

· 临床研究 ·

50 ~ 70 岁人群心脏瓣膜钙化与冠状动脉粥样硬化的关系浅析

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【摘要】目的 探讨 50 ~ 70 岁年龄段人群钙化性瓣膜病与冠状动脉粥样硬化的关系, 试图在冠状动脉粥样硬化引发症状前提供预警。**方法** 选取 2010 年 1 月至 2015 年 6 月在解放军总医院行冠状动脉造影或冠状动脉 CT 血管造影 (CTA) 检查的年龄 50 ~ 70 岁的患者 205 例, 经超声心动图检查, 分为钙化组 ($n = 107$) 和非钙化组 ($n = 98$)。对两组患者血压、血糖、血脂数据进行对比分析, 两组患者冠心病发病率及狭窄血管病变程度与主动脉瓣膜钙化进行相关性分析。**结果** 瓣膜钙化组高血压、高脂血症和糖尿病发生率均显著高于非钙化组, 差异具有统计学意义 ($P < 0.05$), 两组患者除高密度脂蛋白胆固醇无明显差异外, 瓣膜钙化组的血压 (包括收缩压及舒张压)、总胆固醇、低密度脂蛋白胆固醇、甘油三酯、空腹血糖均高于非钙化组, 差异具有统计学意义 ($P < 0.05$)。瓣膜钙化组冠心病发生率高达 64.49%, 其中冠状动脉单支病变为 42.99%, 2 支冠状动脉病变者 13.08%, ≥ 3 支冠状动脉病变者为 8.41%, 而非钙化组冠心病发生率仅 17.35%, 且大多数为单支病变。无论冠心病总发病率, 还是冠状动脉狭窄血管支数, 瓣膜钙化组均明显高于非钙化组, 差异具有统计学意义 ($P < 0.01$)。**结论** 心脏瓣膜钙化与冠状动脉狭窄有相关性, 心脏瓣膜钙化可简便、有效地筛选需进一步接受冠状动脉 CTA 或冠状动脉造影检查的患者。

【关键词】 心脏瓣膜钙化; 冠状动脉疾病; 超声心动描记术

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Correlation of heart valve calcification and coronary atherosclerosis in 50- to 70-year-old adults

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【Abstract】Objective To investigate the correlation of heart valve calcification with coronary atherosclerosis in the adults at the age of 50 - 70 years in order to provide early warning before the symptom appearance induced by atherosclerosis. **Methods** Totally 205 subjects who underwent coronary artery angiography or coronary computed tomographic angiography (CTA) in our hospital from January 2010 to June 2015 were recruited in this study. According to the results of echocardiography, they were divided into calcification group ($n = 107$) and non-calcification group ($n = 98$). The blood pressure, blood glucose level and lipid profiles were measured and compared between the 2 groups. The correlations of the incidence of coronary heart disease and severity of coronary artery lesions were analyzed with heart valve calcification. **Results** The patients in calcification group had significantly higher incidences of hypertension, diabetes and hyperlipemia than those of non-calcification group ($P < 0.05$). Except for high-density lipoprotein cholesterol (HDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and fasting plasma glucose were obviously higher in calcification group than in non-calcification group ($P < 0.05$). The incidence of coronary artery disease was 64.49% in calcification group, with 42.99% of single vessel, 13.08% of 2 vessels, and 8.41% of ≥ 3 vessels of coronary artery lesions. However, in non-calcification group, the incidence of coronary artery disease was only 17.35%, and most of them were single vessel lesion. Both the incidence of coronary artery disease and the involved vessels of coronary artery lesions were remarkably higher in calcification group than in non-calcification group ($P < 0.05$). **Conclusion** Heart valve calcification and coronary artery lesions are correlated. Investigation of heart valve calcification is an easy, fast and effective method to screen the patients needing for CTA or coronary artery angiography.

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【Key words】 heart valve calcification; coronary artery disease; echocardiography

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钙化性心脏瓣膜病是随年龄增长心脏瓣膜结缔组织出现的钙化、纤维化所导致的结构及功能的异常。与年龄、性别、吸烟、高血压、冠心病、糖尿病、高脂血症、钙磷代谢紊乱等因素密切相关^[1-3]。研究表明,钙化性心脏瓣膜病与动脉粥样硬化有关^[4,5]。由于50~70岁年龄段人群为冠状动脉粥样硬化首发症状的高发年龄段,本研究旨在探讨该年龄段人群钙化性心脏瓣膜病与冠状动脉粥样硬化性心脏病的关系,试图在冠状动脉粥样硬化引发症状前提供预警,为临床疾病预防提供有价值的信息。

1 对象与方法

1.1 研究对象

选取2010年1月至2015年6月在解放军总医院行冠状动脉造影或冠状动脉CT血管造影(CT angiography, CTA)检查的年龄50~70岁患者205例。依据瓣膜是否钙化分为两组:钙化组($n=107$)和非钙化组($n=98$)。其中钙化组男101例,女6例,年龄53~70(62.4 ± 7.1)岁;非钙化组男88例,女10例,年龄52~68(60.2 ± 6.9)岁。排除标准:先天性心脏瓣膜疾病、风湿性心脏瓣膜病、心脏瓣膜手术或外伤、心脏急性或慢性炎症患者等。

1.2 方法

1.2.1 一般临床资料的检测 常规检测上肢血压。采集空腹肘正中静脉血,送检验科进行血脂、血糖等检测。

1.2.2 心脏瓣膜钙化情况的检测 采用经胸超声心动图评价心脏瓣膜钙化。患者取平卧位或左侧卧位,一般取心脏常规切面如心底短轴切面、二尖瓣短轴切面、左室长轴切面、心尖四腔切面、心尖五腔切面等,在二维及M型上观察各瓣膜瓣环部、瓣根部、瓣尖部、瓣膜交界的厚度、回声强度及活动度等,测量房室腔大小、室壁厚度、心功能等。应用彩色多普勒及多普勒频谱观察瓣膜反流及反流的部位、程度以及瓣膜的狭窄程度等。

1.2.3 冠状动脉的检查 所有患者均行冠状动脉造影检查或行冠状动脉CTA检查。以直径法计算冠状动脉主要分支管腔狭窄情况,取每支血管的多角度影像的平均值为该血管的狭窄程度。

1.3 诊断标准

(1)瓣膜钙化定义^[6]:凡瓣叶(或瓣环)增

厚 >3 mm和(或)回声强度 $\geq$ 同一切面主动脉根部后壁回声的为瓣膜钙化。(2)根据瓣膜僵硬与钙化程度分为轻、中、重度。轻度:瓣膜轻度增厚、变硬,局灶性点片样回声增强;中度:瓣膜钙化、硬化,有弥漫性斑点状或针状回声增强,瓣环呈多灶样钙化;重度:瓣叶明显增厚、僵硬变形,或瓣叶间粘连,瓦氏窦内结节状钙盐沉积,瓣环区域钙化灶融合成“C”形,回声明显增强或钙化累及周围的心肌组织。(3)冠状动脉病变(冠心病)判断标准依照美国心脏协会(American Heart Association, AHA)指南^[7],以冠状动脉造影或冠状动脉CTA检查提示冠状动脉相关分支狭窄 $>50\%$ 血管管腔直径即可判断,依据病变数量分为单支、双支、多支病变等。

1.4 统计学处理

采用SPSS19.0软件进行统计学分析与处理。计量资料用 $\bar{x} \pm s$ 表示,组间比较采用 t 检验;计数资料用百分率表示,组间比较采用 χ^2 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 钙化组瓣膜钙化情况分析

瓣膜钙化组107例。主动脉瓣膜钙化103例(96.26%),占绝大多数;二尖瓣钙化4例(3.74%);主动脉瓣合并二尖瓣钙化10例(9.34%)。轻度瓣膜钙化72例(67.28%),占多数;中度瓣膜钙化31例(28.97%);重度瓣膜钙化4例(3.74%)。主动脉瓣钙化中无冠瓣钙化59例(57.28%),右冠瓣钙化49例(47.57%),左冠瓣钙化31例(30.10%),多个瓣叶有钙化者为57例(55.34%)。主动脉瓣钙化伴主动脉瓣反流者64例(62.14%),主动脉瓣钙化引发主动脉瓣狭窄者4例(3.88%)。

2.2 两组患者一般资料比较

表1结果表明,两组患者年龄及性别比例差异无统计学意义($P > 0.05$);钙化组高血压、高脂血症和糖尿病发生率均显著高于非钙化组,且差异具有统计学意义($P < 0.05$)。

2.3 两组患者血压、血糖、血脂比较

表2结果表明,两组患者除高密度脂蛋白胆固醇无明显差异外($P > 0.05$),钙化组的血压(包括收缩压和舒张压)、总胆固醇、低密度脂蛋白胆固醇、甘油三酯及空腹血糖均显著高于非钙化组,且差异

具有统计学意义($P < 0.05$)。

表1 两组患者一般临床资料比较

Table 1 Comparison of clinical data between two groups

Item	Calcification group($n = 107$)	Non-calcification group($n = 98$)
Male[$n(\%)$]	101(94.39)	88(89.80)
Age(years, $\bar{x} \pm s$)	62.4 $\pm$ 7.1	60.2 $\pm$ 6.9
Hypertension[$n(\%)$]	71(66.36)*	31(31.63)
Diabetes mellitus[$n(\%)$]	57(53.27)**	24(24.49)
Hyperlipemia[$n(\%)$]	66(61.68)*	34(34.69)

Compared with non-calcification group, * $P < 0.05$, ** $P < 0.01$

表2 两组患者血压、血糖、血脂比较

Table 2 Comparison of blood pressure, free plasma glucose, blood lipid between the two groups ($\bar{x} \pm s$)

Index	Calcification group($n = 107$)	Non-calcification group($n = 98$)
SBP(mmHg)	158 $\pm$ 15**	141 $\pm$ 12
DBP(mmHg)	93 $\pm$ 9**	81 $\pm$ 6
TC(mmol/L)	6.7 $\pm$ 1.3**	5.1 $\pm$ 1.1
LDL-C(mmol/L)	4.3 $\pm$ 0.8*	3.1 $\pm$ 0.6
HDL-C(mmol/L)	1.3 $\pm$ 0.5	1.6 $\pm$ 0.4
TG(mmol/L)	2.5 $\pm$ 0.6*	1.7 $\pm$ 0.2
FPG(mmol/L)	6.6 $\pm$ 1.5*	5.4 $\pm$ 0.9

SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglycerides; FPG: free plasma glucose. 1 mmHg = 0.133 kPa. Compared with non-calcification group, * $P < 0.05$, ** $P < 0.01$

2.4 两组患者冠状动脉狭窄 >50% 及狭窄血管支数比较

表3 结果表明,不管是冠心病总发病率,还是冠状动脉病变支数,钙化组均明显高于非钙化组,且差异具有统计学意义($P < 0.01$)。

表3 两组患者冠状动脉狭窄 >50% 及狭窄血管支数比较

Table 3 Comparison of coronary artery stenosis >50% and the number of coronary artery stenosis [$n(\%)$]

Item	Calcification group($n = 107$)	Non-calcification group($n = 98$)
Coronary artery stenosis >50%	69(64.49)**	17(17.35)
Single vessel disease	46(42.99)**	14(14.29)
Double vessel disease	14(13.08)**	3(3.10)
≥ 3 vessel disease	9(8.41)**	0(0.00)

Compared with non-calcification group, ** $P < 0.01$

2.5 50~70岁人群瓣膜钙化的发病率

随机选取2010年1月至2015年6月在我院门诊及住院的年龄50~70岁的患者3498例,其中男性2659例(76.01%),女性839例(23.99%)。主动脉瓣膜钙化1190例(34.02%),二尖瓣钙化

385例(11.01%),三尖瓣钙化33人(0.009%),肺动脉瓣钙化病例仅2例。

3 讨论

超声心动图对心脏瓣膜病的检测具有特异性,是目前诊断钙化性瓣膜病最敏感、可靠、无创、可重复性强的检查方法,多年来已广泛应用于临床。其不仅可以观察瓣膜的钙化程度及活动度,还可以明确诊断相关的心血管硬化、心肌厚度及活动度、心腔大小及心功能情况等。既往大多数学者认为^[2],钙化性瓣膜病是一种与年龄密切相关的瓣膜老化、退行性病变和钙质沉积所致的老年性疾病,此病变实际上代表了年龄过程的变化。现在已有充分证据表明^[4],退行性瓣膜病变是一个伴有钙化的动脉粥样硬化的瓣膜病变,即心脏瓣膜的钙化与动脉粥样硬化的主动脉炎症过程所致,而且这种关系随年龄增长而更加明显,有高血压、高脂血症、糖尿病等并发症时,则更加速其瓣膜病变的发展。本研究显示瓣膜钙化组高血压、高脂血症和糖尿病发生率均显著高于非钙化组,差异具有统计学意义,与既往的研究结论一致。

心脏瓣膜的退行性变主要有3种形式^[6],即钙化、硬化、黏液变性,通常无瓣膜游离缘受累和瓣叶间粘连,即瓣叶间不发生粘连融合和固定,以此与风湿性心脏瓣膜病及其他炎症所致的瓣膜病变相区别。心脏瓣膜的钙化首先影响到主动脉瓣,且主动脉瓣受累多于二尖瓣,这是由于主动脉瓣相对于左房室瓣膜承受更多的压力负荷及高速血流的冲击。在我们的临床实践及本研究中也呈现这样的现象,瓣膜钙化病变也是以主动脉瓣的钙化病变占大多数,其次为二尖瓣,三尖瓣钙化很少,肺动脉瓣的钙化更少见。主动脉瓣膜病变主要集中在瓣膜主动脉侧内膜下,钙质一般从主动脉面的基底部开始,沿主动脉瓣环沉积,随病变发展,逐渐向瓣膜游离缘扩展,呈米粒状或线性钙化灶,重者钙化斑块可填满瓦氏窦。无冠瓣和右冠瓣的主动脉瓣的钙化病变重于左冠瓣,本研究与此结论相符。钙化可引起主动脉瓣反流,超声心动图表现为在舒张期可见由主动脉反流入左室内的花色反流束,严重钙化可引起主动脉瓣狭窄。钙化性主动脉瓣狭窄主要表现为主动脉瓣增厚、回声增强,收缩期瓣膜开放受限、瓣口流速增快、跨瓣压差增高等。

文献报道显示,钙化性瓣膜病与动脉粥样硬化有关,主动脉瓣膜钙化是动脉硬化进展的独立预测

因子,可作为动脉粥样硬化的标志^[8],是同种疾病的不同表现,可以认为主动脉瓣膜钙化是主动脉粥样硬化的延续,或动脉粥样硬化扩展至心脏瓣膜的一种结果^[9,10]。有学者^[11]研究认为,主动脉瓣钙化对冠状动脉的血流动力学产生影响的根本是降低冠状动脉血流储备。超声心动图对心脏主动脉瓣钙化的早期发现能够从某种程度上预示冠状动脉粥样硬化的可能性。

有研究显示,年龄是瓣膜钙化发病的独立危险因素,>80岁的老年人,瓣膜钙化发病率可高达80%以上^[12,13]。<40岁的成年人,除外风湿性心脏瓣膜病及先天瓣膜疾病,瓣膜钙化发生率较低。故我们选取50~70岁这一年龄段人群,旨在降低年龄对瓣膜的明显影响。本研究显示瓣膜钙化组冠心病发生率高达64.49%,其中冠状动脉单支病变为42.99%,双支冠状动脉病变者13.08%,≥3支冠状动脉病变者为8.41%,而非钙化组冠心病总发生率仅17.35%。不管从冠心病总发病率,还是冠状动脉狭窄血管支数,瓣膜钙化组均明显高于非钙化组,差异具有统计学意义。据报道西方人40~50岁年龄瓣膜钙化组其冠心病发生率>20%,故其在瓣膜外科手术前对>40岁患者常规行冠状动脉造影^[14]。而我国成年人>50岁瓣膜病患者术前做选择性冠状动脉造影为宜。本研究结果显示50~70岁这一年龄段瓣膜钙化人群其冠心病发病率可高达64.49%,虽以单支病变发病为主,但也不乏双支、≥3支冠状动脉病变患者。故我们建议>50岁瓣膜有明显钙化者,宜行冠状动脉CTA或冠状动脉造影等检查以进一步明确冠状动脉情况,并根据冠状动脉检查情况进行适当干预治疗。

总之,心脏瓣膜钙化与动脉粥样硬化密切相关,通过简便的超声心动图对心脏瓣膜钙化进行检测,心脏瓣膜尤其是主动脉瓣钙化的发现可提示冠心病存在的可能性,这与文献报道^[15]相同。主动脉瓣钙化可以作为冠心病无创评估的一个参考指标,而关于冠状动脉受累程度及受累范围则需要进一步冠状动脉CTA或冠状动脉造影等检查以进一步明确。在临床实际工作中,对于50~70岁这一有心脏瓣膜钙化风险的人群进行常规的冠状动脉粥样硬化的检查,对提高冠状动脉粥样硬化的早期诊断、防止心血管事件的突发具有重要临床意义。

【参考文献】

[1] Thanassoulis G, Massaro JM, Cury R, *et al.* Associations of long-term and early adult atherosclerosis risk factors with aortic and

mitral valve calcium [J]. *J Am Coll Cardiol*, 2010, 55 (22): 2491-2498.

- [2] Spadaccio C, Mozetic P, Nappi F, *et al.* Cells and extracellular matrix interplay in cardiac valve disease; because age matters [J]. *Basic Res Cardiol*, 2016, 111(2): 16.
- [3] Wang C, Jiang L, Feng S, *et al.* Risk factor analysis of calcification in aortic and mitral valves in maintenance peritoneal dialysis patients [J]. *Kidney Blood Press Res*, 2013, 37(4-5): 488-495.
- [4] Henein M, Hillgren P, Holmgren A, *et al.* Aortic root, not valve, calcification correlates with coronary artery calcification in patients with severe aortic stenosis: a two-center study [J]. *Atherosclerosis*, 2015, 243(2): 631-637.
- [5] Saha SA, Beatty AL, Mishra RK, *et al.* Usefulness of an Echocardiographic Composite Cardiac Calcium Score to predict death in patients with stable coronary artery disease (from the Heart and Soul Study) [J]. *Am J Cardiol*, 2015, 116(1): 50-58.
- [6] Islas F, Almería C, García-Fernández E, *et al.* Usefulness of echocardiographic criteria for transcatheter aortic valve implantation without balloon predilation: a single-center experience [J]. *J Am Soc Echocardiogr*, 2015, 28(4): 423-429.
- [7] Hope MD, Urbania TH, Yu JP, *et al.* Incidental aortic valve calcification on CT scans; significance for bicuspid tricuspid valve disease [J]. *Acad Radiol*, 2012, 19(5): 542-547.
- [8] Kilsch H, Lehmann N, Mahabadi AA, *et al.* Beyond Framingham risk factors and coronary calcification: does aortic valve calcification improve risk prediction? The Heinz Nixdorf Recall Study [J]. *Heart*, 2014, 100(12): 930-937.
- [9] Owens DS, Budoff MJ, Katz R, *et al.* Aortic valve calcium independently predicts coronary and cardiovascular events in a primary prevention population [J]. *JACC Cardiovasc Imaging*, 2012, 5(6): 619-625.
- [10] Couci AI, Siciliano V, Poggianti E, *et al.* Cardiac calcification by transthoracic echocardiography in patients with known or suspected coronary artery disease [J]. *Int J Cardiol*, 2010, 142(3): 288-295.
- [11] Schwartzberg S, Meledin V, Zilberman L, *et al.* Low circulating monocyte count is associated with severe aortic valve stenosis [J]. *Isr Med Assoc J*, 2013, 15(9): 500-504.
- [12] Thyregod HG, Holmberg F, Gerds TA, *et al.* Heart Team therapeutic decision-making and treatment in severe aortic valve stenosis [J]. *Scand Cardiovasc J*, 2016, 50(3): 146-153.
- [13] Liyanage L, Lee NJ, Cook T, *et al.* The impact of gender on cardiovascular system calcification in very elderly patients with severe aortic stenosis [J]. *Int J Cardiovasc Imaging*, 2016, 32(1): 173-179.
- [14] Chérif A, Farhati A, Ezzar T, *et al.* Coronary arteriography in severe aortic valve disease [J]. *Tunis Med*, 2005, 83(8): 445-447.
- [15] Geng F, Ge YD, Qin X. Study of association between the aortic valve calcification and coronary artery disease [J]. *China Med Pharm*, 2014, 4(12): 229-231. [耿峰,葛艺东,秦信.主动脉瓣钙化与冠心病的关系研究[J].中国医药科学,2014,4(12):229-231.]

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