Bicuspid aortic valve: different clinical profiles for subjects with versus without repaired aortic coarctation

Michelle S Lim,1,2 Paul G Bannon,1,3 David S Celermajer1,2

ABSTRACT

Objectives A small proportion of patients undergoing bicuspid aortic valve (BAV) intervention have had prior repair of aortic coarctation (CoA). We aimed to describe phenotypic differences between BAV patients, comparing those with versus those without previous coarctation repair.

Methods 556 adults with BAV who had undergone aortic valve and/or ascending aortic surgery were identified, and relevant clinical and operative details were retrospectively analysed.

Results Of the total cohort, 532 patients (95.7%) had isolated BAV (‘BAV-only’), and 24 (4.3%) had had a previous successful CoA repair (‘BAV-CoA’). The median age at surgery was significantly lower in BAV-CoA patients compared with BAV-only (median, IQR: 40 years, 26–57 vs 62 years, 51–69, p<0.001). Indications for surgery also differed, with BAV-CoA patients much more likely to undergo surgery for aortic regurgitation (BAV-CoA 38% vs BAV-only 13%, p<0.001); patients with isolated BAV were more likely to require surgery for aortic stenosis (BAV-only 75% vs BAV-CoA 50%, p<0.001). Two different BAV morphotypes were commoner in the BAV-CoA group; type 0 valves (24% vs 8%, p<0.05) and type 2 valves (12% vs 3%, p<0.05). The proportion of patients undergoing concomitant aortic surgery at the time of valve surgery were similar (BAV-only 38% vs BAV-CoA 42%, p=0.8).

Conclusion In adult patients undergoing aortic valve surgery for BAV disease, those with a prior history of repaired CoA underwent surgery at a very much younger age, and a higher proportion required intervention for aortic regurgitation.

INTRODUCTION

Bicuspid aortic valve (BAV) is the most common congenital heart abnormality in adults, and it is well recognised that aortic coarctation (CoA) coexists in a small but significant proportion of these patients. Despite this established link, however, the impact of past CoA repair on the natural history of BAV disease is not well described. Before the advent of repair techniques, aortic dissection accounted for 19% of deaths in patients with coarctation, which was amplified when BAV was also present.1 In the current era of effective CoA repair, however, few studies have specifically sought to investigate the impact of repaired CoA on BAV, and thus far, limited investigation of this important clinical question has led to conflicting results. We, therefore, aimed to identify any differences between patients with BAV alone, and those with BAV and coarctation, in order...
to better understand what clinical bearing coexistent coarctation may have on BAV disease.

METHODS

Patient and public involvement

Patients and the public were not directly involved in the undertaking of this research.

Patient selection

Adult patients (age >17 years) who had undergone aortic valve surgery for a BAV, with or without concomitant aortic surgery, were retrospectively recruited from the Adult Congenital Heart Disease and Cardiothoracic Surgery databases, at Royal Prince Alfred and Strathfield Private Hospitals. Patients were categorised as having BAV without coarctation (‘BAV-only’) or BAV with previous CoA repair (‘BAV-CoA’). We have separately reported the 30-day outcomes for 346 of the BAV-only patients. This paper focuses on the differences in characteristics and outcomes between BAV patients with or without previously repaired coarctation.

We prospectively determined that we would exclude any patients if they had developed any clinically significant recurrence of CoA, however, no such patients were identified in our databases. Patients were also excluded if the presence of a bicuspid valve could not be confirmed (4), the patient underwent transcatheter aortic valve replacement (1), surgery was primarily performed for ischaemic heart disease with aortic valve intervention an incidental/secondary operation (31), the patient had aortic surgery only, without valve intervention (10), had Ehlers Danlos or Marfans syndrome (3), had insufficient clinical information (5), their CoA had not been repaired (2), or they had associated complex congenital heart disease (14) except for patent ductus arteriosus, un repaired ventricular or atrial septal defects, left superior vena cava and/or hypoplastic aortic isthmus.

Study variables and definitions

Patient demographics and surgical data were collected from the databases, medical records, operation reports and echocardiography studies. If the exact date of surgery was not known, but the year of surgery was known, the patient was included and the age at surgery was calculated assuming the surgery was performed on the 30 June of that year. All deidentified data were recorded and stored in a secure password-protected REDCap (Research Electronic Data Capture) database, provided by the Clinical Research Centre at Sydney Local Health District.

BAV morphology: The presence of a BAV was confirmed in all patients from operative reports or preoperative transthoracic or transoesophageal echo studies. BAV morphology was classified according to the number of raphes present, and the orientation of the valve cusps, according to the classification system proposed by Sievers and Schmidtke (figure 1). Morphological classification was not possible in 232 patients due to insufficient operative report descriptions or unclear or unavailable echo studies. A subanalysis of BAV morphotype was, therefore, performed in the 336 (60%) patients in whom classification was possible.

Surgical indications: Patients were first classified according to the primary indication for surgery; valvular dysfunction (either aortic stenosis (AS), aortic regurgitation (AR) or mixed AS/AR), aortic disease, or infective endocarditis. Patients in whom multiple indications were listed, but the primary indication was not flagged, were classified as ‘unknown’. Patients were also secondarily classified according to the valve abnormality; normal, AS, AR, mixed AS/AR or infective endocarditis related valve dysfunction.

Operative details: Data were collected on operation type, valve replacement type and any concomitant coronary artery bypass graft surgery. Data on aortic surgery were also collected, and patients were classified as having no aortic surgery (‘none’), aortic root replacement only (‘proximal’), ascending and/or hemiarch replacement only without aortic root replacement (‘distal’), or both aortic root and ascending and/or hemiarch replacement (‘proximal and distal’). Choice of operation was at the discretion of the managing team (physician, surgeon and for valve type, patient preference was also considered). Generally, concomitant aortic intervention was performed if ascending aortic dimension exceeded 45 mm, and aortic valve intervention was performed if the valve was significantly calcified, was more than mildly stenosed, or was assessed as having haemodynamically significant AR.

Statistics

Continuous variables were non-parametric in distribution and so are reported as median and IQR, and categorical data are expressed as frequency and percentage. Comparison between groups was performed using the Mann-Whitney U test for continuous variables, and the \( \chi^2 \) test or Fischer’s exact tests for categorical variables. Post hoc analyses were carried out using multiple Fischer’s exact tests with Bonferroni correction. A two-tailed level of \( p<0.05 \) was considered statistically significant. All statistical analyses were performed using the SPSS V.25.0.
RESULTS

Patient characteristics
Patient characteristics are presented in table 1. Of the 556 recruited patients, 24 (4.3%) had a history of repaired CoA (‘BAV-CoA’). BAV-CoA patients were significantly younger at the time of surgery than BAV-only patients (median, IQR: 40 years, 26–57 vs 62 years, 51–69, p<0.001). A higher proportion of patients with BAV-CoA had undergone previous balloon aortic valvuloplasty or surgical valvotomy (16.7% vs 4.2%, p=0.022). Even after excluding these patients, however, a significant difference in median age at surgery remained (BAV-CoA 43 years, 29–59 vs BAV-only 63 years, 52–70 p<0.001).

BAV morphology
Data on valve morphotype were available on 60% of patients (table 1). A significantly higher proportion of patients in the repaired coarctation group had type 0 valves compared with patients without (23.5% vs 7.5%, p=0.02), while BAV-only patients were more likely to have type 1 valves (81.2% vs 52.9%, p=0.005). A higher proportion of patients with repaired coarctation had type 2RL/RN valves (11.8% vs 2.5%, p=0.029).

Indications for and types of surgery
Indications for and types of surgery are presented in table 2. There were significant differences in valve abnormalities that led to the aortic valve being replaced; a significantly higher proportion of patients with BAV-CoA required valve surgery for AR (38% vs 13%, p=0.001), while a higher proportion of patients with BAV-only required surgery for AS (75% vs 50%, p=0.007) (figure 2). Due to the higher proportion of patients with BAV-CoA

| Table 1 | Patient characteristics |
|---------|-------------------------|
|         | BAV only n=532 (95.7%)  | BAV and repaired CoA n=24 (4.3%) | p-value |
| Age at surgery | 62 (51–69) | 40 (26–57) | <0.001 |
| Male | 389 (73%) | 20 (83%) |
| Previous valvuloplasty or valvotomy | 22 (4.2%) | 4 (16.7%) | <0.05 |
| Age at surgery if no previous valvotomy/valvuloplasty | 63 (52–70) | 43 (29–59) | <0.001 |
| BAV morphology—data available in 336 (60%) |
| Type 0 | 24 (7.5%) | 4 (23.5%) | <0.05 |
| 0AP | 12 (3.8%) | 4 (23.5%) | <0.001 |
| 0Lat | 12 (3.8%) | 0 |
| Type 1 | 259 (81.2%) | 9 (52.9%) | <0.05 |
| 1RL | 190 (59.6%) | 7 (41.2%) |
| 1RN | 57 (17.9%) | 1 (5.9%) |
| Type 2 (2RL/RN) | 8 (2.5%) | 2 (11.8%) | <0.05 |
| Unicuspid | 3 (0.9%) | 0 |
| Cannot classify | 25 (7.8%) | 2 (11.8%) |

Continuous variables reported as median (IQR). Categorical variables reported as n (%). AP, anterior posterior; BAV, bicuspid aortic valve; CoA, aortic coarctation; Lat, Lateral; 1 LN, type 1 with left and non-coronary cusp fusion; 1 RL, type 1 with right and left coronary cusp fusion; 1 RN, type 1 with right and non-coronary cusp fusion.

| Table 2 | Indications for and types of surgery |
|---------|-----------------------------|
|         | BAV only n=532 (95.7%)  | BAV and repaired CoA n=24 (4.3%) | p-value |
| Primary indication for surgery |
| Valve dysfunction | 397 (74.6%) | 16 (66.7%) |
| Aortic disease | 80 (15.0%) | 6 (25.0%) |
| IE | 19 (3.6%) | 2 (8.3%) |
| Unknown | 36 (6.8%) | 0 | <0.001 |
| Valve haemodynamic |
| Normal function | 10 (1.9%) | 0 (0.0%) |
| AS | 398 (74.8%) | 12 (50.0%) | <0.05 |
| AR | 68 (12.8%) | 9 (37.5%) | <0.001 |
| IE | 19 (3.6%) | 2 (8.3%) |
| Mixed AS/AR | 25 (4.7%) | 0 |
| Unknown | 12 (2.3%) | 1 (4.2%) |
| Type of operation |
| Need for aortic surgery | 200 (37.6%) | 10 (41.7%) |
| Proximal versus distal aortic surgery |
| None | 332 (62.6%) | 14 (58.3%) |
| Proximal only | 46 (8.7%) | 6 (25.0%) |
| Distal only | 54 (10.2%) | 1 (4.2%) |
| Prox and distal | 98 (18.5%) | 3 (12.5%) |
| Type of surgery |
| AVR | 324 (60.9%) | 12 (50.0%) |
| Ross | 8 (1.5%) | 2 (8.3%) |
| AVR plus Aorta | 200 (37.6%) | 10 (41.7%) |
| AVR type | <0.05 |
| Mechanical | 185 (34.8%) | 13 (54.2%) | <0.05 |
| Tissue | 333 (62.7%) | 9 (37.5%) | <0.05 |
| Homograft | 3 (0.6%) | 0 |
| Ross | 9 (1.7%) | 2 (8.3%) | <0.05 |
| Valve repair | 1 (0.2%) | 0 |
| Concurrent CABG | 109 (20.5%) | 2 (8.3%) |
| 30 day mortality | 7 (1.3%) | 0 |

Categorical variables reported as n (%). p<0.001. †p<0.05. AR, aortic regurgitation; AS, aortic stenosis; AVR, aortic valve replacement; BAV, bicuspid aortic valve; CABG, coronary artery bypass graft; CoA, aortic coarctation; IE, infective endocarditis.
DISCUSSION

While the association between BAV and CoA is widely recognised, a history of prior CoA repair has traditionally had minimal impact on the clinical management of the bicuspid valve. The implications of the coexistence of the two conditions are not well appreciated. This study demonstrates for the first time, significant clinical differences between patients with isolated BAV requiring surgery, and those with BAV and prior repaired coarctation. Patients with BAV-CoA developed BAV-related complications requiring surgical intervention over two decades earlier than their BAV-only counterparts, and a significantly higher proportion required valve surgery for AR. These differences suggest that BAV patients with past CoA repair may have an accelerated clinical course, necessitating different surveillance strategies to detect the development of important BAV complications much earlier in life, and contributes to our understanding of the nature of the relationship between these two frequently associated conditions.

The impact of repaired coarctation on the valvular complications of BAV has not been extensively investigated. A small number of studies in children have found that children with BAV-CoA have less AS/AR than children with pure BAV and less valve intervention. While this indicates that repaired CoA does not appear to have deleterious effects on the BAV early in life, the consequences of any prolonged aberrations relating to the repaired CoA may not yet have manifested in this young cohort. No studies of adults have specifically studied the impact of CoA on BAV valve complications, however, one large study of 642 adults with BAV, of whom 25% had a history of CoA, found that a significantly higher proportion of adults with CoA did not experience valve and aortic complications, suggesting that in fact patients with coarctation have a better prognosis. By contrast, a study of patients with aortic coarctation found BAV to be a predictor of developing AR in patients with CoA.

The significance of CoA for the possible ascending aortic complications of BAV has been more widely studied. It appears that the presence of coarctation is not associated with aortic dilatation, as paediatric studies have found children with concomitant CoA actually have smaller aortic dimensions, and slower rates of aortic dilatation. Once again in adulthood, however, the impact of CoA on BAV-related aortic complications is contentious. While some data suggest that BAV-CoA patients are more likely to develop aortic complications (predominantly driven by increased aneurysm risk), although dissection risk also appears to be higher, other data suggest there is no difference in aortic complications. Despite the conflicting evidence, clinically there remains sufficient concern of the potential increase in risk, which is reflected in the lower threshold for aortic surgery for patients with BAV-CoA in the European guidelines.

We propose a few possible explanations for our findings. It has been previously postulated that BAV and CoA are part of a spectrum of manifestations of a single disease process, with shared embryological, histological and clinical features. It is possible, therefore, that patients with both conditions have a unique aortic/valvar profile, both innately and acquired, compared with patients with only one or the other.

At a cellular level, a recent study of neonatal aortic tissue sampled proximal to a coarctation demonstrated significantly different proteomic and histological profiles when BAV was present, compared with TAV. A unique phenotype may also be evident on a macroscopic level. In our cohort, patients with BAV-CoA had a higher frequency of prior valvuloplasty or valvotomy. This may suggest that BAV-CoA patients are born with more severe valve abnormalities, although the paediatric studies referred to earlier did not find this. Alternatively, there may be a preponderance for particular BAV morphotypes to cluster in patients with CoA. We found that while 1-RL BAVs were the most common valve morphotype in both BAV-only and BAV-CoA groups, a significantly higher proportion of BAV-CoA patients had type 0-AP valves.

Figure 2 The indication for valve surgery significantly differs between patients with BAV-only and BAV-CoA. *P<0.001. BAV-CoA, patients with bicuspid aortic valve and prior repaired coarctation. BAV-only, patients with BAV only.
Other series have previously shown that BAV-CoA is associated with 1-RL morphology, however, synthesis of literature on BAV morphotype distribution is challenging, due to variable morphotype classification systems, with many not specifying the presence or absence of a raphe. One study that did compare the differences between BAV with and without raphe was Michałowska et al., who found that CoA was more commonly associated with patients with BAV-without raphe, than BAV with raphe (44.4% vs 13.3%)—findings which are similar to our study findings.

In addition to histological and morphological differences between BAV-only and BAV-CoA patients, disturbed haemodynamic and loading conditions, may be an alternative or contributing cause. Abnormal aortic biomechanics in coarctation has been demonstrated, initially in animal models, and then in humans, with evidence of reduced aortic elasticity and increased stiffness both before and after coarctation repair. Additionally, systemic hypertension is a known complication of repaired coarctation, accounting for a significant proportion of the morbidity affecting these patients. Hypertension is a well-recognised risk factor for the development of aortic valve disease, inclusive of both stenosis and regurgitation. Altered aortic geometry may be an additional differing feature, as previous CoA repair is associated with a ‘gothic’ aortic arch. Mechanobiological studies on the aortic valve have elucidated the intricate relationship between altered leaflet pressure, stretch and shear stresses and the cellular, proteomic and genomic profiles of aortic valves which may be involved in aortic valve dysfunction. These abnormalities in aortic and aortic valve mechanics, therefore, may potentially contribute to the accelerated valvular dysfunction that we observed in the patients with BAV-CoA.

More complex haemodynamic perturbations may also be implicated. Regional disturbances in wall shear stress (WSS) in patients with BAV have been implicated in the haemodynamic theory of BAV-aortopathy. Flow disturbances have also been demonstrated in patients with CoA, with computational fluid dynamic methods showing how these are compounded when BAV is also present. While we did not find a statistically significant difference in the proportion of patients who underwent concomitant ascending aortic surgery, the known role of aortic dilatation in AR raises speculation for a haemodynamic explanation for the higher proportion of patients with AR in the BAV-CoA group. Finally, differences in valve leaflet WSS has been demonstrated in BAVs compared with tricuspid aortic valves and between BAV morphotypes. Whether or not valve leaflet WSS is further disturbed by concomitant CoA has not been studied, but if present, may also potentially contribute to accelerated valve dysfunction, leading to surgery at a younger age in patients with BAV-CoA.

**Study limitations and future directions**

This study has limitations including its retrospective design. The BAV-CoA group was small compared with the BAV-only comparator; however, the 4.3% proportion is consistent with previous reports. This study also includes only patients who have clinically significant BAV related complications requiring surgical intervention. The impact, therefore, of concomitant CoA on patients across the broad spectrum of (milder) BAV disease remains unknown. In this study, quantitative data on aortic dimensions were not collected. While at our two institutions, aortic intervention was undertaken according to international guideline recommendations, the lack of aortic dimension data in our study precludes us from making firm conclusions on the nature of BAV-related aortic disease in our cohort.

Future study of ‘all-comers’ with BAV including longitudinal follow-up will be important, to clarify the applicability of our findings to all patients with BAV. Further clinical, scientific and imaging research, investigating the phenotypic, biological and haemodynamic differences in patients with these co-occurring conditions, is needed to elucidate the mechanisms for our findings, and guide future management strategies.

**CONCLUSION**

In patients undergoing aortic valve replacement for BAV disease, those with a prior history of repaired coarctation had significantly different clinical profiles, requiring surgery over two decades earlier than their BAV-only counterparts and with a higher proportion undergoing surgery for AR. These findings suggest that the coexistence of BAV and CoA may lead to a more aggressive clinical phenotype, requiring that these patients undergo different surveillance strategies to detect the development of important BAV complications, earlier in adult life.

**Acknowledgements** The authors would like to thank Irina Kotchetkova and Lisa Turner for their assistance with utilising the institutional databases.

**Contributors** ML was responsible for the acquisition of data. All three authors made substantial contributions to the conception of the work, analysis and interpretation of the data, drafting and revision of the manuscript, and approval of the final version being submitted. All authors agree to be accountable for all aspects of the work.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The study protocol was approved by the institutional ethics committees at the two hospital sites. The need for written informed consent was waived by the Institutional Ethics Committee in accordance with NHMRC guidelines.

**Provenance and peer review** Not commissioned; internally peer reviewed.

**Data availability statement** Data are available on reasonable request.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

**ORCID iD**

Michelle S Lim http://orcid.org/0000-0001-6416-5566
REFERENCES

1. Abbott ME. Coarctation of the aorta of the adult type: II. A statistical study and historical retrospect of 200 recorded cases with autopsy, of stenosis or obliteration of the descending arch in subjects above the age of two years. Am Heart J 1928;3:574–618.

2. Lim M, Bannon P, Celermajer D. Bicuspid aortic valve disease – valve morphology influences age at and indications for operative treatment. Heart, Lung and Circulation 2019;28:S347.

3. Sievers H-H, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. J Thorac Cardiovasc Surg 2007;133:1228–33.

4. Fernandes SM, Sanders SP, Khairy P, et al. Morphology of bicuspid aortic valve in children and adolescents. J Am Coll Cardiol 2004;44:1648–51.

5. Merkx R, Duijnhouwer AL, Vink E, et al. Aortic diameter growth in children with a bicuspid aortic valve. Am J Cardiol 2017;120:131–6.

6. Tzemos N, Thiriet J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. JAMA 2008;300:1317–25.

7. Lujendijk P, Stevens AWJM, de Bruin-Bon RHACM, et al. Rates and determinants of progressive aortic valve dysfunction in aortic coarctation. Int J Cardiol 2013;167:2841–5.

8. Beaton AZ, Nguyen T, Lai WW, et al. Relation of coarctation of the aorta to the occurrence of ascending aortic dilatation in children and young adults with bicuspid aortic valves. Am J Cardiol 2009;103:266–70.

9. Fernandes S, Khairy P, Graham DA, et al. Bicuspid aortic valve and associated aortic dilation in the young. Heart 2012;98:1014–9.

10. Oliver JM, Alonso-de Grado AC, Zwinderman AH, et al. Aortic valve stenosis and aortic root or ascending aorta complications in patients with bicuspid aortic valve and without coarctation of the aorta. Am J Cardiol 2009;104:1001–6.

11. Eledj MF, Forde I, Edwards WD, et al. Type A aortic dissection in patients with bicuspid aortic valves: clinical and pathological comparison with tricuspid aortic valves. Heart 2013;99:1668–74.

12. Michalowska IM, Kruk M, Kwieta P, et al. Aortic pathology in patients with bicuspid aortic valve assessed with computed tomography angiography. J Thorac Imaging 2014;29:113–7.

13. Michalena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. JAMA 2011;306:1104–12.

14. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J 2014;35:2873–926.

15. Kappetein AP, Gittenberger-de Groot AC, Zwinderman AH, et al. The neural crest as a possible pathogenetic factor in coarctation of the aorta and bicuspid aortic valve. J Thorac Cardiovasc Surg 1991;102:830–6.

16. Lindsay J. Coarctation of the aorta, bicuspid aortic valve and abnormal ascending aortic wall. Am J Cardiol 1988;61:182–4.

17. Wannes OA. Bicuspid aortic valve and coarctation: two villains part of a diffuse process. Heart 2003;89:965–6.

18. Sheffington KL, Bond AR, Abdul-Ghani S, et al. Bicuspid aortic valve alters aortic protein expression profile in neonatal coarctation patients. J Clin Med 2019;8:517.

19. GUPTA TC, WIGGERS CJ. Basic hemodynamic changes produced by aortic coarctation of different degrees. Circulation 1951;3:37–31.

20. Oo P, Celermajer DS, Jolivet O, et al. Increased central aortic stiffness and left ventricular mass in normotensive young subjects after successful coarctation repair. Am Heart J 2008;155:187–93.

21. Clarkson PM, Nicholson MR, Barratt-Boyes BG, et al. Results after repair of coarctation of the aorta beyond infancy: a 10 to 28 year follow-up with particular reference to late systemic hypertension. Am J Cardiol 1983;51:1481–8.

22. Rahimi K, Mohseni H, Kiran A, et al. Elevated blood pressure and risk of aortic valve disease: a cohort analysis of 5.4 million UK adults. Eur Heart J 2018;39:3596–603.

23. Sophocleous F, Biffi B, Milano EG, et al. Aortic morphological variability in patients with bicuspid aortic valve and aortic coarctation. Eur J Cardiothorac Surg 2019;55:704–13.

24. Balachandran K, Sucosky P, Yoganathan AP. Hemodynamics and mechanobiology of aortic valve inflammation and calcification. Int J Inflam 2011;2011:1–15.

25. Farag ES, van Ooij P, Planken RN, et al. Aortic valve stenosis and aortic diameters determine the extent of increased wall shear stress in bicuspid aortic valve disease. J Magn Reson Imaging 2018;48:522–30.

26. Hope MD, Meadows AK, Hope TA, et al. Clinical evaluation of aortic coarctation with 4D flow MR imaging. J Magn Reson Imaging 2010;31:711–8.

27. Keshavarz-Motamed Z, Garcia J, Kadem L. Fluid dynamics of coarctation of the aorta and effect of bicuspid aortic valve. PLoS One 2013;8:e72394.

28. Chandra S, Rajamannan NM, Sucosky P. Computational assessment of bicuspid aortic valve wall-shear stress: implications for calcific aortic valve disease. Biomech Model Mechanobiol 2012;11:1085–96.

29. Cao K, Sucosky P. Computational comparison of regional stress and deformation characteristics in tricuspid and bicuspid aortic valve leaflets. Int J Numer Method Biomed Eng 2017;33:e02798.

30. Roberts WC. The congenitally bicuspid aortic valve. Am J Cardiol 1970;26:72–83.

6  Lim MS, et al. Open Heart 2020;7:e001429. doi:10.1136/openhrt-2020-001429