Cardiac magnetic resonance imaging of congenital bicuspid aortic valves and associated aortic pathologies in adults

Ralf Wassmuth¹,²*, Florian von Knobelsdorff-Brenkenhoff¹,², Henriette Gruettner¹,², Wolfgang Utz¹,², and Jeanette Schulz-Menger¹,²

¹Working Group Cardiac MRI, Humboldt University Berlin, Charite Campus Buch, Experimental and Clinical Research Center, Berlin, Germany; and ²Cardiology and Nephrology Department, HELIOS Klinikum Berlin Buch, 13125, Berlin, Germany

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Aims
Bicuspid aortic valve (BAV) represents the most frequent congenital cardiac abnormality resulting in premature valvular degeneration and aortic dilatation. In a large series of consecutive patients, we evaluated the distribution of BAV types and the associated valvular and aortic abnormalities.

Methods and results
We investigated 266 patients (58 ± 14 years) with BAV using a 1.5 T cardiac magnetic resonance (CMR) scanner. Valve morphology was described according to the Sievers classification. The aortic valve orifice area, aortic regurgitation (AR) fraction, and aortic dilation were quantified. Two hundred and forty-two data sets were available for analysis; 24% had BAV without a valvular lesion. The predominant valvular lesion was aortic stenosis (AS) with 51%. Lone AR was found in 17%. A combined lesion of AS and AR was found in 9%. Those with AS were older than the overall average (64 ± 12 vs. 57 ± 15 years, P < 0.001). The patients with AR and those without valvular abnormality were younger than average (49 ± 13 and 50 ± 12 years vs. 57 ± 15 years, P < 0.01 respectively). Comparing two observers Kappa coefficient was 0.77 for differentiation of six valve morphologies and 0.80 for the differentiation of bicuspid and tricuspid valve. Aortic dilatation was found in 39% of cases with no discernible preference for any specific BAV-type and mainly affecting the ascending aorta.

Conclusion
CMR can non-invasively differentiate various morphologies in BAV with low inter-observer variability. Valvular pathologies vary across age. Aortic dilatation is frequent in BAV independent from valvular morphology or lesion. In future CMR might help to guide management in patients with BAV.

Keywords
Magnetic resonance imaging • Bicuspid aortic valve • Aorta • Aortic stenosis

Introduction
Bicuspid aortic valve (BAV) is the most common cardiac congenital variant with an estimated incidence of 0.5% in population-based studies¹ and 1% in autopsy studies.²,³ Aortic stenosis (AS) and regurgitation (AR) occur earlier and more frequently than in tricuspid aortic valves (TAVs). In addition, aortic dilatation is associated with BAV. Typically transthoracic echocardiography (TTE) is used to evaluate the aortic valve if acoustic window allows sufficient image quality. Cardiovascular magnetic resonance (CMR) imaging is able to depict aortic valve morphology and to AS and AR.⁶–⁸ Moreover, it can depict associated pathologies of the thoracic aorta.⁹–¹² The detection of BAV morphology can be of clinical importance, as the threshold for aortic surgery may differ between bicuspid and tricuspid valves depending on individual risk factors.¹²

We therefore undertook a comprehensive CMR study to investigate the variability of BAV morphology and the associated valvular and aortic pathologies. We tested the reproducibility of CMR in assessing BAV morphology and aortic dilatation.

Methods
The study complies with the declaration of Helsinki. The local ethical committee approved the study.

* Corresponding author. Tel: + 49 30940153536; Fax: + 49 30940153549, Email: ralf.wassmuth@charite.de

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Patients
We retrospectively searched our database (~3000 CMR cases per year) from 2004 to 2009 for CMR reports including the term ‘bicuspid’. From 2010 on, we prospectively enrolled all consecutive patients, in whom BAV was known or incidentally discovered during the CMR scan. All CMR scans were clinically indicated, not only for valvular lesions but also for any other clinical cardiovascular indication, e.g. stress tests.

CMR
All the patients gave written informed consent before CMR using a 1.5 T clinical scanner (Avanto or Sonata, Siemens AG Healthcare Sector, Erlangen, Germany). The left ventricle (LV) was depicted with steady-state-free precession (SSFP) cine sequences during breathhold in three long axes. Typically spatial resolution was $1.8 \times 1.8 \times 6 \text{ mm/voxel}$. Based on an optimized double-oblique view of the left ventricular outflow tract that was based on the centre of the aortic root, we obtained five contiguous SSFP cine slices of 5 mm thickness aligned to the aortic valve plane to depict valvular morphology. In-plane resolution was $1.7 \times 1.7 \text{ mm/pixel}$. The thoracic aorta was covered with axial localizers (steady-state gradient echo, slice thickness 6 mm, no gap, in plane resolution $1.4 \times 1.4 \text{ mm}$) in all cases and additionally with contrast-enhanced three-dimensional (3D) MR angiography ($0.2 \text{ mmol/kg gadoteridol at } 2 \text{ mL/s; voxel size } 1.1 \times 0.9 \times 2 \text{ mm}$) if clinically indicated. If aortic regurgitation was assumed in cine images, we additionally acquired a breathhold segmented phase contrast measurement (echo time $2.3 \text{ ms}$, slice thickness $5.5 \text{ ms}$) perpendicular to the ascending aorta across the sinotubular junction (STJ).

Image analysis
Using Osirix (version 3.9; www.osirix-viewer.com), we visually analysed all images across the aortic valve to categorize valvular morphology. We classified the BAV-type according to the Sievers terminology. First, the presence or absence of a raphe and its number was determined. Second-ly, the position of a raphe between two cusps was determined. The potential subtypes therefore are 0-lateral, 0-AP, 1LR, 1RN, 1LN, 2 (unicuspid) (Figure 1). Valves, that were considered tricuspid or only mimic a congenital bicuspid morphology due to extensive degenerative changes, were excluded. Reasons to classify a valve as tricuspid with secondary fusion were cusps of equal size and an angle of $120^\circ$ between commissures. The true bicuspid valves frequently feature cusps of different size and uneven angles between commissures closer to $160^\circ$ than $120^\circ$. Partly opening raphes with otherwise bicuspid morphology or advanced age alone were not criteria to consider a valve as tricuspid.

All valves, that appeared difficult to classify and might represent TAV by one observer, were seen by an independent second observer. These debatable valves were mixed in random order with 24 randomly chosen valves selected from the study group by a random number generator. Observers had not only to decide between BAV and TAV, but between six different morphologies of BAV.

The aortic valve orifice area was quantified with planimetry on Osirix and considered stenotic if smaller than $2 \text{ cm}^2$. Aortic regurgitation was considered significant if regurgitation fraction based on the CMR flow measurement was $>10\%$.

In those patients with 3D MR angiography two independent investigators measured the aorta at seven landmarks [bulbus, STJ, mid-ascending aorta, proximal arch, mid-arch, proximal descending aorta, distal descending aorta, descending aorta, celiac trunk, superior mesenteric artery, inferior mesenteric artery].

Figure 1  Schematic representation of various aortic valve morphologies adjusted to typical orientation on CMR images. View from the LV towards the aorta in a left-anterior to right-dorsal direction. The aortic valve is depicted in a cross-sectional short axis view with the interatrial septum (IAS) in the right lower corner. The ostium of the right coronary artery (RCA) is depicted on the left side of the image, the left main (LM) is seen on the right side. Note that this view differs from the surgical situs and echocardiography. Top row left shows a TAV compared with various subtypes of BAV according to the Sievers classification.
mid-descending aorta] according to the AHA guidelines.\textsuperscript{15} Measurements were done in an oblique orientation perpendicular to the main direction of flow using a 3D viewer. In cases without 3D CMR angiography, the maximal aortic diameter was measured on axial slices and the aortic root was assessed on cine images. The ascending aorta was considered dilated if larger than 2.1 cm/m² according to European guidelines.\textsuperscript{16}

The aortic arch geometry was described as gothic, crenel, or normal based on its height (A) and transverse diameter (T) as described before by Ou et al.\textsuperscript{17} and similarly by others.\textsuperscript{18} The A/T ratio was calculated.

### Statistical analysis

Calculations were performed with SAS 9.2 (SAS Institute, Inc., Cary, NC, USA). Data are presented as means ± standard deviation. Observed and expected frequencies of valvular abnormalities in various subtypes of BAV were compared with the Chi-test and Fisher’s exact test. We applied ANOVA and t-tests to test for differences in age among different types of valve morphology. Subgroups with <10 patients were not analysed separately. Inter-observer variability for BAV-subtypes was assessed with Cohen’s kappa-statistics. Kappa coefficients were calculated to evaluate the observer agreement. For binary data, the simple kappa coefficient was used, for multinominal data, a weighted kappa was calculated.\textsuperscript{19} For aortic dimensions inter-observer variability was assessed by Bland–Altman analysis.

### Results

We identified 242 patients [58 ± 14 years, range 19–83 years, median 60 years, 179 (75%) male] with BAV and included them into the analysis. In eight additional cases the electronic image data could not be retrieved. Twelve additional valves were considered degenerated tricuspid valves and therefore excluded from analysis. Six additional cases remained unclear.

<table>
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<th>Table 1 Distribution of BAV morphology</th>
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<td><strong>One raphe</strong></td>
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BAV, bicuspid aortic valve. Owing to rounding percentages do not exactly add up to 100.

**Figure 2** Typical SSFP cine CMR still frames of BAV. An oblique orientation is given through the aortic valve according to anatomic scheme in Figure 1. The perspective is from the left-anterior side of the LV towards the aorta. CMR visualizes different types of BAV in diastole (top row) and systole (bottom row). Type 1 LR (left), type 0-lateral (centre), and type 0-AP (right).
Aortic valve morphology

Table 1 describes the distribution of aortic valve morphology. The 1LR type (one raphe between left and right cusp) was the predominant type found in 60% of patients, followed by type 1RN in 16%. All other types were rather infrequent. Examples are given in Figure 2.

Valvular dysfunction

Table 2 describes the distribution of valvular dysfunction and age. Nearly one-quarter of patients (24%) had BAV with normal valvular function. The predominant valvular lesion was AS with 51%. Planimetry of the aortic valve orifice area revealed an average of 1.6 ± 1.2 cm². Patients with AS had an orifice area of 0.9 ± 0.3 cm². The degree of AS did not differ among BAV-subtypes. Sole AR was found in 17%. A combined lesion of AS and AR was found in 9%. In both, the subgroup with Type 1 RN and the small subgroup with type 0-AP we found fewer patients with AS than expected (AS overall 51%, in 1RN 44%, in 0-AP 38%). In 0-AP 44% of the patients had normal valvular function compared with 24% in the overall group. However, these discrepancies between observed and expected frequencies did not reach significance in Fisher’s statistics.

Age distribution

Patients with AS, regurgitation, or normal valvular function differed in age (P < 0.001; Table 2). Those with AS were older (64 ± 12 years) than the overall average (P < 0.001). The patients with AR and those without valvular abnormality were younger than those with AS (49 ± 13 years; P < 0.001 and 50 ± 12 years, P < 0.001 respectively). Patients with a mixed lesion of stenosis and regurgitation were older than those with pure regurgitation (P = 0.012) and those with normal valvular function (P < 0.04).

Aortic morphology

In 84 patients (35% of the total group) contrast-enhanced 3D CMR angiography was available for evaluation (Figure 3). On average maximal aortic diameter was 2.07 ± 0.4 cm²/m² (range 1.1–3.2 cm²/m²). Aortic dilatation was found in 95% of cases (39%) based on diameters indexed for the body surface area. Among

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<th>Table 2</th>
<th>Frequency of valvular lesions and age distribution</th>
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<td>51</td>
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<td>Age (years)</td>
<td>64 ± 12*</td>
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AS, aortic valve stenosis; AR, aortic valve regurgitation. Owing to rounding percentages do not exactly add up to 100. Age is given as SD ± mean.

*P < 0.001 vs. total.
†P < 0.001 vs. AS.
‡P < 0.012 vs. NS.

Figure 3 Anterolateral view of a maximal intensity projection contrast-enhanced 3D magnetic resonance angiography depicts different aortic geometry patterns: gothic aortic arch [height–width ratio 1.05 (A) vs. dilated ascending aorta with height-width ratio of 0.55 (B) vs. crescent aortic arch including an aneurysm underneath the arch (C, height-width 0.37)].
cases with aortic dilatation, there was no discernible preference for any specific BAV-type. Predominantly, the ascending aorta was dilated (maximal aortic diameter for the whole group at the mid-ascending aorta with 44 ± 7 mm) while aortic root dilatation was found in five cases only (Figure 4). Coarctation or a surgically corrected coarctation was present in five cases. Among 47 patients with apparently normal valvular function still 15 (32%) had aortic dilatation. The A/T ratio was 0.54 ± 0.15 on average. A gothic aortic arch (A/T 0.86 ± 0.17) was found in five cases, a crescent aortic arch in two cases (A/T 0.37).

**Inter-observer variability**

Nineteen aortic valves (8% of the total study group) were considered difficult to classify or potentially tricuspid valves and mixed together with 24 randomly chosen bicuspid valves. Two independent observers agreed in 39/43 cases (91%) whether the valve was bicuspid or tricuspid. In three additional cases they disagreed about the BAV-subtype resulting in an overall agreement about aortic valve morphology in 36/43 cases (84%).

The kappa coefficient of the two observers across the six categories (1LR, 1RN, 1LN, 0-AP, 0-lat, and TAV) was 0.77 (95% CI: 0.60; 0.95). When TAV was compared against non-TAV, the kappa coefficient of the two observers was found to be 0.80 (95% CI: 0.61; 0.99). There was a low variability between two observers for aortic dimensions (r = 0.99). The mean difference between observers was 0.20 ± 0.88 mm with narrow limits of agreement (−1.52 to 1.93 mm).

**Discussion**

To the best of our knowledge, we present the largest series of CMR imaging in patients with BAV so far. We applied the Sievers classification that not only describes the orientation of the bicuspid orifice, but also includes the number and presence of a raphe and thereby results in a more detailed characterization of valvular morphology. In addition, we included inter-observer analysis corroborating substantial inter-observer agreement in detecting BAV and its morphologic subtypes and thereby underscore the quality of CMR imaging for the aortic valve.

Our results indicate that CMR can clearly depict the morphology of bicuspid aortic valve and reliably discern anatomic variants as well as the associated aortic pathologies. Our experience suggests that a single slice is not sufficient to assess aortic valve morphology due to inherent through plane valvular motion. A raphe might be visible in one slice, but easily be overlooked in the next. Therefore, it appears mandatory to evaluate valvular morphology in multiple slices across the valve.

**Aortic valve morphology and function**

The distribution of BAV-subtypes found in our patients is in accordance with autopsy and surgical series described before. The great majority of cases features one raphe mostly in the LR-position. AS was the most frequent valvular lesion. Patients with aortic regurgitation were younger than those with AS. Different BAV-subtypes tended to result in valvular pathologies to a different degree, but these trends did not reach statistical significance and might still be due to chance in smaller subgroups of patients.

Cardiac surgeons have suggested that determination of commissural orientation and coaptation height might be important for the success of bicuspid valve repair. The image quality and the low inter-observer variability achieved in our study show that CMR can provide detailed anatomical information in this regard.

**Aortic morphology**

Aortic dilatation is common in bicuspid aortic valve due to both, genetically induced changes in aortic wall structure and haemodynamic sequelae of valvular dysfunction. We could confirm in our series aortic dilatation as a frequent finding that mostly affected the tubular ascending aorta. This supports observations by Fernandes et al. in paediatric patients. One third of those patients with normal valvular function in our group nevertheless had aortic dilatation underscoring the genetic aetiology independent from pure haemodynamic reasons for dilatation. In our series, we did not find geometric patterns like gothic or crenel to be very helpful for diagnostic analysis as only a small minority of patients fell into these categories. BAV-subtype was not related to the incidence of aortic dilatation in our patient group. This is in accordance with previous reports. Two studies found more aortic dilation in type 1LR and 0-AP, but both studies relied on TTE alone for imaging the aortic valve and the aorta.

Cutting edge four-dimensional flow visualization using CMR indicates that bicuspid aortic valve morphology has an impact on aortic flow patterns and aortic wall stress. This illustrates the potential of CMR for further clinical risk stratification in patients with BAV.

**Imaging modalities**

TTE remains the first-line diagnostics for aortic valvular diseases. However, delineation of morphologic details, e.g. identification of a raphe can be difficult as even echo experts conceded.
groups have described BAV morphology using CMR before.4,33–35 CMR was superior in detecting BAV compared with TTE with intra-operative inspection as the gold standard.13,36 In children 3D TTE might be of benefit in characterizing BAV morphology.37 Cardiac computed tomography (CT) is able to depict bicuspid morphology and the associated aortic changes,38–40 but is limited by radiation exposure and temporal resolution. Lee et al.42 found almost identical sensitivity and specificity of CT and CMR in differentiating bicuspid from tricuspid aortic valve morphology. Multiplane transoesophageal echocardiography yielded a sensitivity of 87% and a specificity of 91% for the detection of BAV (not BAV-subtype) compared with surgical inspection.43 We demonstrated that CMR can depict detailed BAV morphology and the associated pathologies without radiation. Therefore, CMR appears as a useful tool for monitoring and pre-surgical planning in these patients.

Limitations

The study has not been designed for direct comparison of echocardiography. In a substantial number of cases, BAV was detected by chance during a CMR study for other purposes. In other cases, an aortic valve problem had been described by echo before but trans-thoracic echo had not described valve morphology.

Our analysis is not free from referral bias. We did include both, patients referred for a known valve problem and those with incidental detection of BAV. We did only see those patients that had sought medical advice for any cardiovascular problem. Therefore, we cannot assess the true incidence and distribution of BAV-subtypes.

Aortic geometry is not only determined by aortic valve morphology, but also by age and pulse pressure.18 In our analysis, we did not account for this when describing aortic geometry. Only in a subgroup of patients the aorta has been imaged with 3D MRA. However, earlier work demonstrated, that aortic diameters are comparable between axial and 3D imaging methods.44

Conclusion

CMR can discern various morphologic subtypes of BAV with high reproducibility and assess its associated valvular and aortic abnormalities. The valvular pathologies tend to vary across BAV-subtypes and age. Aortic dilatation is frequent and independent from BAV-type or valvular lesion. In the future, CMR might therefore help to guide management in patients with BAV.

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References

Giant saphenous vein graft aneurysm presenting as stridor

Yasir Parviz1*, William Parker2, Peter Brown3, and John N. West1

1Department of Cardiology, Sheffield Teaching Hospitals NHS Trust, Herries Road, Sheffield S5 7AU, UK; 2Department of Medicine, Chesterfield Royal Hospital, Chesterfield, UK; and 3Department of Radiology, Sheffield Teaching Hospitals NHS Trust, Sheffield, UK

* Corresponding author. Tel: + 44 1142375583; fax: + 44 1142711863. Email: drlyasar@hotmail.com

A 68-year-old male with a history of previous coronary artery bypass (CABG) surgery and chronic obstructive pulmonary disease presented with stridor and dyspnoea.

CABG using long saphenous vein conduits to the right coronary artery and circumflex had been performed in 1984 and 1986. A chest X-ray showed a mass lesion adjacent to the right heart border with consolidation in the right upper zone (Panel A). The lesion was further evaluated by CT coronary angiography (Panel B). A large false aneurysm arising from the proximal aspect of the right coronary graft measuring ~10 cm in diameter with thrombus within it was confirmed. The aneurysm was causing pressure atelectasis of the right middle lobe due to bronchial compression.

Saphenous vein graft aneurysm is a rare complication of CABG which can present in a wide variety of ways including chest pain, dyspnoea, wheeze, and haemoptysis.

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