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RESEARCH LETTER
Infectious/communicable diseases

Aortic valve endocarditis: comparing clinical outcomes in bicuspid versus tricuspid aortic valves

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Infective endocarditis (IE) of a bicuspid aortic valve (BAV) is a well-established complication. The incidence of bicuspid aortic valve infective endocarditis (BAV-IE) has been reported at 2% in contemporary BAV cohorts with an estimated risk of developing BAV-IE 11 times that of the general population with a trileaflet aortic valve (TAV).[1]

The aim of this study was to ascertain if those with BAV-IE are at a higher risk of adverse sequelae by comparing clinical outcomes with a cohort of individuals with trileaflet aortic valve infective endocarditis (TAV-IE).

In this retrospective observational cohort study, two physicians interrogated the clinical records of all patients (>16 years old) with a definitive diagnosis of native aortic valve IE by Duke's criteria who were admitted to a large tertiary referral centre in the UK between 2015 and 2022.[2] Clinical, echocardiographic, and microbiological data were obtained. The primary outcome was death and/or surgical aortic valve intervention during the indexed hospital admission.

Secondary outcomes included cardiac complications (including aortic root abscess or fistula formation, IE affecting another valve, or high-degree atrioventricular block requiring temporary or permanent pacemaker insertion). Extra-cardiac complications included embolic phenomena and thrombotic events.

Statistical analyses were performed using R (version 4.3.0) utilizing the RStudio IDE tool (version 2023.03.01). Wilcoxon rank sum test was used to test differences between non-parametric variables. Where computationally feasible, Fisher's exact tests were used to test differences between categorical variables. Step-wise logistic regression methods were performed to assess if BAV carries a mortality risk after correcting for confounders. The level of statistical significance was set as $P < 0.05$. The study conformed to the principles outlined in the Declaration of Helsinki.

A total of 83 patients were included (BAV-IE 34; TAV-IE 49). Patients with BAV-IE were significantly younger at presentation than patients with TAV-IE (mean age BAV-IE 50 ± 16 years vs. 60 ± 13 years for TAV-IE; $P = 0.007$) (*Table 1*).

When adjusted for age, gender, and co-morbidities, there was no significant difference in the risk of inpatient mortality between the two groups (OR 0.34, 95% CI 0.09–1.08; $P = 0.2$). Furthermore, the risk of other cardiac complications was similar, with aortic root abscess formation being the most common cardiac manifestation in both groups.

There was a significantly higher prevalence of at least moderate aortic regurgitation (AR) in the BAV-IE group [88% (30/34) BAV-IE vs. 67% (33/49) TAV-IE; $P = 0.03$]. Furthermore, a higher proportion of those in the BAV-IE group had aortic valve intervention during the admission [70% (24/34) BAV-IE vs. 43% (21/49) TAV-IE, $P = 0.013$].

When classified by Siever's nomenclature, the vast majority of BAV morphology was right–left coronary cusp fusion (64.7%; $n = 22$) and right–non-coronary cusp fusion (20.6%; $n = 7$) (*Figure 1*).[3] Streptococcal species accounted for the majority of IE cases (23/49 TAV-IE; 11/34 BAV-IE), with staphylococcal species being the next most common causative organism (13 TAV-IE; 10 BAV-IE).

Despite the BAV-IE group being younger with less predisposing co-morbidities, we did not find a significant difference in the risk of inpatient mortality, the presence of high-grade atrioventricular block, abscess or fistula formation, or concomitant endocarditis of an additional valve when comparing BAV-IE with TAV-IE. Previous studies have however identified that individuals with BAV were more likely to develop an aortic root abscess.[4,5]

Acute surgical intervention has previously been estimated to be required in up to 50% of all-comers with IE.[6] Our study showed significantly higher rates of acute aortic valve replacement (AVR) in patients with BAV-IE (71% vs. 47%, $P = 0.013$). Though many patients with TAV-IE may be older, more comorbid, and therefore poorer surgical candidates, the higher rate of AVR in BAV-IE may also be due to the higher rates of significant AR developing in those with a BAV. Due to its structure, BAVs are inherently predisposed to developing AR, and if endocarditis develops, a vegetation could potentially cause more rapid destruction of the valvular apparatus than in a trileaflet valve.

This single-centre study is limited by the relatively small number of cases included. The presence of on-site cardiothoracic services may introduce a referral bias where individuals with severe IE are referred

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Table 1 Demographics and clinical outcomes of both bicuspid and trileaflet aortic valve endocarditis patients

	Bicuspid aortic valve ($n = 34$)	Trileaflet aortic valve ($n = 49$)	*P*-value
Age at initial presentation (standard deviation)	50.2 (±16)	60.3 (±13)	**0.007**[a]
Male; *n* (%)	32 (94)	38 (78)	**0.04**[b]
Co-morbidities			
Type 2 diabetes; *n* (%)	4 (12)	12 (22)	0.07[b]
Intravenous drug use; *n* (%)	2 (6)	2 (4)	0.99[c]
Hypertension; *n* (%)	6 (18)	14 (29)	0.25[c]
Ischaemic heart disease; *n* (%)	0 (0)	4 (8)	0.99[b]
Malignancy; *n* (%)	0 (0)	5 (10)	0.64[c]
End-stage renal failure; *n* (%)	0 (0)	6 (12)	0.08[c]
Length of hospital stay; median days (IQR)	33 (22–51)	52 (34–69)	**0.007**
Blood culture organism; *n* (%)			0.65[c]
• Streptococcus	11 (32)	23 (47)	
• Staphylococcus	10 (29)	13 (27)	
• Enterococcus	5 (15)	5 (10)	
• Negative	7 (21)	8 (16)	
• Other	1 (3)	0 (0)	
Cardiac complications			
Developed at least moderate AR; *n* (%)	30 (88)	33 (67)	**0.03**[c]
High-grade AVB/CHB; *n* (%)	3 (9)	5 (10)	0.73[c]
Aortic root abscess; *n* (%)	7 (21)	6 (12)	0.30[b]
Fistula; *n* (%)	3 (9)	1 (2)	0.30[c]
MV endocarditis; *n* (%)	4 (8)	4 (12)	0.71[c]
Extra-cardiac manifestations			
Emboli; *n* (%)	15 (44) (Cerebral 8 – 3 acute strokes)	19 (39) (Cerebral 10 – 4 acute strokes)	0.66[b]
Acute aortic valve surgery; *n* (%)	24 (71)	23 (47)	**0.013**[b]
Death during admission; *n* (%)	4 (12)	14 (29)	**0.006**[a]

AR, aortic regurgitation; AVB, atrioventricular block; CHB, complete heart block; MV, mitral valve; IQR, interquartile range. All in bold are statistically significant, based on $p < 0.05$.
[a]Wilcoxon rank sum text.
[b]Pearson's chi-squared test.
[c]Fisher's exact test.

and thereby more likely to require surgical intervention, whereas those with more indolent clinical courses may be treated at their local centre. Similarly, there may be an immortal time bias where suitable surgical candidates were referred to our centre whereas those with more severe presentations died in their local centre before being referred. However, these concepts are applicable to both the TAV-IE and BAV-IE cohorts. Owing to this potential bias, the high rates of AVR seen in our cohort may not necessarily be able to be extrapolated to the general IE population. Furthermore, the vast majority of patients had no previous TTE performed, and so the degree of pre-existing valvular dysfunction is unknown.

In contrast to prior recommendations, current international guidance does not recommend the routine use of antibiotic prophylaxis prior to medical or dental procedures.[4,7] It is not the aim of this study to challenge these recommendations, but the most common causative organisms in this study were streptococcal and staphylococcal species, in line with previous studies.[5,8] This reinforces the importance of mitigating sources of infection through optimal dental and cutaneous hygiene, and antibiotic prophylaxis in select, high-risk patients should be considered as outlined in the existing guidelines.[4] The risk of IE should be explained to individuals when a BAV is detected so that these aforementioned precautions can be made. Furthermore, prompt medical attention and treatment of suspected IE cases are of utmost importance in individuals with BAV as degeneration of the valve and other cardiac complications can occur rapidly.

Overall, despite its population prevalence of 1–2%, BAV accounted for 41% of all native aortic valve endocarditis cases in our cohort over a 7-year period. Moreover, the high incidence of cardiac complications in comparatively young individuals with BAV highlights the significant risk of adverse sequelae if individuals with BAV develop IE.

Author contributions

N.C., J.D., A.M., A.B., and M.T.E. contributed to the conception or design of the work. N.C., J.D., N.K., R.H., U.B., S.F., and R.B. contributed to the acquisition, analysis, or interpretation of data for the work. N.C., J.D., S.F., R.B., and U.B. drafted the manuscript. M.T.E., M.P., and A.M. critically revised the manuscript. U.B. revised the manuscript from a statistical method perspective. All gave final approval and agree to be accountable for all aspects of the work ensuring integrity and accuracy.

Conflict of interest: None declared.

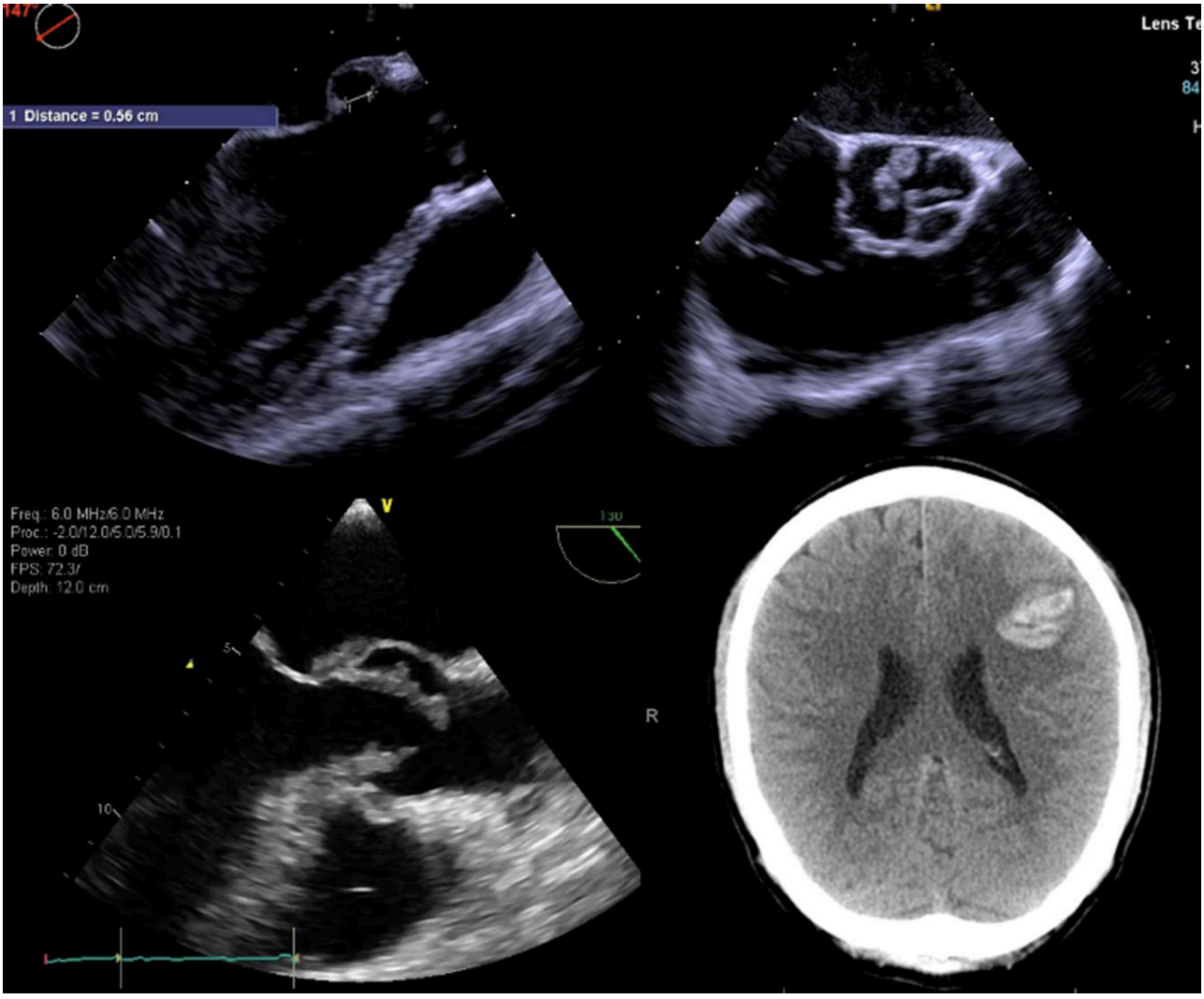

Figure 1 Imaging findings in bicuspid aortic valve infective endocarditis (BAV-IE). *Top left*, transoesophageal echocardiogram (TOE) in a 35-year-old lady with an aortic root abscess and 5.6 cm communication between the aorta and the left ventricle; *top right*, TOE demonstrating a BAV with a large vegetation on the non-coronary cusp, which had partially ruptured; *bottom left*, TOE demonstrating large vegetations on both aortic leaflets. These resulted in significant aortic regurgitation. *Bottom right*, unenhanced axial computed tomography head in the same patient showing acute intraparenchymal haemorrhage in the left frontal lobe.

Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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