升主动脉扩张及主动脉瓣功能障碍对二叶式主动脉瓣患者主动脉弹性影响的磁共振成像研究

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【摘要】 **目的** 通过磁共振成像研究升主动脉扩张和主动脉瓣功能障碍对二叶式主动脉瓣(bicuspid aortic valve, BAV)患者中段升主动脉(middle ascending aorta, mid-AA)和近端降主动脉(proximal descending aorta, PDA)弹性的影响。**方法** 前瞻性选取复旦大学附属中山医院2019年10月至2021年3月间130名BAV患者和30名健康志愿者做3.0 T磁共振检查,测量其主动脉扩张度。根据升主动脉直径和主动脉瓣功能将BAV患者分为4组:BAV伴正常或轻度瓣膜功能障碍且升主动脉不扩张组(BAV-CTL组, n=30);BAV伴正常或轻度瓣膜功能障碍且升主动脉扩张组(Dilated BAV-NF组, n=40);BAV伴中重度主动脉瓣狭窄(aortic stenosis, AS)且升主动脉扩张组(Dilated BAV-AS组, n=30);BAV伴中重度主动脉瓣关闭不全(aortic insufficiency, AI)且升主动脉扩张组(Dilated BAV-AI组, n=30)。在右肺动脉平面测量mid-AA和PDA的面积,计算其扩张度。采用Student's t检验和Mann-Whitney U检验比较连续性变量,卡方检验或Fisher精确检验比较分类变量。**结果** 在无严重瓣膜功能障碍者中,BAV伴升主动脉扩张组较不扩张组mid-AA扩张度降低[2.77(IQR:1.45～6.26) *vs.* 1.52 (IQR:1.08～2.19), P=0.004]。在升主动脉扩张者中,BAV伴中重度AI组主动脉扩张度较伴正常或轻度瓣膜功能障碍组高[mid-AA:1.52(IQR:1.08–2.19) *vs.* 2.29 (IQR:1.60～4.08), P=0.006; PDA:3.70(IQR:2.89～4.70) *vs.* 4.79 (IQR:2.93～6.80), P=0.024]; BAV伴中重度AI组主动脉扩张度较伴中重度AS组高[mid-AA:1.60 (IQR:0.99～2.26) *vs.* 2.29 (IQR:1.60～4.08), P=0.022; PDA:3.73 (IQR:2.38～4.40) *vs.* 4.79 (IQR:2.93～6.80), P=0.014]。**结论** 升主动脉扩张和AI是影响BAV患者主动脉弹性的主要因素,主动脉扩张对弹性的影响局限于升主动脉,而AI对主动脉弹性的影响范围更广。

【关键词】 二叶式主动脉瓣(BAV); 主动脉扩张度; 主动脉瓣狭窄(AS); 主动脉瓣关闭不全(AI); 磁共振成像(MRI)

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Effects of ascending aorta dilatation and aortic valve dysfunction on aortic elasticity of patients with bicuspid aortic valve: a magnetic resonance imaging study

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【**Abstract**】 **Objective** To study the effects of ascending aorta dilatation and aortic valve dysfunction on the elasticity of the middle ascending aorta (mid-AA) and proximal descending aorta (PDA) in patients with bicuspid aortic valve (BAV) by using magnetic resonance imaging (MRI). **Methods** From Oct

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2019 to Mar 2021, a total of 130 BAV patients and 30 healthy volunteers from Zhongshan Hospital, Fudan University were prospectively undergone 3.0 T MRI for aortic distensibility. BAV patients were categorized into 4 groups according to the diameter of ascending aorta and aortic valve function as follows: BAV with normal or mild aortic valve dysfunction and nondilated ascending aorta (AA) (BAV-CTL, n=30), BAV with normal or mild aortic valve dysfunction and dilated AA (Dilated BAV-NF, n=40), BAV with moderate to severe aortic stenosis and dilated AA (Dilated BAV-AS, n=30), and BAV with moderate to severe aortic insufficiency and dilated AA (Dilated BAV-AI, n=30). The cross-sectional areas and distensibility of mid-AA and PDA were assessed at the level of right pulmonary artery. Student's t test and Mann-Whitney U test were used to compare the continuous variables between the groups, while chi-square test or Fisher exact test was used to compare the categorical variables. **Results** Dilated BAV-NF group had decreased mid-AA distensibility [2.77 (IQR: 1.45–6.26) *vs.* 1.52 (IQR: 1.08–2.19), P=0.004] than BAV-CTL group. Compared with the Dilated BAV-NF, Dilated BAV-AI had elevated distensibility at mid-AA and PDA [mid-AA: 1.52 (IQR: 1.08–2.19) *vs.* 2.29 (IQR: 1.60–4.08), P=0.006; PDA: 3.70 (IQR: 2.89–4.70) *vs.* 4.79 (IQR: 2.93–6.80), P=0.024]. Compared with the Dilated BAV-AS, Dilated BAV-AI again showed elevated distensibility at mid-AA and PDA [mid-AA: 1.60 (IQR: 0.99–2.26) *vs.* 2.29 (IQR: 1.60–4.08), P=0.022; PDA: 3.73 (IQR: 2.38–4.40) *vs.* 4.79 (IQR: 2.93–6.80), P=0.014]. **Conclusion** Ascending aorta dilatation and aortic insufficiency are the main factors affecting aortic elasticity in patients with BAV. The effect of aortic dilatation on aortic elasticity is limited to the ascending aorta, while the effect of aortic insufficiency on aortic elasticity is more extensive.

【Key words】 bicuspid aortic valve (BAV); aortic distensibility; aortic stenosis (AS); aortic insufficiency (AI); magnetic resonance imaging (MRI)

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先天性二叶式主动脉瓣(bicuspid aortic valve, BAV)是最常见的先天性心脏畸形,发病率约1%～2%[1-2]。BAV常伴有主动脉瓣狭窄(aortic stenosis, AS)、主动脉瓣关闭不全(aortic insufficiency, AI)、主动脉瘤及主动脉夹层[3-4]。虽然目前对于引起BAV患者主动脉壁弹性变化的机制仍存在争议,但BAV患者表现出的异常血流动力学模式长期作用于主动脉壁,使主动脉弹性下降,最终导致主动脉瘤和主动脉夹层形成是被证实的机制[5]。

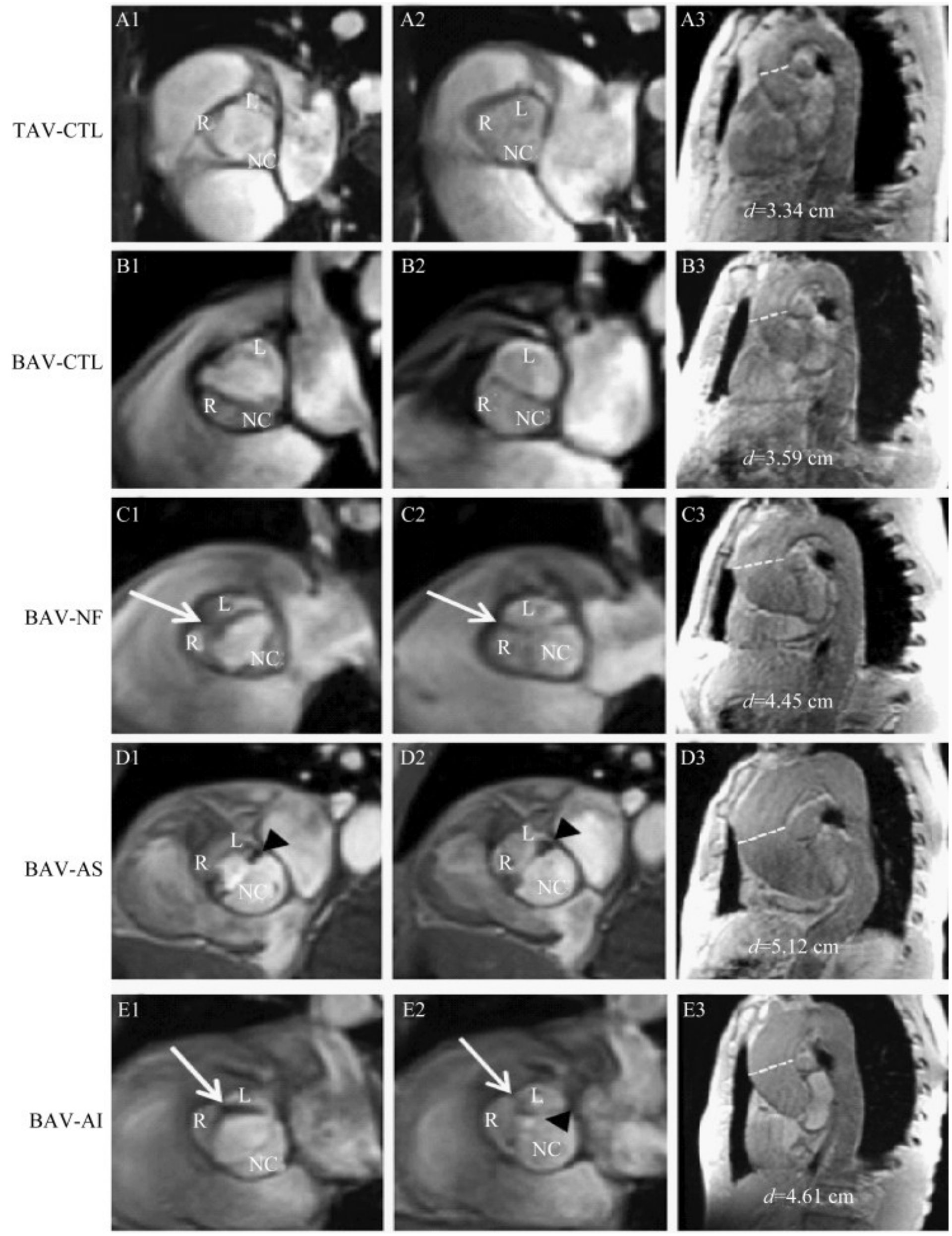
早期、准确评估主动脉弹性的变化可以为了解BAV患者主动脉壁重塑和BAV相关主动脉病提供更多信息[6]。主动脉扩张度是指一个心动周期内,在动脉血压压力变化的作用下,主动脉横截面积的相对变化[7]。主动脉扩张度可以通过磁共振成像(magnetic resonance imaging, MRI)直接获得,且在一次扫描中可以同时获得中段升主动脉(middle ascending aorta, mid-AA)和近端降主动脉(proximal descending aorta, PDA)的弹性参数。

对于正常三叶式主动脉瓣(tricuspid aortic valve, TAV)者,有研究表明升主动脉扩张是导致主动脉弹性减低的重要因素[8]。此外,目前已研究证实,主动脉瓣功能正常的BAV患者就可存在主动脉弹性减退,且减退程度在BAV伴升主动脉扩张者中更加明显[8-9]。然而,对于伴有升主动脉扩张的BAV患者,主动脉瓣功能障碍是否会加速主动脉壁重塑、导致其顺应性进一步下降,目前尚不清楚。我们的研究假设是升主动脉扩张和主动脉瓣功能障碍会影响BAV患者的主动脉弹性,目的是利用MRI测量mid-AA和PDA的直径、面积和扩张度,比较BAV伴升主动脉扩张和/或AS/AI的患者与健康对照组间两段主动脉的弹性差异。

资 料 和 方 法

研究对象 前瞻性选取复旦大学附属中山医院门诊2019年10月至2021年3月经临床和超声诊

断为BAV的患者130例。根据升主动脉直径和主动脉瓣功能,将BAV患者分为4组:BAV伴正常或轻度瓣膜功能障碍且升主动脉不扩张组(BAV-CTL,n=30);BAV伴正常或轻度瓣膜功能障碍且升主动脉扩张组(Dilated BAV-NF,n=40);BAV伴中重度主动脉瓣狭窄且升主动脉扩张组(Dilated BAV-AS,n=30);BAV伴中重度主动脉瓣关闭不全且升主动脉扩张组(Dilated BAV-AI,n=30)(图1B~E)。4组配对内容包括:年龄、性别、体表面积、收缩压、糖化血红蛋白水平和血清总胆固醇水平。诊断标准为:MRI上测得升主动脉直径≥40 mm定义为主动脉扩张。根据美国心脏协会/美国心脏病



A: TAV-CTL, systole (A1), diastole (A2) and nondilated ascending aorta (A3); B: BAV-CTL, systole (B1), diastole (B2) and nondilated ascending aorta (B3), RN fusion; C: BAV-NF, systole (C1), diastole (C2) and dilated ascending aorta (C3), LR fusion (white arrow: raphe); D: BAV-AS (black arrowhead), systole (D1), diastole (D2) and dilated ascending aorta (D3), LR fusion; E: BAV-AI (black arrowhead), systole (E1), diastole (E2) and dilated ascending aorta (E3), LR fusion (white arrow: raphe). NC: Non-coronary sinus; R: Right coronary sinus; L: Left coronary sinus; d: Diameter.

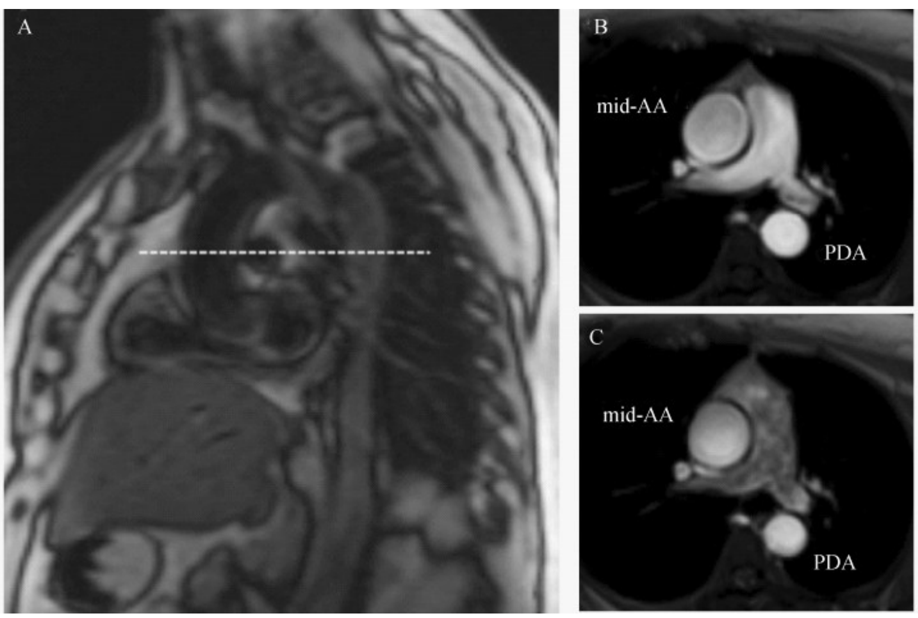
图1 TAV和BAV各组主动脉瓣形态和中段升主动脉直径

Fig 1 Aortic valve morphology and diameter of mid-AA in TAV and BAV subjects

学会指南,主动脉瓣轻、中、重度狭窄者,平均跨瓣压差分别为<20 mmHg、20~40 mmHg、>40 mmHg(1 mmHg=0.133 kPa,下同);主动脉瓣轻、中、重度关闭不全者,反流分数分别为<30%、30%~49%、≥50%[10]。排除标准:(1)同时存在中重度主动脉瓣狭窄和关闭不全;(2)主动脉缩窄和/或其他形式的先天性心脏病;(3)马方综合征或马方综合征家族史;(4)既往心血管手术史;(5)有MRI检查禁忌证。另外选取本院体检合格的30名TAV志愿者作为健康对照组(TAV-CTL,n=30)(图1A)。本研究获得复旦大学附属中山医院伦理委员会的批准(伦理号:B2020-232R)。所有参与者签署本研究的书面知情同意书。

超声检查 采用Philips iE33彩色多普勒超声诊断仪对所有受试者进行常规超声心动图检查。BAV可根据瓣膜融合形态分为:左右冠状窦融合型(left and right cusp fusion type,LR),右无冠状窦融合型(right and non-coronary cusp fusion type,RN)和左无冠状窦融合型(left and non-coronary cusp fusion type,LN)[11](图1)。本次试验未纳入LN型BAV患者。左心室容积通过Teichholz校正公式计算。

磁共振检查 采用3.0T(Verio,德国Siemens Medical Systems公司),磁共振稳态自由进动序列(steady-state free precession sequence,SSFP),8通道体部线圈,常规胸腹部定位扫描。在横断位、冠状位、矢状位定位图基础上,取右肺动脉平面,心电门控,屏气采集,获取一个心动周期mid-AA和PDA横断位图像(图2、3)。TR 45.3 ms,TE 2.4 ms,反转角12°,层厚6 mm,视野276 mm×340 mm,矩阵156×192,时间分辨率26~32 ms。



A: Oblique sagittal pilot image of the aorta is used to select the level of right pulmonary artery (dashed line) and measure diameter and cross-sectional area of mid-AA and PDA; B: Images of mid-AA and PDA acquired during systole; C: Images of mid-AA and PDA acquired during diastole.

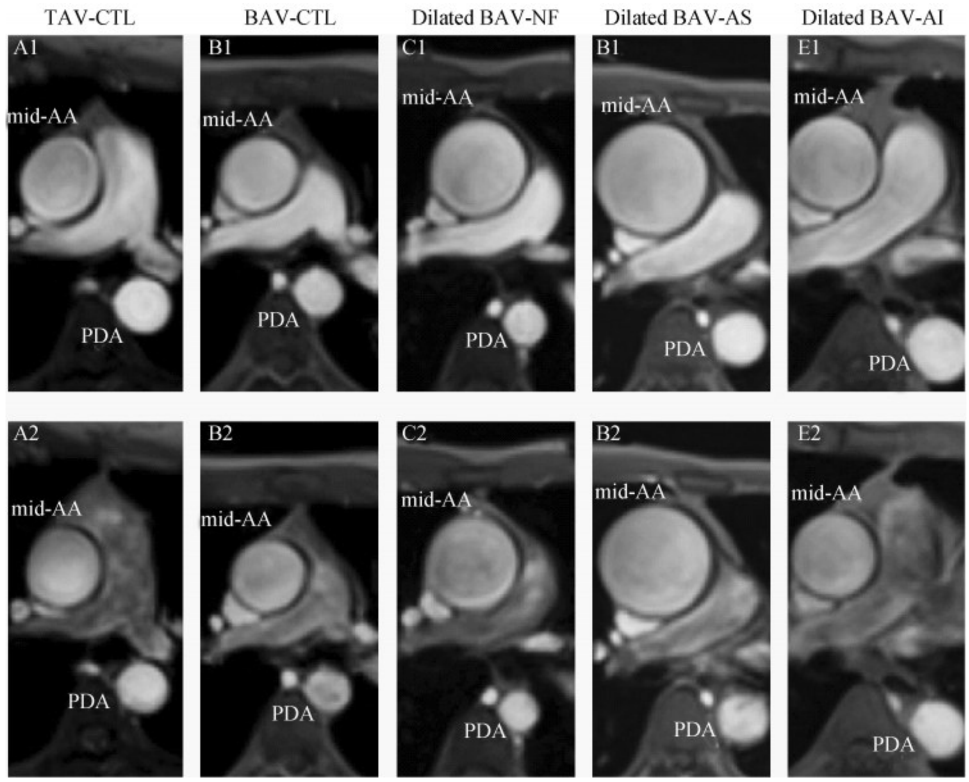
图2 健康对照组主动脉扩张度测定

Fig 2 Aortic distensibility calculation in a TAV-CTL

观察指标 TAV及BAV各组mid-AA和PDA直径、横截面积及主动脉扩张度。应用Syngo MR B14工作站,测量mid-AA和PDA的直径以及舒张期和收缩期的主动脉横截面积(图3)。结合动脉血压,根据公式[7]:[(Amax-Amin)/Amin]/(SBP-DBP),得到主动脉扩张度。Amax和Amin分别为主动脉收缩期的最大横截面积和舒张期的最小横截面积,SBP和DBP分别为所测得的肱动脉收缩压和舒张压。

在MRI检查前测得受试者右臂肱动脉收缩压和舒张压。

统计学分析 采用SPSS 20.0统计软件进行数据



A1, B1, C1, D1, E1: The maximum aortic cross-sectional areas of mid-AA and PDA in TAV-CTL, BAV-CTL, Dilated BAV-NF, Dilated BAV-AS, Dilated BAV-AI, respectively; A2, B2, C2, D2, E2: The minimum aortic cross-sectional areas of mid-AA and PDA in TAV-CTL, BAV-CTL, Dilated BAV-NF, Dilated BAV-AS, Dilated BAV-AI, respectively.

图3 TAV和BAV各组中段升主动脉和近端降主动脉的最大(上排)和最小横截面积(下排)

Fig 3 The maximum (top) and minimum (bottom) aortic cross-sectional area of mid-AA and PDA in TAV and BAV subjects

处理。采用Shapiro-Wilk检验、直方图和Q-Q图对连续型变量进行正态性检验。连续型变量以$\bar{x}\pm s$或中位数(四分位数)表示,分类型变量以数值(百分比)表示。服从正态分布的连续型变量采用Student's t检验,不符合正态分布则采用Mann-Whitney U检验。分类型变量用卡方检验或Fisher精确检验。对mid-AA和PDA扩张度的前后两次测量值采用组内相关系数分析(intraclass correlation coefficient,ICC)进行比较。$P<0.05$为差异有统计学意义。

结 果

患者基本情况 表1显示了TAV和BAV受试者的临床信息。BAV患者各组间在年龄、性别、体表面积、心率、共存疾病、用药情况以及瓣膜亚型上差异均无统计学意义。Dilated BAV-AI患者舒张压较Dilated BAV-AS患者小(F=4.682,t=2.685,P=0.010),脉压差较Dilated BAV-NF(F=18.196,t= −2.141,P=0.040)和Dilated BAV-AS大(F=8.852,t=−2.783,P=0.008),左心室容积和左心室容积指数较Dilated BAV-NF(左心室容积:F=40.774,t=−6.563;左心室容积指数:F=43.250,t=−6.703;P均<0.001)和Dilated BAV-AS大(左心室容积:F=18.851,t=−6.320;左心室容积指数:F=17.890,t=−6.302;P均<0.001)。Dilated BAV-AS患者平均跨瓣压差较Dilated BAV-NF(F=28.697,t=−11.181,P<0.000 1)和Dilated BAV-AI患者大(F=24.761,t=11.351,P<0.001)。

动脉直径、面积和扩张度 TAV-CTL和BAV-CTL两组间主动脉直径、升降主动脉横截面积和扩张度差异均无统计学意义。与BAV-CTL组相比,Dilated BAV-NF组的mid-AA直径和横截面积增大(直径:Z=−6.275;最大横截面积:Z=−6.210;最小横截面积:Z=−6.084;P均<0.001),mid-AA扩张度明显降低(Z=−2.854,P=0.004),而PDA直径、横截面积和扩张度差异均无统计学意义。与Dilated BAV-NF相比,Dilated BAV-AI患者mid-AA横截面积较大(最大横截面积:Z=−2.454,P=

表1 TAV对照组和BAV患者的临床特征

Tab 1 Baseline characteristics of BAV patients and TAV volunteers

Clinical characters	TAV-CTL (*n*=30)	BAV-CTL (*n*=30)	Dilated BAV-NF (*n*=40)	Dilated BAV-AS (*n*=30)	Dilated BAV-AI (*n*=30)	*P* values				
						TAV-CTL *vs.* BAV-CTL	BAV-CTL *vs.* Dilated BAV-NF	Dilated BAV-NF *vs.* Dilated BAV-AS	Dilated BAV-NF *vs.* Dilated BAV-AI	Dilated BAV-AS *vs.* Dilated BAV-AI
Age (y)	52.60±11.03	49.70±10.49	51.03±9.33	52.87±10.50	50.04±12.31	0.400	0.621	0.441	0.716	0.362
Male/Female	16/14	15/15	22/18	17/13	15/15	0.796	0.678	0.890	0.678	0.605
Body surface area (m^2)	1.70±0.14	1.70±0.15	1.71±0.15	1.69±0.20	1.75±0.12	0.815	0.733	0.677	0.276	0.216
SBP (mmHg)	125.70±8.76	125.90±5.49	123.53±9.00	123.10±8.94	126.36±7.83	0.931	0.284	0.845	0.199	0.160
DBP (mmHg)	70.40±11.49	72.75±4.84	74.18±6.76	76.90±8.84	68.56±13.27	0.407	0.405	0.148	0.068	**0.010**
Pulse pressure (mmHg)	55.30±8.87	53.15±5.98	49.35±8.58	46.20±10.45	57.80±18.53	0.374	0.081	0.171	**0.040**	**0.008**
Heart rate (bpm)	68.20±9.98	71.90±14.96	67.23±8.98	71.60±11.05	71.48±7.70	0.363	0.136	0.072	0.064	0.962
Comorbid conditions										
Hypertension	3 (10.0)	1 (3.3)	2 (5.0)	3 (10.0)	2 (6.7)	0.612	1.000	0.645	1.000	1.000
Diabetes	0	1 (3.3)	2 (5.0)	0	1 (3.3)	0.429	1.000	0.503	1.000	1.000
Dyslipidemia	1 (3.3)	2 (6.7)	1 (2.5)	1 (3.3)	0	1.000	0.573	1.000	1.000	1.000
Current medications										
Beta-blocker therapy	2 (6.7)	0	0	1 (3.3)	1 (3.3)	0.492	–	0.429	0.429	1.000
ACEI/ARB therapy	0	0	1 (2.5)	1 (3.3)	1 (3.3)	–	1.000	1.000	1.000	1.000
BAV subtype										
LR	–	15 (50.0)	16 (40.0)	14 (46.7)	13 (43.4)	–	0.405	0.577	0.779	0.795
RN	–	15 (50.0)	24 (60.0)	16 (53.5)	17 (56.7)					
Echocardiographic Parameter										
Mean gradient (mmHg)	11.55±5.34	10.80±5.18	12.23±6.03	45.13±15.25	11.76±4.72	0.502	0.371	**<0.001**	0.744	**<0.001**
LVEF (%)	64.15±3.31	64.90±2.73	64.58±3.13	65.67±4.42	63.40±5.25	0.475	0.694	0.230	0.319	0.088
LVEDV (mL)	96.38±17.02	95.33±16.02	103.88±15.88	103.14±23.29	174.74±52.50	0.843	0.065	0.876	**<0.001**	**<0.001**
LVEDV index (mL/m^2)	56.86±9.71	56.32±9.11	60.82±7.94	61.10±12.74	99.55±28.20	0.857	0.069	0.915	**<0.001**	**<0.001**

Data are reported as mean±standard deviation or number (percentage), *P* value resulted from Student-*t* test or Chi-square/Fisher exact test. TAV-CTL: Tricuspid aortic valve control (healthy control); SBP: Systolic blood pressure; DBP: Diastolic blood pressure; LR: Left and right cusp fusion type; RN: Right and non-coronary cusp fushion type; LVEF: Left ventricular ejection fraction; LVEDV: Left ventricular end-diastolic volume.

0.014;最小横截面积:Z=−2.933,*P*=0.003),mid-AA扩张度增加(Z=−2.737,*P*=0.006),PDA直径和横截面积增大(直径:Z=−4.936;最大横截面积:Z=−4.881;最小横截面积:Z=−4.362;*P*均<0.001),PDA扩张度稍增高(Z=−2.238,*P*=0.024)。与Dilated BAV-AS相比,Dilated BAV-AI患者mid-AA最小横截面积稍大(Z=−2.020,*P*=0.043),mid-AA扩张度增加(Z=−2.282,*P*=0.022),PDA直径和横截面积增大(直径:Z=−5.198;最大横截面积:Z=−5.026;最小横截面积:Z=−4.471;*P*均<0.001),PDA扩张度稍增高(Z=−2.468,*P*=0.014)。Dilated BAV-NF和Dilated BAV-AS两组在主动脉直径、横截面积及扩张度上差异均无统计学意义(表2,图4)。

BAV各组中LN型和RN型患者中段升主动脉和近端降主动脉直径、横截面积及扩张度差异均无显著统计学意义(图5)。

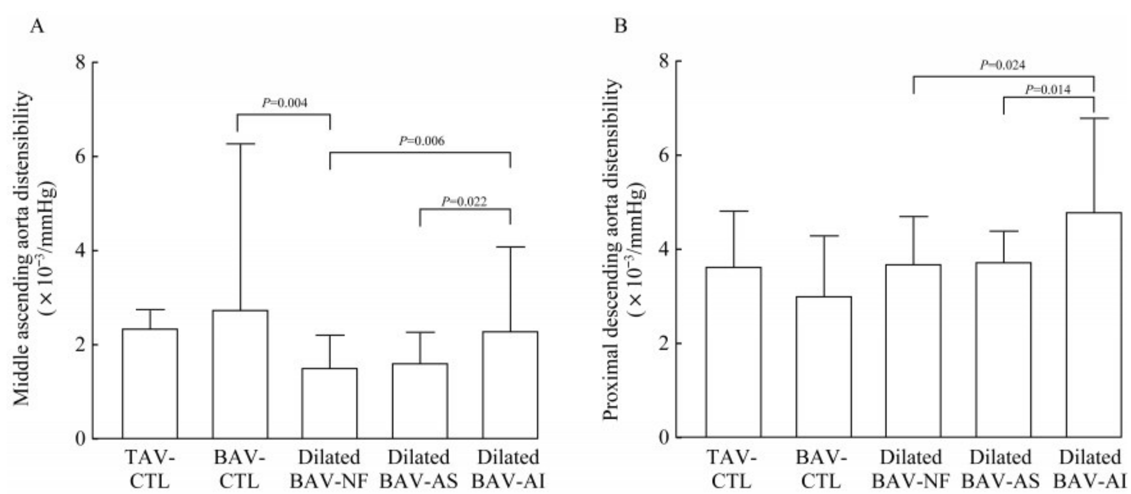
重复性分析 随机选取40个受试者的MRI图像,由两名测量者独立测量主动脉横截面积且计算主动脉扩张度,其中一名间隔1周重复测定。mid-AA和PDA扩张度在观察者内和观察者间均具有良好的一致性,mid-AA扩张度观察者内的差异性ICC为0.971(95%CI:0.939~0.986),观察者间的差

表 2 TAV 对照组和 BAV 患者的 MRI 检查指标比较

Tab 2 Comparison of MRI parameters in BAV patients and TAV volunteers

MRI parameters	TAV-CTL (*n*=30)	BAV-CTL (*n*=30)	Dilated BAV-NF (*n*=40)	Dilated BAV-AS (*n*=40)	Dilated BAV-AI (*n*=40)	*P* values				
						TAV-CTL *vs.* BAV-CTL	BAV-CTL *vs.* Dilated BAV-NF	Dilated BAV-NF *vs.* Dilated BAV-AS	Dilated BAV-NF *vs.* Dilated BAV-AI	Dilated BAV-AS *vs.* Dilated BAV-AI
mid-AA diameter (cm)	3.50 (3.31,3.61)	3.67 (3.34,3.89)	4.59 (4.40,4.94)	4.55 (4.35,4.94)	4.45 (4.21,4.68)	0.093	**<0.001**	0.643	0.082	0.237
PDA diameter (cm)	2.45 (2.28,2.72)	2.34 (2.16,2.51)	2.26 (2.12,2.54)	2.27 (2.15,2.42)	2.75 (2.58,2.99)	0.267	0.616	0.891	**<0.001**	**<0.001**
mid-AA $area_{max}$ (cm^2)	9.56 (8.92, 11.26)	11.85 (9.03,12.65)	18.09 (16.40,19.00)	17.19 (15.15,19.56)	15.50 (14.49,18.22)	0.088	**<0.001**	0.176	**0.014**	**0.240**
mid-AA $area_{min}$ (cm^2)	8.59 (7.84,9.33)	9.99 (7.37,11.23)	16.86 (15.04,17.59)	15.81 (13.66,18.17)	13.79 (12.23,16.76)	0.091	**<0.001**	0.204	**0.003**	**0.043**
PDA $area_{max}$ (cm^2)	5.06 (4.29,5.99)	4.72 (4.24,5.45)	4.69 (3.91,5.85)	4.78 (3.97,5.28)	7.31 (6.09,7.91)	0.433	0.778	0.744	**<0.001**	**<0.001**
PDA $area_{min}$ (cm^2)	4.18 (3.82,5.23)	3.90 (3.64,4.78)	3.92 (3.27,4.97)	4.11 (3.34,4.65)	5.71 (4.67,6.51)	0.579	0.760	0.939	**<0.001**	**<0.001**
mid-AA distensibility ($\times 10^{-3}$/mmHg)	2.35 (1.83,2.76)	2.77 (1.45,6.26)	1.52 (1.08, 2.19)	1.60 (0.99, 2.26)	2.29 (1.60, 4.08)	0.607	**0.004**	0.943	**0.006**	**0.022**
PDA distensibility ($\times 10^{-3}$/mmHg)	3.61 (2.27,4.82)	3.01 (2.33,4.29)	3.70 (2.89,4.70)	3.73 (2.38,4.40)	4.79 (2.93,6.80)	0.433	0.145	0.610	**0.024**	**0.014**

Data were reported as median (IQR); *P* values were resulted from Mann-Whitney *U* test.



P-value were resulted from Mann-Whitney U *t*-test.

图 4 TAV 对照组和 BAV 患者中段升主动脉(A)和近端降主动脉(B)扩张度的差异

Fig 4 Distensibility of mid-AA (A) and PDA (B) in TAV controls and BAV patients

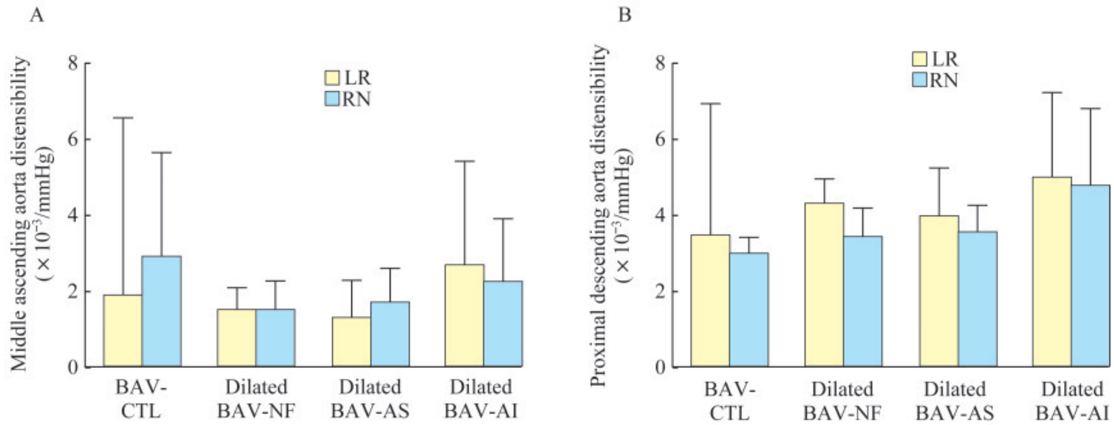


图5 BAV患者LR型和RN型中段升主动脉(A)和近端降主动脉(B)扩张度的差异

Fig 5 Distensibility of mid-AA (A) and PDA (B) in LR-BAV and RN-BAV patients

异性ICC为0.989(95%CI:0.960～0.997),PDA扩张度观察者内的差异性ICC为0.962(95%CI:0.921～0.981),观察者间的差异性ICC为0.965(95%CI:0.933～0.996)。

讨 论

BAV常伴随大血管病变和主动脉瓣病变,其相关主动脉病的病因机制复杂,近年来愈来愈成为国内外研究的热点。既往文献报道[12-13],主动脉壁重塑与年龄、血压、主动脉直径等相关,但目前对于合并升主动脉扩张和主动脉瓣病变的BAV患者主动脉弹性特征鲜有报道。本研究在匹配年龄、血压等临床资料后,采集了130例BAV患者主动脉MRI图像,以探讨不同并发症下BAV患者主动脉弹性特点。对比超声检查,MRI具有无创、软组织分辨率高、操作者依赖性小、视野大、可动态观察主动脉形态变化、精确显示管腔情况等特点,对研究BAV相关主动脉病的价值更高。

主动脉作为主要的弹性血管,可将心室的间断性射血转变为血液在血管中的连续流动,减少心动周期中血压的波动幅度。主动脉顺应性减低意味着其对血压缓冲能力减弱,是反映主动脉结构和功能受损的重要指标。与既往的MRI研究结果一致[8-9],我们发现BAV-CTL患者与TAV-CTL主动脉扩张度无明显差异,而Dilated BAV-NF组中段升主动脉扩张度显著降低,这提示主动脉直径大于40 mm可能是主动脉弹性受损的重要标志。组织学研究表明BAV患者主动脉中层易发生囊变坏死,胶原纤维增加,弹性纤维裂解,导致主动脉管壁扩张、弹性减弱[14-15]。此外,随着主动脉直径增加,升主动脉内皮功能损伤,管壁炎性反应和氧化应激反应增加,引起主动脉壁发生重塑[9]。反之,升主动脉弹性减弱也是导致主动脉进一步扩张的重要因素之一[8,13],有研究认为和马方综合征相似[16],主动脉弹性可以作为BAV患者升主动脉扩张的独立预测因子[17]。另外,我们发现PDA弹性受到主动脉瓣膜形态或升主动脉扩张的影响不大,这说明BAV患者中主动脉弹性受损可能具有位置局限性。PDA和mid-AA平滑肌细胞起源不同可能是导致这一现象产生的原因[18]。BAV相关的主动脉疾病,如主动脉瘤、主动脉夹层等多发生在升主动脉,进一步证实了BAV患者具有主动脉区域性重塑的特征[4,19]。

为了解主动脉瓣膜功能障碍对主动脉弹性的影响,我们比较了在主动脉直径大于40 mm时,BAV伴AS和AI的患者mid-AA和PDA的扩张度。我们观察到Dilated BAV-AS和Dilated BAV-NF两组间主动脉扩张度无明显差异,而Dilated BAV-AI患者mid-AA和PDA扩张度相对更高,左心室容积指数更大。与之前的超声研究结果一致[20-21],主动脉管壁重塑与AS无显著相关性,这可能与中重度AS的患者心脏收缩期射血量明显减少有关。相反,当伴有中重度AI时,患者的心脏射血量和左心室后负荷增加[13],同时,患者的收缩压升高,舒张压降低,脉压差明显增大。为了适应左心室容积增加所引起的变化,主动脉通过提高管壁顺应性作为早期的调节机制[22]。另外,血压变化对主动脉可产生连续的、整体性的影响,因此除了mid-AA外,PDA扩张度也相应有所升高。然而,有研究对儿童BAV伴升主动脉不扩张的患者进行了超声检查,发现伴

有AS者主动脉弹性增加,而伴有AI者主动脉弹性受损更严重[23]。和该研究不同的是,我们选取了升主动脉扩张且伴有瓣膜功能障碍的BAV成年人作为研究对象,采用MRI检查探讨在主动脉弹性功能已经出现损伤的基础上,主动脉瓣功能障碍是否加速主动脉重塑的过程。

有研究证明肱动脉血压和有创方法所测得的中心动脉血压有良好的一致性[24],并且肱动脉测量血压作为一种无创的检查手段,可常规应用于临床工作。本研究采用了肱动脉血压代替中心动脉压来计算主动脉扩张度。另有研究显示,LR型BAV和RN型BAV在升主动脉扩张部位上表现出一定的差异性,LR型以主动脉根部扩张为主,RN型以远端升主动脉和主动脉弓部扩张为主[25-26]。本研究的局限性为:(1)为横断面研究,未来需要对患者进行长期随访,监测主动脉壁弹性的动态变化,以确定导致主动脉弹性降低的真正因素。(2)只测量和计算了mid-AA和PDA的直径和扩张度,主动脉根部和主动脉弓等多部位主动脉弹性差异需要进一步研究。

综上,主动脉扩张和AI是影响BAV患者主动脉弹性的重要因素。主动脉扩张对主动脉弹性的影响局限于升主动脉,而AI对主动脉弹性的影响范围更广。在对BAV患者进行长期随访过程中,定量评估主动脉弹性可能有助于了解BAV相关主动脉病的发生,并对其进行及时干预。

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利益冲突声明 所有作者均声明不存在利益冲突。

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复旦大学基础医学院袁正宏/陈捷亮团队揭示乙肝病毒微染色体逃避清除的表观调控机制

近日,肝病学领域国际学术期刊*Hepatology*在线发表了复旦大学基础医学院病原生物学系暨医学分子病毒学教育部/卫健委重点实验室袁正宏/陈捷亮团队题为"Hepatitis B Virus cccDNA Minichromosomes in Distinct Epigenetic Transcriptional States Differ in Their Vulnerability to Damage"的研究论文(DOI: 10.1002/hep.32245)。该研究基于多种体内外乙型肝炎病毒(HBV)微染色体模型,首次系统阐明不同转录活性和表观状态的HBV微染色体在稳定性和抗清除方面存在差异,并由此提出促进HBV基因储存库清除的新对策。该研究首次揭示了转录活性和表观调控对HBV cccDNA微染色体稳定性的影响,加深了对cccDNA异质性存留方式和清除机制的认知,为研发靶向清除HBV基因储存库的策略提供了新视角和理论技术支撑。

附论文链接:https://aasldpubs.onlinelibrary.wiley.com/doi/abs/10.1002/hep.32245。

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