Coronary Artery Ectasia Are Frequently Observed in Patients With Bicuspid Aortic Valves With and Without Dilatation of the Ascending Aorta

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Background—The presence of coronary artery ectasia (CAE) is influenced by genetic factors and related to the presence of aneurysms in other vascular beds. Bicuspid aortic valve (BAV) disease is frequently accompanied by ascending aortic aneurysm. Because the aortic valve and the proximal parts of the coronary arteries share a common embryonic origin, we hypothesized that CAE is associated with BAV disease.

Methods and Results—One hundred seventy-seven patients with suspected aortic valve disease (n=94 BAV, n=83 tricuspid aortic valve) underwent both cardiac magnetic resonance imaging and coronary angiography. To confirm the association of CAE with BAV, the frequency of CAE was evaluated in an in-house BAV registry (n=600, n=231 with available coronary angiogram) and compared with the frequency of CAE in the German Myocardial Infarction (MI) Family Study, in which the heritability of CAE was formerly established (n=899). Furthermore, the frequency of CAE was investigated in an observational registry of real-life patients undergoing coronary angiography for clinically indicated reasons (n=3.097) and in a subgroup of the KORA MI study (Cooperative Health Research in the Region of Augsburg), which is a population-based MI registry (n=403). Compared with tricuspid aortic valve disease, CAE occurred more than twice as frequently in cardiac magnetic resonance–confirmed BAV disease (17% versus 44%; *P*<0.0001) and CAE was observed similarly often in subjects with BAV with (37%) and without (54%, *P*=0.11) ascending aortic pathology. The common appearance of CAE in patients with BAV could be independently confirmed in the BAV registry (frequency 37%), whereas CAE was found less frequently in family history of positive MI patients (21%), sporadic MI without familial disposition (10%), and rarely in unrelated real-life catheterization patients (6%).

Conclusions—To our knowledge, our data show for the first time that ectatic coronary artery disease is a common appearance of BAV disease with and without ascending aortic ectasia. (*Circ Cardiovasc Interv*. 2016;9:e004092. DOI: 10.1161/CIRCINTERVENTIONS.116.004092.)

Key Words: aneurysm ■ bicuspid aortic valve ■ coronary aneurysm ■ coronary artery disease ■ genetics

Coronary artery ectasia (CAE) is characterized by inappropriate dilatation of coronary vessel segments.[1–3] There is yet no consensus about the exact pathogenesis, prognostic significance, and morbidity related to this clinical entity encountered during diagnostic cardiac catheterization.

Details on frequency data of CAE mainly report an incidence ranging from 1.5% to 5%,[2–7] with male predominance.[8] Notably, various methods have been used for defining CAE: exemplarily, a commonly used angiographic definition of CAE is a diameter of the ectatic segment being >1.5 times larger compared with an adjacent healthy reference diameter.[1–3] However, because the distribution of CAE is variable

and not always focal, normal reference segments may not be readily apparent, and this definition potentially underestimates the true incidence of the disease. In this regard, higher frequency values have been described in an Indian patient cohort with ischemic coronary artery disease (CAD).[9] Data by our own group also revealed frequent appearance of ectatic CAD in subjects with a strong positive family history of myocardial infarction (MI). Specifically, ≈50% of the variability of this morphological phenotype is found to be inherited.[10] Thus, genetic effects most likely influence the presence of CAE.

Nevertheless, it is postulated that atherosclerosis is the main contributor to the development of CAE. Because of the

WHAT IS KNOWN

- The presence of coronary artery ectasia (CAE) is influenced by genetic factors and is related to the presence of aneurysms in other vascular beds.
- Bicuspid aortic valve disease, the most common congenital cardiac abnormality, is another heritable disorder and is known to have an increased risk of ascending aortic aneurysm.
- Genetic abnormalities contributing to the development of aortic aneurysm have been studied extensively, and several of these factors have overlapped in patients with CAE.

WHAT THE STUDY ADDS

- Our data show for the first time that CAE is a common appearance of bicuspid aortic valve disease.
- CAE was observed similarly often in subjects with bicuspid aortic valve disease with and without ascending aortic pathology.
- Our findings may corroborate the fact that CAE is related to genetic factors.

frequent presence of associated obstructive CAD, it is considered to be a maladaptive process of atherosclerosis.[11]

However, it has been documented that CAE is associated with the presence of aneurysms in other vascular beds, such as aortic aneurysms and aneurysms of the pulmonary arteries.[1,12] These findings may corroborate the fact that CAE is related to genetic abnormalities. In fact, the genetic abnormalities contributing to the development of aortic aneurysm have been studied extensively, and several of these factors have overlapped in patients with CAE.[13] Interestingly, in contrast to aneurysms of the descending or abdominal aorta, ascending aortic aneurysms are not commonly a result of atherosclerosis.[14] In contrast, ascending aortic aneurysm is regularly a clinical component among heritable connective tissue disorders, such as Marfan or Ehlers-Danlos syndrome.[15,16]

Bicuspid aortic valve (BAV) disease, the most common congenital cardiac abnormality,[17,18] is another heritable disorder and is known to have an increased risk of ascending aortic aneurysm.[19] Up to 50% to 70% of patients with this aortic valve dysfunction have evidence of aortic dilatation, which typically involves the aortic root and ascending aorta, but not the descending aorta. Most often, root dilatation is observed in younger men with BAV and is independent of the presence or severity of an aortic valve stenosis.[15,20]

The aorta in BAV and Marfan syndrome patients and ectatic coronary arteries may share common histopathologic findings, including increased matrix metalloproteinase activity.[16] Moreover, the aortic valve, the proximal part of the coronary arteries, the ascending aorta, and the pulmonary trunk share a common embryonic origin, each developing from the neural crest.[21–23]

On the basis of this evidence, we hypothesized that CAE may be commonly observed in patients with BAV disease. To

the authors' knowledge, the relationship between BAV and CAE has never been studied before. To test this hypothesis, we studied cohorts of patients with BAV disease diagnosed by cardiac magnetic resonance (CMR) with available coronary angiograms.

Methods

Study Populations

Aortic Valve CMR Study

The study population was selected from a series of cardiovascular CMR, which analyzed tricuspid (TAV) and bicuspid (BAV) aortic valve disease for clinically indicated reasons. CMR studies were performed on a 1.5-T scanner (Sonata and Avanto, Siemens Medical Solutions). Details of the CMR image acquisition, determination of aortic valve disease severity, as well as BAV categorization, are described elsewhere.[19,24] In this study, 303 patients with aortic valve disease were investigated by CMR at the University Hospital of Regensburg, Germany. All patients gave informed consent. In 180 cases of BAV and TAV, coronary angiograms were available for detailed review. BAV and TAV were classified by the consensus of all investigators.[24] Three patients had been excluded because of uncertain diagnosis of BAV or TAV because of unacceptable image quality. Thus, the final sample for the present analysis consisted of 94 BAV and 83 TAV patients (n=177). The aortic valves were further phenotyped with regard to valve dysfunction (ie, stenosis or insufficiency), as well as the pattern of cusp fusion in BAV.[24] In subjects with BAV, n=64 (61%) had predominant or pure aortic stenosis (AVA<1.5 cm²) and 30 patients (29%) had predominant aortic insufficiency (greater than or equal to grade II). Because of the small sample size, the fusion types were categorized into the typical pattern, corresponding to the most common RL fusion pattern (involving the right and left cusps resulting in an anterior-posterior leaflet orientation), and atypical patterns, corresponding to all other rare fusion patterns. Furthermore, diameters of the ascending aorta were investigated. For these reasons, a definition of aortic ectasia being ≥40 mm was used.

To verify the results obtained from the aortic valve CMR study, 4 additional study cohorts were collected.

The Regensburg retrospective BAV registry included 600 patients in whom the diagnosis of BAV has been documented in charts of the University hospital between June 1999 and December 2013. After transesophageal echocardiographic review, definite diagnosis of BAV could be confirmed in 364 cases by consensus of all investigators. Of these, coronary angiograms were available for clinical investigation in 231 cases.

The GoKard registry is an observational registry of unselected real-life patients undergoing coronary angiography for clinically indicated reasons (n=3.097) at the University Hospital Regensburg, Germany. This study cohort served as a real-life comparative control group aiming to collect clinical data, as well as distinct morphological patterns and manifestations of CAD, including CAE. In this registry, the frequency of CAE was assessed irrespective of aortic valve status.

MI cases from the German MI Family Study with available coronary angiograms (n=899) had a strong positive family history for CAD and an early onset of disease, that is, were enriched for a strong genetic component. Patients were identified after their admission for acute treatment of MI or in cardiac rehabilitation clinics throughout Germany. This study cohort, in which a strong genetic component of CAE was formerly established by the use of variance component heritability analysis,[10] served as a genetic or familial comparative group.

Patients for this study were drawn from the MONICA/KORA MI Registry (Monitoring Trends and Determinants in Cardiovascular Disease/Cooperative Health Research in the Region of Augsburg). This is a population-based MI registry in Augsburg, Germany, which was established in 1984 as part of the World Health Organization MONICA Project. This registry comprises all hospitalized cases of

acute nonfatal MI at least surviving 24 hours and coronary deaths occurring in inhabitants of a defined study region, the city of Augsburg and the 2 surrounding counties, who are aged between 25 and 74 years. The registry has been described in detail elsewhere.[25,26] For the present study, coronary angiograms were retrospectively analyzed in a subgroup of 403 MI patients. In contrast to familial MI cases from the German MI Family Study, MI cases from the KORA registry represent nonselected MI patients of the same urban area. This study was performed in accordance with standards of the local ethics committee.

Angiographic Evaluation

In the Aortic Valve CMR Study, coronary angiograms were scored systematically and in random order by 2 experienced interventional cardiologists blinded to clinical status and CMR results (BAV or TAV). The coronary vasculature was categorized into the left main artery, the left anterior descending, the circumflex artery, and the right coronary artery to evaluate angiographic phenotypes. Angiographic CAD was defined as stenosis ≥50% and classified as 1-, 2-, or 3-vessel disease, accordingly. Coronary blood supply was divided into right-dominant, balanced, and left-dominant. All coronary arteries were evaluated in multiple angulated views. CAE was defined as dilatation of the arterial segment to a diameter of ≥150% of the adjacent healthy normal artery or normal segments of the same vessel (Figure 1). If no adjacent normal segments could be identified, the diameter of the largest healthy coronary artery of the patient was considered as the reference normal value. This approach includes the case if the entire artery was conspicuously large without a normal segment. If CAE was diagnosed, the localization of CAE was described, that is, proximal, distal, or whole vessel according to the CASS classification.[27]

In each study, phenotyping was particularly focused to the presence of CAE. From the individual studies, we gathered information about the presence and location of CAEs, angiographic CAD, specifically on the number of diseased major epicardial vessels and criteria
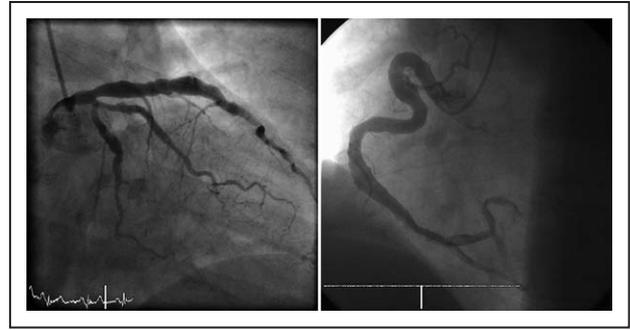

Figure 1. Example of coronary artery ectasia (CAE) of left anterior descending and circumflex artery in a patient with bicuspid aortic valve (BAV) and normal ascending aorta (**left**) and CAE of right coronary artery in a patient with BAV with ascending aortic aneurysm (**right**).

used to define disease, as well as clinical data on the history of coronary events, such as MI or revascularization procedures. Moreover, in each study, we collected clinical and anthropometric data, such as sex, age, and cardiovascular risk factors.

Statistical Analysis

Statistical analysis was performed with JMP 11 (SAS Institute, Cary, NC). The values are presented as counts or means±SDs. The Fisher exact test was used to identify differences in categorical variables between BAV and TAV patients, as well as between BAV patients with and without CAE. For normally distributed continuous variables, the Student t test was used to assess mean differences between groups, and the nonparametric Wilcoxon-Mann-Whitney U test was applied when the data have not met the assumption of normality. A P value of <0.05 was reported as statistically significant.

Table 1.   Baseline Characteristics of Patients With BAV and TAV as Diagnosed by Cardiac MRI

	BAV (n=94)	TAV (n=83)	P Value
Age, y (SD)	56.2 (13.9)	70.3 (9.9)	<0.0001
Male sex, n (%)	76 (81)	45 (54)	0.0001
BMI, kg/m² (SD)	27.8 (4.0)	27.6 (4.8)	0.71
Arterial hypertension, n (%)	57 (61)	71 (86)	0.0002
Smoking, n (%)	51 (54)	37 (45)	0.20
Hypercholesterolemia, n (%)	32 (34)	37 (44)	0.15
Type 2 diabetes mellitus, n (%)	18 (19)	32 (39)	0.004
Severe aortic stenosis, n (%)	31 (33)	42 (51)	0.02
AVA, cm² (SD)	1.7 (1.2)	1.2 (0.9)	0.003
Aortic regurgitation ≥grade 2	16 (19.1)	21 (26.3)	0.27
Aortic ectasia, n (%)	59 (63)	12 (15)	<0.0001
Aorta ascendens diameter, mm (SD)	44.1 (6.4)	35.4 (4.6)	<0.0001
Significant CAD, n (%)	21 (23)	70 (77)	<0.0001
Circulation			0.28
Right dominant, n (%)	38 (57)	36 (54)	
Left dominant, n (%)	18 (27)	13 (19)	
Balanced, n (%)	11 (16)	18 (27)	
Coronary artery ectasia, n (%)	41 (44)	14 (17)	<0.0001

AVA indicates aortic valve area; BAV, bicuspid aortic valve (disease); BMI, body mass index; CAD, coronary artery disease; MRI, magnetic resonance imaging; and TAV, tricuspid aortic valve (disease).

Results

Patient Characteristics

In Table 1, patient characteristics of the CMR cohort are shown. Patients with BAV were predominantly men (n=76, 81%), whereas patients with TAV were male in 54% (n=45). As expected, patients with BAV were younger compared with patients with TAV. Accordingly, patients in the TAV group presented more often with diabetes mellitus and arterial hypertension. Moreover, CAD occurred more frequently in patients with TAV than in patients with BAV. Aortic ascending ectasia were found in 63% of BAV and 15% in TAV patients ($P<0.0001$). Subjects with TAV had more often severe aortic stenosis, that is, aortic valve area ≤ 1 cm^2, and the mean aortic valve area was significantly lower in TAV than in BAV patients.

The frequency of CAE in BAV patients was more than twice the frequency in TAV patients (44% versus 17%; $P\leq0.0001$). CAE occurred almost always in the more proximal parts of the coronary vessels or were distributed along the whole vessel, but never occurred solely in the distal parts of a coronary vessel (data not shown).

Table 2 presents the comparison of BAV subjects with and without CAE. With the exception of a slightly higher frequency of arterial hypertension and the male predominance in BAV subjects with CAE, both groups of patients with and without CAE were well comparable with respect to clinical and angiographic characteristics, including the coprevalence of ascending aortic ectasia, as well as tubular and aortic root diameters.

We evaluated whether CAE occurs independently of ectasia of the aorta in patients with BAV. In the aortic valve CMR study diameters of the aorta were measured by CMR in 164 of 177 cases. Ascending aortic aneurysm or ectasia was diagnosed in 59 subjects with BAV disease (63%), but the frequency of CAE was not different in subjects with (37%) and without (54%) ascending aortic dilatation ($P=0.11$). Because CMR studies have shown that the RL fusion pattern results in an increase in regional wall shear stress because of a flow jet that is directed toward the anterior wall, we investigated whether the valve fusion pattern is connected with dilatation of the aortic root, dilatation of the tubular ascending aorta, and CAE. Table 3 indicates the aortic dimensions and frequencies of CAE according to BAV type. No differences could be observed between the common typical RL fusion pattern and all other atypical fusion patterns with respect to dimensions of tubular ascending aorta, aortic root, and the frequency of aortic dilatation. Moreover, CAE occurred equally often in typical and atypical BAV types.

Replication of Increased CAE Frequency in BAV Disease

To confirm the association of CAE with BAV, the frequency of CAE was evaluated in several independent study populations. Specifically, the prevalence of CAE was analyzed in the in-house BAV registry (n=231), the German MI Family Study (n=899), the KORA MI registry (n=403), as well as in the observational GoKard registry of real-life patients

Table 2.   Bicuspid Aortic Valve Phenotypes According to the Presence of CAE (CMR Study)

	BAV With CAE (n=41)	BAV Without CAE (n=53)	P Value
Age, y (SD)	56.8 (13.0)	55.8 (14.6)	0.72
Male gender, n (%)	37 (90)	39 (74)	0.04
BMI, kg/m^2 (SD)	28.3 (4.0)	27.4 (4.0)	0.32
Arterial hypertension, n (%)	31 (76)	26 (49)	0.009
Smoking, n (%)	22 (54)	29 (55)	0.92
Hypercholesterolemia, n (%)	16 (39)	16 (30)	0.37
Type 2 diabetes mellitus, n (%)	8 (20)	10 (19)	0.94
Significant CAD, n (%)	13 (33)	8 (16)	0.06
Severe aortic stenosis, n (%)	10 (24)	21 (40)	0.10
AVA, cm^2 (SD)	1.7 (1.1)	1.7 (1.2)	0.92
Aortic regurgitation ≥grade 1, n (%)	35 (85)	45 (85)	0.45
Aortic regurgitation ≥grade 2, n (%)	9 (25)	7 (15)	0.23
Circulation			0.77
Right dominant, n (%)	17 (57)	21 (57)	
Left dominant, n (%)	9 (30)	9 (24)	
Balanced, n (%)	4 (13)	7 (19)	
Aortic ectasia, n (%)	22 (54)	37 (70)	0.11
Tubular ascending aorta, mm (SD)	45.2 (6.2)	43.4 (6.4)	0.22
Diameter aortic root, mm (systolic)	31.0 (5.4)	29.0 (4.2)	0.15

AVA indicates aortic valve area; BAV, bicuspid aortic valve (disease); BMI, body mass index; CAD, coronary artery disease; CAE, coronary artery ectasia; and CMR, cardiac magnetic resonance.

Table 3. Aortic Dimensions and Frequency of CAE According to BAV Type

	Typical BAV Pattern (n=56)	Atypical BAV Pattern (n=23)	P Value
Tubular ascending aorta (SD)	44.2 (6.4)	44.7 (6.3)	0.45
Diameter aortic root (systolic)	29.3 (4.3)	30.7 (5.1)	0.30
Aortic dilatation, n (%)	36 (64)	15 (65)	0.97
CAE, n (%)	27 (48)	8 (35)	0.27

Typical BAV pattern, RL fusion type (involving the right and left cusps); atypical BAV pattern, all other fusion types. BAV indicates bicuspid aortic valve; and CAE, coronary artery ectasia.

undergoing coronary angiography for clinically indicated reasons (n=3.097). Figure 2 depicts the relative frequencies of CAE in these study cohorts. Notably, the high frequency of CAE observed in subjects with BAV in the aortic valve CMR Study could be independently replicated in the Regensburg BAV registry. In contrast, CAE was less frequently diagnosed in subjects with TAV disease. CAE occurred more frequently in MI patients with a positive family history of MI than in unselected MI patients, suggesting that genetic factors influence the existence of CAE. Moreover, CAE occurred more often in subjects with acute coronary events than in unselected subjects undergoing coronary catheterization, implicating increased coronary risk associated with CAE.

Discussion

To our knowledge, we showed for the first time that ectatic CAD is a common appearance of BAV disease. Interestingly, CAE occurred with and without dilatation of the ascending aorta, another frequent appearance of BAV disease.[15,19,20] By retrospective review of coronary angiograms, CAE was found more than twice as frequently in CMR-confirmed BAV disease compared with TAV disease, and notably, the common coincidence of CAE and BAV disease could be independently confirmed in our in-hospital BAV registry. In this validation study, the sample size of subjects with BAV was more than twice the size of subjects with BAV disease in the initial CMR exploration study.

The physiological context connecting the association between BAV disease and ectatic CAD remains speculative. Although several mechanisms have been suggested, the pathogenesis of CAE is still uncertain. Likewise, no consensus exists about the natural history, the clinical management, and optimal treatment of this condition, despite CAE represents not only an anatomic variant but also a clinical constellation of CAD that has been associated with an increased risk for acute coronary syndromes.[5]

CAE is usually considered a variant of CAD; however, a definite link has not yet been confirmed. Nevertheless, atherosclerosis is considered the most common pathogenic factor responsible for the majority (ie, >50%) of cases in adults.[2,5,28,29]

However, CAE also exist in children or young adults without overt CAD. Here, Kawasaki disease has been suggested as a common cause,[4,28,30] but coincidence with other vasculitides or mixed connective tissue diseases has been reported,[5] implying an association with inflammatory tissue disease as well.[1,8,31]

Although atherosclerosis predominantly causes narrowing of the vessel lumen, the exact mechanism of luminal dilation in atherosclerotic vessels is still a subject of current scientific research. As a result of a phenomenon referred to as arterial remodeling, some types of atherosclerotic lesions do not reduce luminal size, presumably because of expansion of the media and the external elastic membrane during atheroma development.[32] In CAE patients, cystic medial necrosis has been described repeatedly,[4] and previous studies have shown that proteolytic enzymes such as matrix metalloproteinases play key roles in the pathogenesis of CAE.[13,33] Indeed, overexpression of matrix metalloproteinases has been associated with CAE.[34] Characteristic histopathologic changes in CAE are extensive destruction of musculoelastic elements, including degradation of elastin fibers, a decreased number of smooth muscle cells,[4,35] overproduction of type I collagen, increased degradation of type III collagen, and a reduction in the total collagen volume.[1]

Besides atherosclerosis and inflammatory tissue diseases mentioned above, in ≈20% to 30% of CAE cases a congenital origin has been postulated.[5] Genetic predisposition of CAE
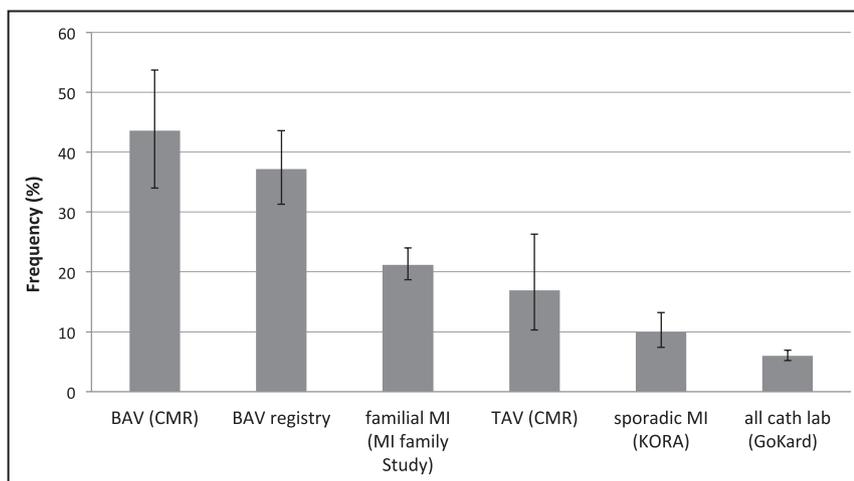

Figure 2. Frequency (sample proportions with 95% confidence intervals) of coronary artery ectasia in different populations. BAV indicates bicuspid aortic valve (disease); CMR, cardiac magnetic resonance; KORA, Cooperative Health Research in the Region of Augsburg; MI, myocardial infarction; and TAV, tricuspid aortic valve (disease).

could be suggested from its association with polymorphisms in HLA-DR B1 and DQ B1,[36] angiotensin-converting enzyme DD genotype,[37] endothelial nitric oxide synthase gene,[38] as well as associations with various hereditary conditions, such as familial hypercholesterolemia,[39] isolated congenital coronary artery fistulas,[40] and heritable connective tissue disorders, such as Marfan syndrome and Ehlers-Danlos syndrome.[15,16] Data by our own group also revealed frequent appearance of ectatic CAD in subjects with a strong positive family history of MI. Specifically, ≈50% of the variability in this morphological phenotype are found to be inherited. Moreover, because CAE is much more common in MI patients with positive family history than in unselected MI patients as revealed in our present investigation, a genetic susceptibility is likely to explain why certain individuals are at risk of developing CAE.

Our new finding that CAE is associated with BAV disease, the most common heritable abnormality of the human heart, underscores the theory that genetic effects influence the presence of CAE. Thus, the intriguing question is whether both phenotypes BAV disease and CAE share common genetic variations.

Because BAV disease is known to have an increased risk of ascending aortic aneurysm as well, BAV ectatic aortic disease and ectatic coronary disease may exhibit similar pathogenetic findings. Indeed, the autosomal-dominant inherited Marfan aortic disorder and BAV aortic disease share similar histopathologic characteristics, including degeneration of the medial layer, decreased fibrillin-1 in the vessel wall, and increased matrix metalloproteinase activity, which in part have been also conjectured to be involved in the pathogenesis of CAE.[16,41] The development of BAV disease is part of a spectrum of structural congenital impairments involving the aortic valve, the aortic annulus, sinuses of Valsalva, sinotubular junction, ascending aorta, the proximal parts of the coronary arteries, as well as the pulmonary trunk because they share a common embryonic origin developing from neural crest cells.[22,23] In fact, abnormal migration of neural crest cells has been proposed as a common pathway leading to BAV and aorthopathy.[21,42] This process may also affect the coronary vessels. Interestingly, studies have shown an increased incidence of left coronary arterial dominance associated with BAV.[43] In our study, coronary blood supply did not differ in subjects with BAV and TAV disease, as well as in BAV disease with and without coronary ectasia. However, it might be demanding to distinguish ectatic coronary vessels from coronary artery dominance in some cases, particularly when the ectatic lesion is not focal and adjacent normal segments are difficult to circumscribe.

Although there is objective evidence that BAV is heritable, controversies still exist regarding the pathogenesis of dilatation of the ascending aorta. In this respect, the development of BAV aortopathy has been attributed to both hemodynamic and genetic bases; both theoretically might also be involved in the pathogenesis of coronary dilatations. Arguments supporting the genetic origin of BAV aortopathy are the recurrence risk of aortopathy in relatives of BAV patients and evident modes of inheritance,[21,44] the high prevalence of aortic dilatation even in people with apparently normal functioning BAV,[21,42,44] and observed cases with progressive aortic enlargements even after aortic valve replacement.[45]

In contrast, the concept that hemodynamic factors, that is, abnormal valve dynamics, lead to BAV aortopathy is supported by the observation that even normally functioning BAV can have abnormal transvalvular flow patterns, resulting in regional hemodynamic shear stress on the aortic wall induced by eccentric turbulent flow through the bicuspid valve. An increased shear stress has also been postulated as a central component in the pathophysiology of coronary ectasia in general[46] and, thus, can also be responsible for the coincidence of BAV and coronary ectasia. However, the fact that CAE occurs similarly with and without ascending aortic ectasia in BAV disease in our study may contradict hemodynamic causes.

Small CMR studies have demonstrated that the RL fusion pattern (fusion occurs between the right coronary and left coronary leaflets) results in a flow jet directly toward the right anterior aortic wall and, conversely, the RN fusion pattern (fusion occurs between the right coronary and noncoronary leaflets) in a flow toward the posterior aspect of the aorta.[47–49] These associations between different BAV morphologies and specific dilatation patterns of the proximal aorta support the hemodynamic theory of BAV aortopathy. Interestingly, we did not observe a relationship of coronary ectasia, BAV fusion type, and ascending aortic ectasia in our study. However, from the preliminary observations in small samples of patients in the above-mentioned CMR studies and our study sample, it might not be possible to draw definite conclusions and require further clarification in larger unselected populations.

Besides our relatively small sample size of available CMR and coronary angiography, the retrospective analysis of CAE frequency without knowledge of the true incidence of BAV disease in the replication study samples has to be criticized. However, ≈1% to 2% of the general population are affected by BAV,[17,50] making the introduction of a severe bias unlikely.

In conclusion, to our knowledge, we have shown for the first time that BAV disease is not only connected with the already accepted increased incidence of ascending aortic dilatation but also with CAE.

Thus, in subjects in whom CAE was found incidentally on coronary angiography, assessment for BAV disease and aortopathy may enable early diagnosis and may help to improve patient care and outcome.

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Disclosures

None.

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