表 1)。正性重构临床上多见于急性冠脉综合征,而负性重构多见于稳定性心绞痛,两组比较差异有统计学意义(表 1)。

表 1 重构与患者临床背景及临床表现的关系

| 组别   | n         | 年龄(岁)     | 女性例(%)    | 糖尿病例(%)     | 高血压例(%)    |
|------|-----------|-----------|-----------|-------------|------------|
| 负性重构 | 40        | 61.4±8.5  | 14(35.0%) | 13(32.5%)   | 14(35.0%)  |
| 正性重构 | 44        | 59.4±7.9  | 9(20.5%)  | 16(36.4%)   | 17(38.6%)  |
| 组别   | 吸烟例(%)    | 高血脂例(%)   | 饮酒例(%)    | 急性冠脉综合征例(%) | 稳定性心绞痛例(%) |
| 负性重构 | 10(25.0%) | 15(37.5%) | 18(45.0%) | 12(30.0%)   | 28(70.0%)  |
| 正性重构 | 12(27.3%) | 15(34.1%) | 21(47.7%) | 27(61.4%)*  | 17(38.6%)* |

注:与负性重构组比较,\* $P < 0.01$

**2.2 重构与斑块大小及性状的关系** 根据血管造影把病变狭窄程度分为轻度( $\leq 50\%$ )、中度( $50\% \sim 75\%$ )和重度( $\geq 75\%$ )狭窄。可见重构与狭窄程度有关,正性重构多见于轻度狭窄,而负性重构多见于重度狭窄,两组比较差异有统计学意义(表 2)。正性重构虽然狭窄程度较轻,但血管面积、斑块面积及体积均较大;负性重构虽狭窄程度较重,但斑块面积及体积较小,两组比较差异有统计学意义(表 2)。正性重构以偏心性斑块、软斑块、斑块破裂多见,钙化性斑块(18.2%)较少;而负性重构以硬斑块(其中钙化斑块 52.5%)多见,斑块破裂发生率较低,两组比较差异有统计学意义(表 2,图 1)。



正性血管重构:血管面积增大,并可见斑块面积较大的偏心性的软斑块

图 1 正性血管重构图像

3 讨论

冠脉粥样硬化斑块进展时有两种代偿方式,一种为侧支循环形成,另一个为血管重构。侧支循环形成较晚,而血管重构可以在较早的时期内发生,先于血管造影发现的侧支循环。因而有时临床有冠心病而血管造影却正常<sup>[6]</sup>。从形态学角度看,代偿性扩张能够延缓冠脉管腔狭窄,而血管皱缩则进一步减少心肌血供。

笔者研究发现,血管重构和冠心病的临床表现明显相关,正性重构的患者更多的表现为急性冠脉综合征,血管病变更多为偏心性软斑块,且较少含有钙化;负性重构则相反。这与其他研究相同<sup>[6,7]</sup>。同时笔者还通过二维及三维 IVUS 发现正性重构虽然狭窄程度较轻,但斑块的面积及体积较大,提示管腔的狭窄是斑块形成和血管重构交互作用的结果,依赖于斑块生长与血管重构过程的平衡,正性重构血管代偿增大导致管腔狭窄较轻,因此从狭窄程度来评价血管重构有一定的局限性。正性重构虽可使冠脉血流增加,心肌缺血症状减轻,但斑块的不稳定性增加,易于破裂;而负性重构虽然使心肌缺血症状加重,但斑块的稳定性增加。这也可部分解释为何急性冠状动脉综合征多发于轻中度狭窄的病变。

血管重构发生的具体机制还不确定,可能与病变局部机械力学因素(血流剪切应力和压力)、体液因素(血管活性物质、生长介质和炎症介质)和斑块组成有关。同时不同类型的血管重构发生机制也可能不同。正性重构的偏心性斑块使血管壁局部剪切力增加,刺激无病变的血管壁内皮依赖性的血管扩张;正性重构的软斑块比纤维组织和钙化组织僵硬程度小,所以当管腔面积减少时,富含脂质的组织在剪切应力的作用下更易扩张。负性重构的纤维钙化性斑块则可限制血管适应性反应,血管代偿性扩张减小。正性重构与负性重构的关系仍不清楚,一般认为正性重构发生较早,负性重构发生较晚<sup>[8]</sup>。以脂质、疏松结缔组织为主的病变是较早期的粥样硬化,随着粥样硬化的进展,斑块的纤维组织和钙化增多。因此正性重构出现在粥样硬化的早期阶段,此时病变处于增殖期,有更多的脂质成分和炎症细胞浸润,这样斑块较不稳定,易于破裂而发生急性冠脉综合征。但正性重塑作为一种保护性的代偿反应,可维持有效的管腔面积和血供。随着冠脉粥样硬化的发

表 2 重构与斑块大小及性状的关系

| 组别   | n                        | ≤50%狭窄                 | 50%~75%狭窄              | ≥75%狭窄                 | 血管外弹力膜                 | 斑块面积               |
|------|--------------------------|------------------------|------------------------|------------------------|------------------------|--------------------|
|      |                          | 例(%)                   | 例(%)                   | 例(%)                   | 面积(mm <sup>2</sup> )   | (mm <sup>2</sup> ) |
| 负性重构 | 40                       | 6(15.0%)               | 12(30.0%)              | 22(55.0%)              | 13.6±4.9               | 9.5±4.8            |
| 正性重构 | 44                       | 24(54.6%)*             | 13(29.5%)              | 7(15.9%)*              | 17.8±7.0*              | 12.2±5.5*          |
| 组别   | 斑块体积(mm <sup>3</sup> )   | 硬斑块 例(%)               | 软斑块 例(%)               | 偏心性斑块 例(%)             | 斑块破裂 例(%)              |                    |
| 负性重构 | 217.9±78.7               | 29(72.5%)              | 11(27.5%)              | 13(32.5%)              | 5(12.5%)               |                    |
| 正性重构 | 303.6±123.4 <sup>#</sup> | 16(36.4%) <sup>#</sup> | 28(63.6%) <sup>#</sup> | 29(65.9%) <sup>#</sup> | 14(31.8%) <sup>#</sup> |                    |

注:与负性重构组比较,\* $P < 0.05$ , $^{\#}P < 0.01$

- [17] Wu L. Antioxidative properties of acetylsalicylic acid on vascular tissues from normotensive and spontaneously hypertensive rats. *Circulation*, 2002, 106: 105: 387-392.
- [18] Mehta JL, Chen J, Yu F, et al. Aspirin inhibits ox-LDL-mediated LOX-1 expression and metalloproteinase-1 in human coronary endothelial cells. *Cardiovasc Res*, 2004, 64: 243-249.
- [19] Svensson P, De FU, Hoshide S, et al. Comparative effects of ramipril on ambulatory and office blood pressure in hypertension patients. *Hypertens Res*, 2004, 27: 15-20.
- [20] Kohno I, Iwasaki H, Okutani M, et al. Administration time dependent effects of diltiazem on the 24-hour blood pressure profile of essential hypertension patients. *Chronobiol Int*, 1997, 14: 71-84.
- [21] Kitahara Y, Saito F, Akao M, et al. Effect of morning and bedtime dosing with cilnidipine on blood pressure, heart rate, and sympathetic nervous activity in essential hypertensive patients. *J Cardiovasc Pharmacol*, 2004, 43: 68-73.
- [22] Pickering TG, Levenstein M, Walmsley P. Night-time dosing of doxazosin has peak effect on morning ambulatory blood pressure. *Am J Hypertens*, 1994, 7: 844-847.

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展,斑块被纤维成分所替代并有钙盐沉积,此时病变相对稳定,但管腔失去了代偿性反应,则更多表现为负性重构。斑块易损性与血管重构的关系亦不清楚,研究认为正性重构的血管段多伴内皮功能障碍<sup>[9]</sup>,血管段生物活性更强<sup>[10]</sup>,是发生斑块破裂的因素之一;同时炎性物质也是一个重要环节,Varnava 等<sup>[11]</sup>发现正性重构的病变含有更多的脂质成分和巨噬细胞,而富含脂质和大量巨噬细胞浸润是斑块易损的标志。

冠脉重构在冠心病介入治疗中的指导作用已日益引起重视。研究发现,正性重构的病变介入治疗后不良事件发生率较高,而负性重构介入治疗后再次狭窄发生率较高<sup>[12]</sup>。由于血管重构,冠脉造影不能真实反映冠脉病变程度,常低估冠脉病变。因此介入术前使用 IVUS 检查有益于治疗决策。

#### 参考文献

- [1] Glagov S, Weisenberg E, Zarins CK, et al. Compensatory enlargement of human atherosclerotic coronary arteries. *N Engl J Med*, 1987, 316: 1371-1375.
- [2] 陈文强,张立,张梅,等. 血管内超声和病理学分析对比研究动脉粥样硬化兔不稳定斑块的破裂和血栓形成. *中华超声影像学杂志*, 2004, 13: 777-779.
- [3] 李俊峡, 鹰津良树, 宫本忠司, 等. 急性冠脉综合症与稳定型心绞痛患者冠脉病变的血管内超声比较研究. *中华超声影像学杂志*, 2004, 13: 256-258.
- [4] Kruk M, Jakub P, Lukasz K, et al. Cumulative incidence of coronary lesions with vulnerable characteristic in patients with stable angina pectoris: an intravascular ultrasound and angiographic study. *Int J Cardiol*, 2005, 102: 201-209.
- [5] 李俊峡, 鹰津良树, 宫本忠司, 等. 冠脉病变的血管内超声与冠脉造影的比较研究. *第四军医大学学报*, 2005, 26: 1191-1193.
- [6] Schoenhagen P, Ziada KM, Kapadia SR, et al. Extent and direction of arterial remodeling in stable versus unstable coronary syndromes. An intravascular ultrasound study. *Circulation*, 2000, 101: 598-603.
- [7] Fududa D, Kawarabayashi T, Tanaka A, et al. Lesion characteristics of acute myocardial infarction: an investigation with intravascular ultrasound. *Heart*, 2001, 85: 402-406.
- [8] Ward MR, Pasterkamp G, Yeung AC, et al. Arterial remodeling: mechanisms and clinical implication. *Circulation*, 2000, 102: 1186-1191.
- [9] 祁春梅, 李东野, 夏勇, 等. 血管内超声及冠脉内多普勒联合应用评价冠状动脉血管重构的实验研究. *徐州医学院学报*, 2003, 23: 491-494.
- [10] Dangns G, Mini GS, Mehran R, et al. Preintervention arterial remodeling as an independent predictor of target-lesion revascularization after nonstent coronary intervention—an analysis of 777 lesions with intravascular ultrasound imaging. *Circulation*, 1999, 99: 3149-3154.
- [11] Varnava AM, Mills PG, Davies MJ, et al. Relationship between coronary artery remodeling and plaque vulnerability. *Circulation*, 2002, 105: 939-943.
- [12] Endo A, Hirayama H, Yoshida O, et al. Arterial remodeling influences the development of intimal hyperplasia after stent implantation. *J Am Coll Cardiol*, 2001, 37: 70-75.