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ORIGINAL ARTICLE

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Effect of age and aortic valve anatomy on calcification and haemodynamic severity of aortic stenosis

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ABSTRACT

Objective To evaluate the effect of age and aortic valve anatomy (tricuspid (TAV) vs bicuspid (BAV) aortic valve) on the relationship between the aortic valve calcification (AVC) and the haemodynamic parameters of aortic stenosis (AS) severity.

Methods Two hundred patients with AS and preserved left ventricular ejection fraction were prospectively recruited in the PROGRESSA (Metabolic Determinants of the Progression of Aortic Stenosis) study and underwent a comprehensive Doppler echocardiography and multidetector CT (MDCT). Mean transvalvular gradient (MG) measured by Doppler echocardiography was used to assess AS haemodynamic severity and AVC was evaluated by MDCT using the Agatston method and indexed to the left ventricular outflow tract area to obtain AVC density (AVCd). All analyses were adjusted for sex.

Results Thirty-nine patients had a BAV and 161 a TAV. Median age was 51 and 72 years for BAV and TAV patients, respectively. There was a modest correlation between MG and AVCd (ρ=0.51, p<0.0001) in the whole cohort. After dichotomisation for valve anatomy, there was a good correlation between AVCd and MG in the TAV group (ρ=0.61, p<0.0001) but weak correlation in the BAV group (ρ=0.32, p=0.046). In the TAV group, the strength of the AVCd–MG correlation was similar in younger (<72 years old; ρ=0.59, p<0.0001) versus older (≥72 years old; ρ=0.61, p<0.0001) patients. In the BAV group, there was no correlation between AVCd and MG in younger patients (<51 years old; ρ=0.12, p=0.65), whereas there was a good correlation in older patients (≥51 years old; ρ=0.55, p=0.009). AVCd (p=0.005) and age (p=0.02) were both independent determinants of MG in BAV patients while AVCd (p<0.0001) was the only independent determinant of MG in TAV patients.

Conclusions In patients with TAV as well as in older patients with BAV, AVCd appears to be the main factor significantly associated with the haemodynamic severity of AS and so it may be used to corroborate AS severity in case of uncertain or discordant findings at echocardiography. However, among younger patients with BAV, some may have a haemodynamically significant stenosis with minimal AVCd. The results of MDCT AVCd should thus be interpreted cautiously in this subset of patients.

Trial registration number NCT01679431; Pre-results.

INTRODUCTION

Bicuspid aortic valve (BAV), characterised by a two-leaflet aortic valve instead of a trileaflet aortic valve, is the most common congenital heart disease and affects 1%–2% of the population.[1] This condition is known to be associated with multiple vascular and/or valvular dysfunctions such as calcific aortic stenosis (AS), aortic regurgitation or dilatation of the aorta.[2] AS is the third most common cardiovascular disease in the developed countries,[3] affecting 2%–4% of the population over 65 years old and nearly 10% of the population over 80 years old.[4 5] Calcific AS is the main aetiology of the disease in the Western countries and is characterised by a progressive mineralisation and fibrosis of aortic valve leaflets, which is accompanied by inflammation.[4 6 7] AS is the most common disorder associated with BAV and compared with patients with a normal tricuspid aortic valve (TAV), BAV patients are more at risk to develop AS and generally it occurs 10–20 years earlier than in TAV patients.[1 8–11] Until now, there is no pharmacological treatment available to slow down or to stop the progression of AS and the only available treatment is the implantation of a prosthetic heart valve.[12] According to the 2014 American Heart Association/American College of Cardiology (AHA/ACC) practice guidelines, patients with symptoms and a severe AS have a class I indication for aortic valve replacement.[12] Doppler echocardiography is routinely used in clinical practice and is the reference method to assess the haemodynamic severity of AS. Parameters such as peak aortic jet velocity, mean transvalvular gradient (MG) and aortic valve area are the criteria commonly used; however, about 30% of the patients with AS present a discordance between these parameters of AS severity.[13 14] The most frequent discordance is the combination of a low MG (<40 mm Hg) suggesting a moderate AS with a small aortic valve area (<1.0 cm^2) rather consistent with a severe AS.[13 14] In such situations, another imaging modality may be useful to corroborate actual severity of the stenosis. Aortic valve calcification (AVC) can be easily and accurately measured by multidetector CT (MDCT).[15 16] Several studies have previously shown a good relationship between the AVC reflecting the anatomic severity of AS and the echocardiographic parameters reflecting the haemodynamic

severity of AS.[14 17–20] Aggarwal *et al*[21] recently reported that this relationship is different in men versus women, that is, women reach haemodynamically severe AS with less amount of AVC. This difference persisted even after indexing the AVC for body surface area or the cross-sectional area of the aortic annulus (AVC density).[14] However, the effect of age and of the aortic valve anatomy (ie, BAV vs TAV) on the relationship between AVC and haemodynamic parameters of AS severity has yet to be evaluated.

METHODS

Patient population

Two hundred patients with AS and preserved left ventricular ejection fraction (LVEF) were prospectively recruited in the PROGRESSA (Metabolic Determinants of the Progression of Aortic Stenosis) study (Clinical Trial register: NCT01679431) between 2005 and 2015. The PROGRESSA study is an observational cohort study focusing on the identification of metabolic determinants as well as imaging biomarkers of the progression of AS.[22–24] Patients underwent a comprehensive Doppler echocardiography and MDCT within a period of 3 months. The inclusion criteria were age >21 and peak aortic jet velocity >2.0 m/s. Patients were excluded if they had symptomatic AS, moderate to severe aortic regurgitation, significant mitral valve disease (mitral stenosis or moderate to severe mitral regurgitation), LVEF<50%, rheumatic valvular disease or endocarditis, previous aortic/mitral valve repair or replacement, previous ascending aorta repair or replacement and if they were pregnant or lactating. The study was approved by the Ethics Committee of the Quebec Heart and Lung Institute and patients signed a written informed consent at the time of inclusion.

Clinical data

Clinical data included age, sex, height, weight, body surface area, body mass index, systolic and diastolic blood pressures, previous diagnosis of hypertension (patients receiving antihypertensive medications or having known but untreated hypertension (blood pressure ≥140/90 mm Hg)), dyslipidemia (patients receiving cholesterol-lowering medication), diabetes (patients receiving antidiabetic medication), coronary artery disease (history of myocardial infarction or coronary artery stenosis on coronary angiography defined as at least one lesion ≥50%) and history of smoking.

Doppler echocardiography data

All Doppler echocardiographic examinations were performed and analysed in the same laboratory according to the current recommendations of the American Society of Echocardiography.[25] Stroke volume was calculated by multiplying the left ventricular outflow tract (LVOT) area by the velocity time integral obtained by pulsed wave Doppler in the LVOT and was indexed to body surface area (stroke volume index). The LVOT diameter was measured at the base of the valve leaflets and was used to calculate the LVOT cross-sectional area. The Doppler echocardiographic parameters of AS severity included peak aortic jet velocity measured by continuous wave Doppler, MG obtained with the modified Bernoulli equation and aortic valve area calculated by the standard continuity equation.

As a measurement of global left ventricular haemodynamic load, we calculated the valvuloarterial impedance according to the formula: (systolic blood pressure+MG)/stroke volume index. Finally, the systemic arterial compliance was calculated according to the formula: stroke volume index/(systolic blood pressure−diastolic blood pressure).

Multidetector CT data

Non-contrast multidetector CT (MDCT) scans were performed with a dual-source MDCT scanner (Somatom Definition, Siemens Medical systems, Fordheim, Germany). The acquisitions were performed and analysed by trained technicians blinded to the clinical, laboratory and Doppler echocardiography data. The protocol for the acquisition and interpretation of MDCT scans was previously described.[14] Briefly, a scan run consisted of a prospective acquisition of contiguous transverse slices, with a thickness of 3 mm and triggered at 60%–80% of the ECG R-to-R wave interval. Image analyses were performed offline on dedicated workstations with validated software (Aquarius iNtuition, TeraRecon, Foster City, California, USA) for the measurement of AVC using the Agatston method and results were expressed in arbitrary units.[26] For measurement of AVC, we paid particular attention to exclude any calcification from the aorta wall, the mitral valve annulus or the coronary arteries, so that AVC only included calcification of the aortic valve leaflets. Calcification was defined as four adjacent pixels with density >130 Hounsfield units. AVC load was summated from all contiguous MDCT planes and was expressed as an absolute value or as AVC density (AVCd).[14] Total radiation exposure related to this study was <4 mSV.

Statistical analysis

The continuous variables were tested for normality of distribution and homogeneity of variances with the Shapiro-Wilk and Levene tests, respectively. Continuous data were expressed as mean±standard deviation. AVC and AVCd were expressed as median (interquartile range) and transformed with the use of square root for normalisation. Comparisons between aortic valve anatomy groups (TAV vs BAV) were done with Student's t-test or Wilcoxon-Mann-Whitney test as appropriate. Categorical data were expressed as percentage and compared with the χ^2 test or Fisher's exact test as appropriate. The TAV and BAV groups were subdivided into two subgroups according to the respective median of age (72 years for TAV and 51 years for BAV). To assess the relationship between anatomic and haemodynamic severity of AS, we analysed the correlations between AVCd and MG using Spearman's rank correlation coefficients (ρ, rho coefficient). Multivariable linear regression analyses were used to identify the independent determinants of MG among age, AVCd, aortic valve anatomy (BAV vs TAV), anthropometric parameters (height, weight, body surface area and body mass index) and risk factors including hypertension, diabetes, dyslipidemia, history of smoking and coronary artery disease. Age, sex, AVCd and valve anatomy were forced into the multivariable models, whereas other factors were entered in the models if their p value on univariable analysis was <0.10. Statistical analyses were performed with SPSS (V.23, SPSS, Chicago, Illinois, USA) and SigmaPlot (V.11.0, Systat Software, San Jose, California, USA) and a p value <0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

The clinical, Doppler echocardiography and MDCT data of the study population are presented in table 1. Among the 200 patients included in this study, 161 (80%) patients had a TAV and 39 (20%) patients had a BAV. The mean age was 67 ±13 years, with the TAV patients being older than the BAV patients (71±9 vs 49±11 years, p<0.0001). Men represented 73% of the total cohort, accounting for 76% of the TAV

Table 1 Characteristics of the study population according to the aortic valve anatomy

Variables	Total (n=200)	TAV (n=161)	BAV (n=39)	p Value
Clinical data				
Age, years	67±13	71±9	49±11	**<0.0001**
Men, %	73	76	56	**0.01**
Height, cm	167±8	166±8	168±9	0.28
Weight, kg	79±16	80±16	76±16	0.12
Body surface area, m²	1.88±0.21	1.88±0.20	1.85±0.23	0.38
Body mass index, kg/m²	29±5	29±5	27±4	**0.01**
Systolic blood pressure, mm Hg	136±18	138±18	127±15	**0.0004**
Diastolic blood pressure, mm Hg	75±9	74±9	80±8	**0.002**
Heart rate, bpm	62±9	62±9	65±8	**0.03**
Hypertension, %	80	88	44	**<0.0001**
Dyslipidemia, %	71	80	33	**<0.0001**
Diabetes, %	23	27	5	**0.003**
Coronary artery disease, %	38	47	3	**<0.0001**
History of smoking, %	67.5	70.8	53.8	**0.04**
Doppler echocardiography data				
Bicuspid aortic valve, %	20	–	–	
Left ventricular outflow tract diameter, mm	22.0±2.1	21.7±1.75	23.3±2.8	**0.002**
Systemic arterial compliance, mL/mm Hg/m²	0.73±0.23	0.67±0.17	0.98±0.29	**<0.0001**
Valvuloarterial impedance, mm Hg/mL/m²	3.86±0.72	3.94±0.71	3.53±0.70	**0.002**
Stroke volume, mL	78.3±14.5	77.4±13.1	81.7±18.9	0.10
Stroke volume index, mL/m²	41.8±6.9	41.2±6.2	44.2±9.0	**0.02**
Peak aortic jet velocity, cm/s	300±55	295±52	319±59	**0.01**
Mean transvalvular gradient, mm Hg	21.1±8.7	20.2±7.9	24.9±10.6	**0.002**
Aortic valve area, cm²	1.12±0.28	1.13±0.27	1.11±0.30	0.79
Indexed aortic valve area, cm²/m²	0.60±0.13	0.60±0.13	0.60±0.14	0.94
Left ventricular ejection fraction, %	65±5	65±5	65±4	0.94
MDCT data				
Aortic valve calcification, AU	949 (452–1593)	975 (580–1591)	672 (22–1604)	0.08
Aortic valve calcification density, AU/cm²	256 (132–416)	269 (158–435)	170 (5–345)	**0.01**

Significant p values are highlighted in bold.
AU, arbitrary units; BAV, bicuspid aortic valve; MDCT, multidetector CT; TAV, tricuspid aortic valve.

patients and 56% of the BAV patients (p=0.01). The BAV group had significantly lower body mass index (p=0.01) and systolic blood pressure (p=0.0004) and lower prevalence of hypertension (p<0.0001), dyslipidemia (p<0.0001), diabetes (p=0.003), coronary artery disease (p<0.0001) and history of smoking (p=0.04) than the TAV group. However, BAV patients presented higher diastolic blood pressure (p=0.002) and heart rate (p=0.03).

With regard to Doppler echocardiography data, BAV patients had a significantly larger LVOT diameter (p=0.002), higher systemic arterial compliance (p<0.0001), lower valvuloarterial impedance (p=0.002), higher stroke volume index (p=0.02), peak aortic jet velocity (p=0.01) and MG (p=0.002). However, aortic valve area, indexed aortic valve area and LVEF were similar in both groups (all p>0.05). AVCd was significantly higher (p=0.01) in the TAV group than in the BAV group, whereas there was a trend (p=0.08) towards a higher AVC in the TAV group. Thus, BAV patients had less valvular calcification despite similar haemodynamic severity of AS.

Relationship between valve calcification and haemodynamic severity

There was a modest association between MG and AVCd in the whole cohort (ρ=0.51, p<0.0001; online supplementary figure S1). However, there were significant interactions between AVCd and age (p=0.0006) and between AVCd and aortic valve anatomy (p=0.002) with regard to the relationship with MG. After stratification for sex, these interactions remained statistically significant for both age (p=0.0006) and aortic valve anatomy (p=0.002).

After dichotomisation according to the valve anatomy, the TAV group showed a good AVCd–MG correlation (ρ=0.61, p<0.0001; figure 1), whereas there was a weak correlation in the BAV group (ρ=0.32, p=0.046; figure 2). The strength of the correlation was similar in the younger (n=77) (<72 years old (median of age in the TAV group); ρ=0.59, p<0.0001; figure 3 and online supplementary figure S2) and in the older (n=84) (≥72 years old; ρ=0.61, p<0.0001; figure 4 and online supplementary figure S2) TAV patients. However, in the BAV patients, no correlation was found between MG and AVCd in the younger patients (n=18) (<51 years old (median of age in the BAV group); ρ=0.12, p=0.65; figure 5 and online supplementary figure S3) while there was a good correlation in the older patients (n=21) (≥51 years old; ρ=0.55, p=0.009; figure 6 and online supplementary figure S4). Of note, the majority of false-negative cases with MDCT (ie, cases with low AVCd score despite a significant MG) were young women with a BAV. Out of seven people with an MG≥18 mm Hg and an AVC score equal to zero, five were young women with BAV. Similar correlations and results were obtained when using the non-indexed AVC scores.

Determinants of AS haemodynamic severity

Linear univariable and multivariable analyses are presented in table 2. In the whole cohort, the independent determinants of

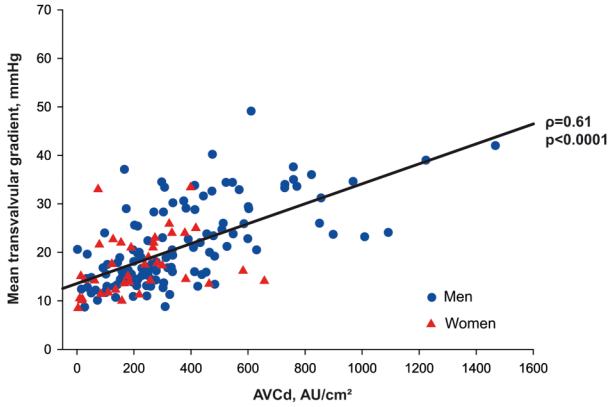

Figure 1 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the tricuspid aortic valve subgroup (n=161). Men are represented by blue dots and women are represented by red triangles.

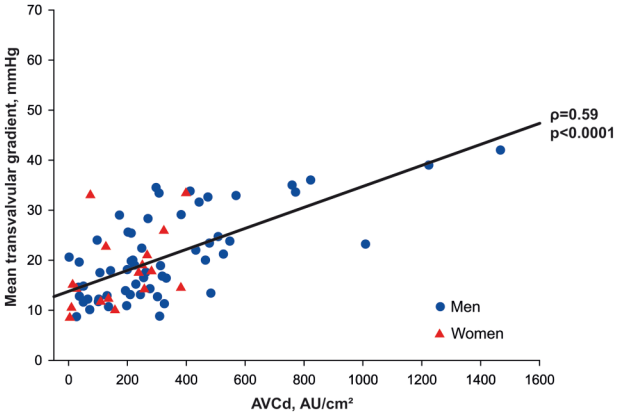

Figure 3 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the tricuspid aortic valve subgroup <72 years old (n=77). Men are represented by blue dots and women are represented by red triangles.

higher MG were age (p=0.02), BAV anatomy (p=0.04) and higher AVCd (p<0.0001). In the TAV group as well as in the subgroup of older patients (≥72 years old), AVCd was the only independent determinant of higher MG (all p<0.0001). In the subgroup of younger patients (<72 years old), AVCd (p<0.0001) remained an independent determinant of higher MG while diabetes (p=0.02) was an independent determinant of lower MG. In the BAV group, higher AVCd (p=0.005) and older age (p=0.02) were independent determinants of higher MG. In the BAV age subgroups (<51 and ≥51 years old), AVCd remained independently associated with a higher MG only in the older BAV patients (p=0.002). These results remained similar after stratification for sex.

DISCUSSION

The main findings of this study are that AVCd is an independent predictor of MG in TAV patients independent of age whereas in the BAV patients there was a major interaction between AVCd and age on determining MG. Indeed, association between AVCd and MG was strong in TAV patients and older BAV patients, whereas there was no association between AVCd and MG in the young BAV patients.

Effect of valve anatomy and age on the relationship between haemodynamic and anatomic severity

Subjects with BAV are more susceptible of developing AS than subjects with TAV and they develop the disease generally one decade earlier compared with TAV subjects.[8–11] This explains the major differences found in the present study between the BAV and TAV groups with respect to age and prevalence of comorbidities examined in the present study.[27 28] Interactions found between age or valve anatomy and the association between AVCd and MG suggest that these two factors influence the relationship between anatomic severity (AVCd) and haemodynamic severity (MG). Thus, these factors must be taken into account when analysing the results of AVC to corroborate AS severity.

Several studies have shown a good relationship between AVC and the haemodynamic severity of AS[14 17–20] and some recent studies have well demonstrated that sex modulates this relationship.[14 21] The results of the present study further confirm these previous findings. Furthermore, the subanalyses presented in this study with respect to aortic valve anatomy and age reveal new insights into the complex relationship between anatomic and haemodynamic severity of AS. A previous study by Roberts *et al*[29] reported in aortic valves retrieved at necropsy that BAV

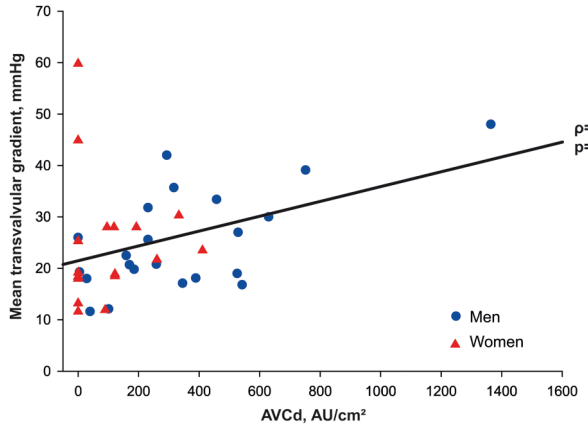

Figure 2 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the bicuspid aortic valve subgroup (n=39). Men are represented by blue dots and women are represented by red triangles.

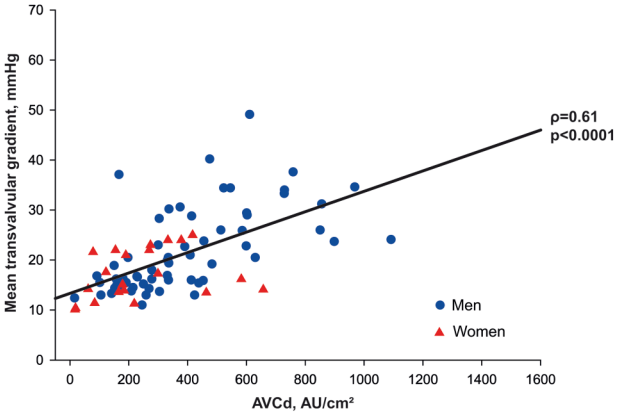

Figure 4 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the tricuspid aortic valve subgroup ≥72 years old (n=84). Men are represented by blue dots and women are represented by red triangles.

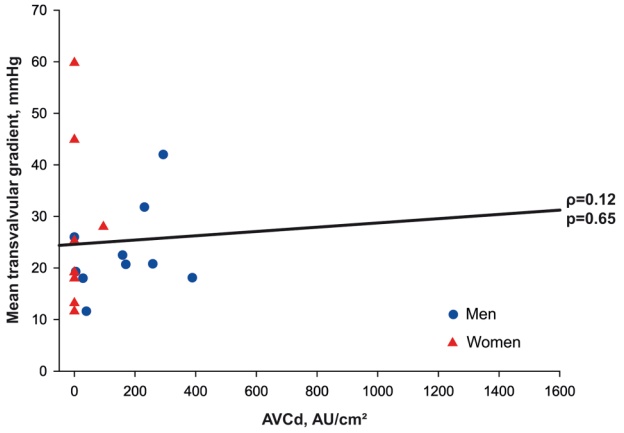

Figure 5 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the bicuspid aortic valve subgroup <51 years old (n=18). Men are represented by blue dots and women are represented by red triangles.

patients had more severely calcified and remodelled valves than TAV patients as assessed by the pathologist. However, in this previous study, the BAV and TAV patients were not necessarily at the same stage of AS anatomic/haemodynamic severity. Furthermore, AVC was assessed visually in the study of Roberts *et al* versus by a quantitative MDCT in the present study. On the other hand, a study showed in surgically explanted stenotic aortic valves that the fibrocalcific remodelling score was independently determined by the sex (male) and BAV.[30] In the present study, we found that despite having higher MG, BAV patients had lower AVCd (p=0.01). Also, following adjustment we identified that BAV was independently related with MG. In the BAV group, AVCd was associated with MG but only in the older group (≥51 years). Taken together, these data suggest that (i) AVCd is a good correlate of haemodynamic severity of AS in TAV and older BAV patients (≥51 years), (ii) BAV is independently related to AS severity despite lower AVCd level and (iii) fibrosis of aortic valve leaflets, which is not evaluated with MDCT, may play a significant role in determining AS severity particularly in younger BAV patients. This latter point is supported by the fact that despite having lower amount of calcium as evaluated by MDCT, BAVs have higher remodelling score.[30] Hence, it is likely that compared with TAV, fibrosis is

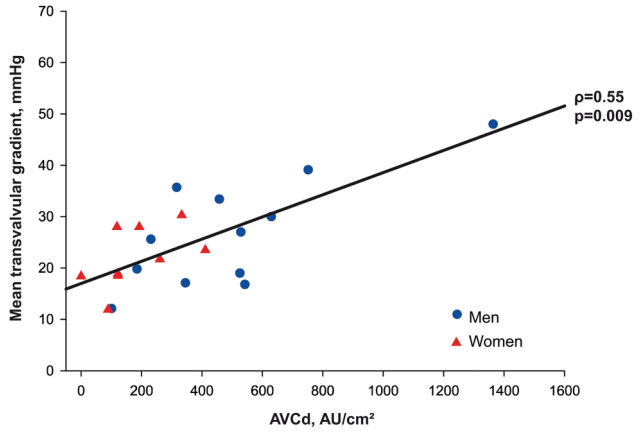

Figure 6 Correlation between the mean transvalvular gradient and the aortic valve calcification density (AVCd) in the bicuspid aortic valve subgroup ≥51 years old (n=21). Men are represented by blue dots and women are represented by red triangles.

accentuated in BAV and alter valve haemodynamics significantly. In this regard, in 477 surgically explanted stenotic aortic valves, Côté *et al*[31] identified that BAV anatomy was independently associated with higher fibrosis score. In a small-size study, Ferda *et al* found a significant correlation between AVC and haemodynamic severity of AS but they did not find significant differences in AVC between BAV and TAV patients. They thus concluded that the valvular anatomy did not interact with the correlation between AVC and haemodynamic severity.[20] In the latter study, however, the investigators did not index AVC for the size of the aortic valve, as calculated by AVCd. Given that BAV patients generally have a larger LVOT and aortic annulus cross-sectional areas compared with TAV patients, this may explain, at least in part, the apparent discrepancy between the present findings and the study by Ferda *et al*.

In patients with BAV, other factors besides calcification and fibrosis of leaflets may contribute to reduce the valve orifice and alter valvular haemodynamics. The morphology of the valve leaflets and the shape of the valve orifice are abnormal and may lead to a reduction in the effective valve orifice area and an increase in pressure gradient, independent of the presence of calcification and fibrosis. Moreover, in BAV patients, the transvalvular flow jet is often very eccentric and is directed towards the wall of the aortic root, thus causing important flow turbulences and a significant pressure drop, even if the valve orifice area is only mildly or moderately reduced.[32] Hence, in younger BAV patients, AVCd does not appear to be the main causal factor of AS, and other factors including abnormal valve orifice shape, fibrotic remodelling of valve leaflets and/or disturbed flow pattern may contribute to the haemodynamic severity of AS. Further work is needed to examine this hypothesis.

We observed that most of the false-negative patients at MDCT, that is, patients with low or no calcification despite a significant MG at echocardiography, were young women with BAV (five out of seven people with MG ≥18 mm Hg and AVC=0). Previous studies have shown that women reach haemodynamically severe AS with lower AVC and AVCd.[14 21] To explain these findings, some investigators have suggested that women may have relatively less valve calcification compared with men but more fibrosis on the valve leaflets. It is thus possible that in young women with BAV, the predominant cause of AS is pronounced valvular fibrosis with little or no calcification.

Clinical implications

MDCT is a non-invasive, simple, reproducible and accurate modality to assess AVC. This method may be useful to corroborate AS severity in patients who have uncertain or discordant findings at echocardiography. Our study shows that AVCd is the main determinant of haemodynamic severity in TAV patients, regardless of age, and in the older BAV patients. Older patients with AS have more comorbidities that may predispose to the development of LV diastolic and systolic dysfunction and thus contribute to reduce the stroke volume and transvalvular flow rate. Low-flow state is the most frequent cause of discordant grading (ie, small aortic valve area with low MG) at echocardiography. Furthermore, older patients with AS often have markedly reduced aortic compliance that may also contribute to an aortic valve area–MG discordance even in the presence of normal flow. Hence, it is not surprising that up to 30% of patients with AS have discordant grading of AS severity at echocardiography. This situation raises uncertainty about the actual severity of the disease and thus about the therapeutic management, particularly if the patient is symptomatic. The results of the present study confirm the clinical utility of AVCd measured

Table 2 Univariable and multivariable regression analyses of the predictors of mean transvalvular gradient

	Univariable analysis		Multivariable analysis	
	Standardised β	p Value	Standardised β	p Value
Whole cohort (n=200)				
Age	−0.10	0.15	−0.21	**0.02**
Men	0.10	0.16	−0.06	0.36
Height	0.07	0.36	–	–
Weight	−0.05	0.48	–	–
Body mass index	−0.09	0.23	–	–
Body surface area	−0.009	0.90	–	–
√AVCd	0.44	**<0.0001**	0.59	**<0.0001**
BAV	0.22	**0.002**	0.18	**0.04**
Hypertension	−0.01	0.88	–	–
Dyslipidemia	−0.01	0.84	–	–
Diabetes	−0.14	**0.046**	−0.08	0.18
History of smoking	−0.11	0.11	–	–
Coronary artery disease	−0.07	0.33	–	–
TAV (n=161)				
Age	0.15	0.054	−0.06	0.36
Men	0.19	**0.02**	0.01	0.82
Height	0.10	0.23	–	–
Weight	−0.03	0.70	–	–
Body mass index	−0.07	0.40	–	–
Body surface area	0.02	0.84	–	–
√AVCd	0.63	**<0.0001**	0.65	**<0.0001**
Hypertension	0.14	0.08	0.02	0.78
Dyslipidemia	0.11	0.15	–	–
Diabetes	−0.11	0.17	–	–
History of smoking	−0.04	0.61	–	–
Coronary artery disease	0.02	0.79	–	–
BAV (n=39)				
Age	−0.13	0.43	−0.49	**0.02**
Men	0.02	0.90	−0.32	0.10
Height	−0.07	0.66	–	–
Weight	−0.02	0.92	–	–
Body mass index	0.01	0.94	–	–
Body surface area	−0.03	0.87	–	–
√AVCd	0.24	0.14	0.67	**0.005**
Hypertension	0.005	0.98	–	–
Dyslipidemia	0.003	0.99	–	–
Diabetes	−0.09	0.58	–	–
History of smoking	−0.21	0.20	–	–
Coronary artery disease	−0.11	0.52	–	–
TAV<72 years old (n=77)				
Men	0.13	0.25	−0.04	0.67
Height	0.06	0.60	–	–
Weight	0.02	0.85	–	–
Body mass index	0.03	0.81	–	–
Body surface area	0.05	0.67	–	–
√AVCd	0.66	**<0.0001**	0.63	**<0.0001**
Hypertension	0.25	**0.03**	0.13	0.16
Dyslipidemia	0.18	0.12	–	–
Diabetes	−0.22	0.06	−0.21	**0.02**
History of smoking	−0.08	0.52	–	–
Coronary artery disease	0.08	0.48	–	–
TAV≥72 years old (n=84)				
Men	0.25	**0.02**	0.08	0.37
Height	0.15	0.17	–	–
Weight	−0.07	0.51	–	–
Body mass index	−0.17	0.13	–	–
Body surface area	0.004	0.97	–	–
√AVCd	0.60	**<0.0001**	0.58	**<0.0001**
Hypertension	0.03	0.76	–	–
Dyslipidemia	0.04	0.70	–	–
Diabetes	−0.005	0.96	–	–
History of smoking	−0.009	0.94	–	–

Continued

Table 2 Continued

	Univariable analysis		Multivariable analysis	
	Standardised β	p Value	Standardised β	p Value
Coronary artery disease	−0.05	0.65	–	–
BAV<51 years old (n=18)				
Men	−0.18	0.48	−0.32	0.36
Height	−0.28	0.27	–	–
Weight	0.05	0.84	–	–
Body mass index	0.24	0.33	–	–
Body surface area	−0.03	0.90	–	–
√AVCd	−0.005	0.99	0.21	0.55
Hypertension	−0.05	0.83	–	–
Dyslipidemia	−0.09	0.73	–	–
Diabetes	–	–	–	–
History of smoking	−0.35	0.15	–	–
Coronary artery disease	−0.14	0.59	–	–
BAV≥51 years old (n=21)				
Men	0.27	0.24	−0.18	0.41
Height	0.17	0.46	–	–
Weight	−0.11	0.64	–	–
Body mass index	−0.28	0.22	–	–
Body surface area	−0.02	0.93	–	–
√AVCd	0.67	**0.001**	0.77	**0.002**
Hypertension	0.08	0.74	–	–
Dyslipidemia	0.09	0.68	–	–
Diabetes	−0.15	0.51	–	–
History of smoking	−0.09	0.69	–	–
Coronary artery disease	–	–	–	–

Significant p values are highlighted in bold.
AVCd, aortic valve calcification density; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

by MDCT to corroborate stenosis severity in TAV patients as well as in older BAV patients presenting discordant findings at echocardiography. Our study also reveals that the younger patients with BAV may have a significant haemodynamic severity despite no or little AVC at MDCT. Hence, the results of MDCT should be interpreted with caution in this subset of patients.

Limitations

The main limitation of the present study is the small sample size of BAV patients. This limits the statistical power of the subanalyses with respect to valve anatomy and age. Also, we had few patients with a haemodynamically severe AS. Further studies with larger number of patients with severe AS will be necessary to determine whether the previously reported sex-related differences in the AVC–MG relationship[14 21] persist after exclusion of younger women with BAV.

We carefully examined the valve morphology (TAV vs BAV) in multiple views by echocardiography. Nevertheless, we cannot exclude that a few patients have been misclassified, especially in the subset of older patients with more extensive valve calcification. However, given that the correlation between gradient and AVCd was similar in older TAV patients versus older BAV patients, such misclassification, if any, would have no impact on the results and conclusions of this study.

CONCLUSION

In patients with TAV and in older patients with BAV, AVCd appears to be the main factor significantly associated with the haemodynamic severity of AS. Hence, in these patients, AVCd measured by MDCT may be used to corroborate AS severity in patients who have uncertain or discordant findings at echocardiography. However, among younger patients with BAV, some may have a haemodynamically significant stenosis with no/minimal AVC. The results of MDCT AVC should thus be interpreted with caution in this subset of patients.

Key messages

What is already known on the subject?
Aortic valve calcification (AVC) measured by CT is well correlated to the haemodynamic parameters of aortic stenosis (AS) assessed by Doppler echocardiography. In patients with a discordant grading severity of AS at Doppler echocardiography, AVC can be useful to determine the actual severity of the stenosis, that is, truly severe or moderate AS. However, the effect of age and aortic valve anatomy of the patients remains unknown on this correlation between AVC and haemodynamic severity.

What might this study add?
This study shows that independent of age, AVC is well correlated to mean transvalvular gradient (MG) in patients with a tricuspid aortic valve (TAV). In bicuspid aortic valve (BAV) patients, AVC is an independent determinant of MG but only in older patients.

How might this impact on clinical practice?
AVC may be useful to corroborate AS severity in patients with discordant findings at echocardiography in TAV as well as in older BAV patients. In younger BAV patients, some may have a haemodynamically significant stenosis with no or minimal AVC. The results of AVC measured by CT should thus be interpreted with caution in this subset of patients.

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Heart

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