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# Unlocking insights in bicuspid aortic valve management in adult patients: the vital role of cardiac imaging

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## Abstract

The bicuspid aortic valve (BAV) presents a multifaceted clinical challenge due to its diverse morphologies and associated complications. This review aims to elucidate the critical role of cardiac imaging in guiding optimal management strategies for BAV patients. BAV, with a prevalence of 1-2%, has genetic underpinnings linked to the *NOTCH1* gene mutation. Variability in BAV morphology necessitates tailored surgical approaches. The three primary types of BAV morphology - right-left cusp fusion, right-noncoronary cusp fusion, and left-noncoronary cusp fusion - demand nuanced considerations due to their distinct implications. Valvular dysfunction results in aortic stenosis or regurgitation, attributed to altered valve structure and turbulent hemodynamics. Cardiac imaging modalities, including echocardiography, magnetic resonance imaging, and computerized tomography, are instrumental in assessing valve function, aortic dimensions, and associated complications. Imaging helps predict potential complications, enabling informed treatment decisions. Regular follow-up is crucial to detecting alterations early and intervening promptly. Surgical management options encompass aortic valve repair or replacement, with patient-specific factors guiding the choice. Post-surgical surveillance plays a vital role in preventing complications and optimizing patient outcomes. The review underscores the significance of advanced cardiac imaging techniques in understanding BAV's complexities, facilitating personalized management strategies, and improving patient care. By harnessing the power of multimodal imaging, clinicians can tailor interventions, monitor disease progression, and ultimately enhance the prognosis and quality of life for individuals with BAV.

## Introduction

The aortic valve plays a vital role in maintaining optimal blood flow within the heart. It is a crucial component, ensuring smooth blood passage from the left ventricle to the aorta. However, when abnormalities arise, such as the bicuspid aortic valve (BAV), it can lead to various complications necessitating careful surgical intervention [1]. This condition, with a prevalence ranging from 1% to 2%, has genetic origins, with the *NOTCH1* gene mutation being a frequently observed genetic factor in BAV patients [2,3].

While some individuals with BAV might not experience symptoms, the condition presents a spectrum of potential issues requiring consideration. BAV is linked to an increased susceptibility to valvu-

lar problems, including aortic stenosis or regurgitation, due to altered valve structure and blood flow patterns [3-5]. Additionally, BAV cases often show an inclination toward developing aortic aneurysms, emphasizing the need for careful monitoring and timely medical intervention [4,6,7]. This heightened risk of aortic dilation highlights the importance of thoroughly assessing aortic dimensions and shape in individuals diagnosed with BAV.

Interestingly, BAV also slightly raises the risk of infective endocarditis [5]. The mechanisms behind this heightened vulnerability are intricate and warrant further exploration.

Furthermore, some individuals with BAV may eventually display symptoms like chest pain, fatigue, and difficulty breathing [6,8]. These symptoms stem from altered blood flow, valve dysfunction, and potential concurrent cardiovascular conditions.

Given these multifaceted implications, a comprehensive grasp of various aspects of BAV-related issues is crucial. Effective management strategies should rely on thorough clinical evaluations, vigilant monitoring, and a nuanced understanding of the interplay between genetic predisposition, valve dynamics, and associated cardiovascular risks.

This article aims to delve into the complexities of BAV, explore its implications, and examine the surgical strategies employed to address this condition.

## Variations in bicuspid aortic valve morphology

The spectrum of the BAV extends beyond a singular form, encompassing diverse morphological configurations, each carrying distinctive implications for clinical and surgical management [3-5]. The heterogeneity in BAV morphology underscores the necessity for customized surgical strategies. Every morphology presents unique hemodynamic profiles, valvular dynamics, and susceptibilities of the aorta. Decisions regarding follow-up and surgical intervention should be guided by a comprehensive assessment of valve functionality, aortic dimensions, and associated risks.

Type 1 BAV morphology (right-left cusp fusion): this variant of BAV involves fusion between the right and left coronary cusps, inducing altered hemodynamics that might predispose individuals to aortic stenosis or regurgitation [3]. Surgical intervention becomes pivotal as valvular dysfunction advances, necessitating repair or replacement to restore proper valve operation and avert complications.

Type 2 BAV morphology (right-noncoronary cusp fusion): type 2 BAV morphology entails fusion between the right coronary cusp and the noncoronary cusp, resulting in distinct flow patterns and mechanical stress on the aortic wall [4]. Those with this morphology face an elevated risk of aortic enlargement and aneurysm development. Surgical indications may be governed by aortic measurements, rupture risk, and potential valve irregularities.

Type 3 BAV morphology (left-noncoronary cusp fusion): marked by fusion between the left coronary cusp and the noncoronary cusp, type 3 BAV morphology presents its unique set of complexities [5]. This morphology is tied to disturbances in hemodynamics that can lead to valvular dysfunction and aortic complications. Surgical considerations encompass an evaluation of valve performance, aortic dimensions, and aneurysm risk.

Figures 1-4 show imaging of the different types of BAV morphologies and associated anomalies of the thoracic aorta.

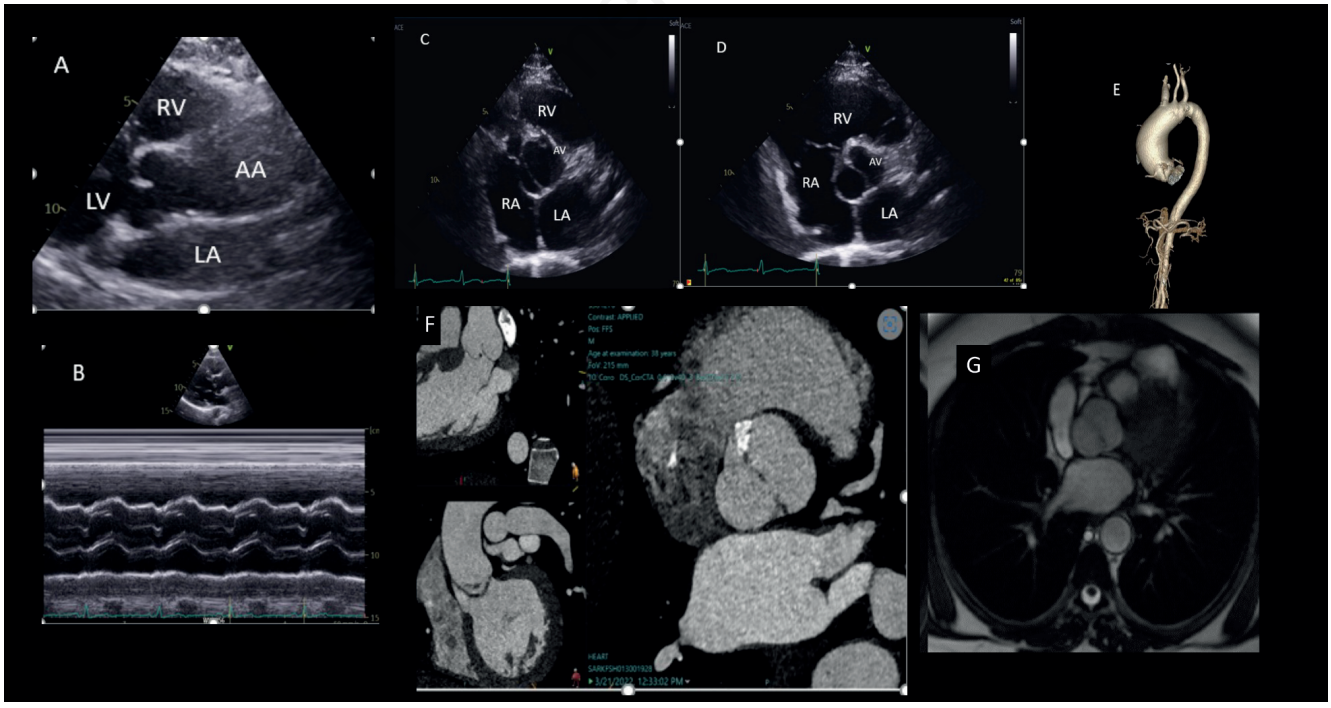


**Figure 1.** Type 1 with raphe: right and left coronary cusp fusion with the raphe in the anterior position. A) 2D transthoracic echocardiography with bicuspid aortic valve with dilatation of ascending aorta; B) M mode transthoracic echocardiography on aortic valve with eccentric valve closure in diastole; C,D) 2D transthoracic echocardiography short axis parasternal aortic level there is a raphe at 2 o'clock between right and left cusps; E) 3D cardiac computed tomography shows dilatation of ascending aorta; F) cardiac computerized tomography, bicuspid aortic valve; G) cardiac magnetic resonance imaging, type 1 bicuspid aortic valve. LV, left ventricular; RV, right ventricular; LA, left atrium; RA, right atrium; AV, aortic valve.

## Valvular dysfunction and hemodynamic derangements

Valvular dysfunction stands as a principal concern in BAV instances, often culminating in significant aortic stenosis or regurgitation [3]. Hemodynamic perturbations arising from the atypical valve morphology predispose individuals to turbulent hemodynamics and the emergence of valvular aberrations.

The mechanism underpinning aortic stenosis in BAV revolves around progressive cusp thickening and calcification [3]. The irregular cuspal morphology engenders an uneven distribution of

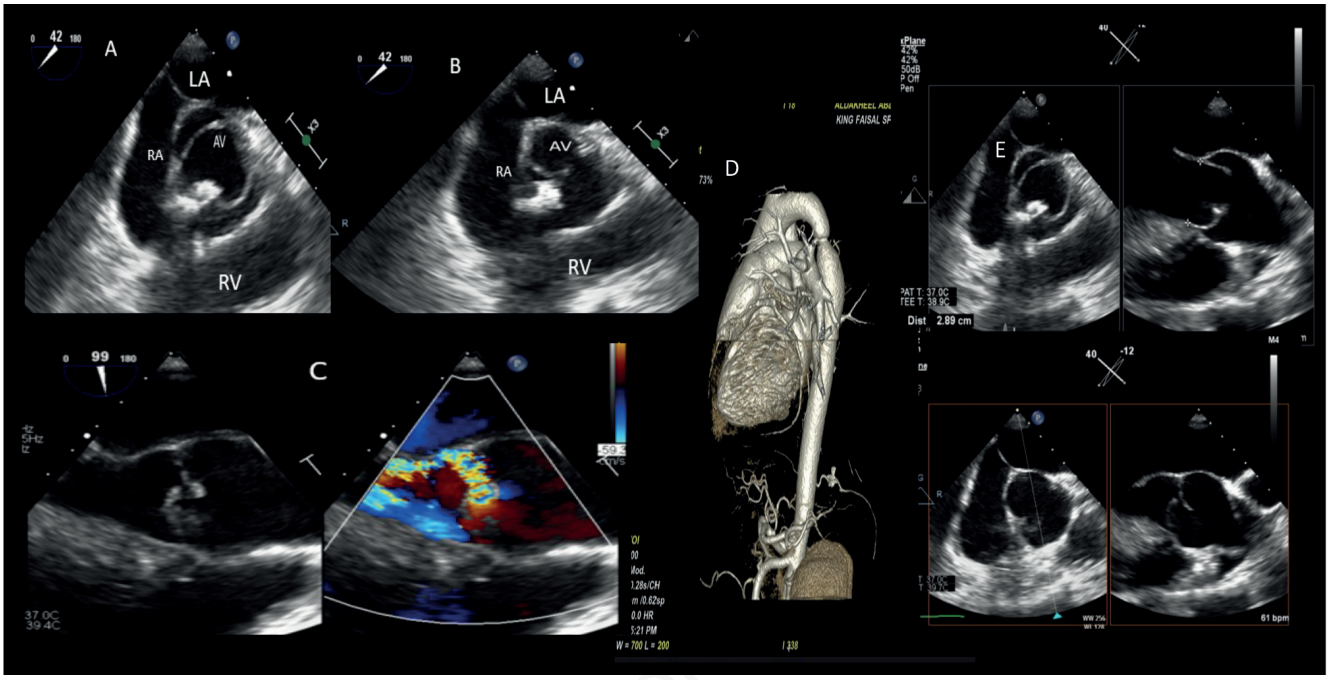


**Figure 2.** Type 1 without raphe. A,B) 2D transesophageal echocardiogram bicuspid aortic valve with fusion of the right and left without a raphe; C) 2D with color transesophageal echocardiogram in long parasternal view shows severe very eccentric aortic regurgitation; the jet is impinging on the anterior mitral valve; D) 3D cardiac computerized tomography shows coarctation of aorta; E) 2D X plane transesophageal echocardiogram, systole and diastole. RV, right ventricular; LA, left atrium; RA, right atrium; AV, aortic valve.

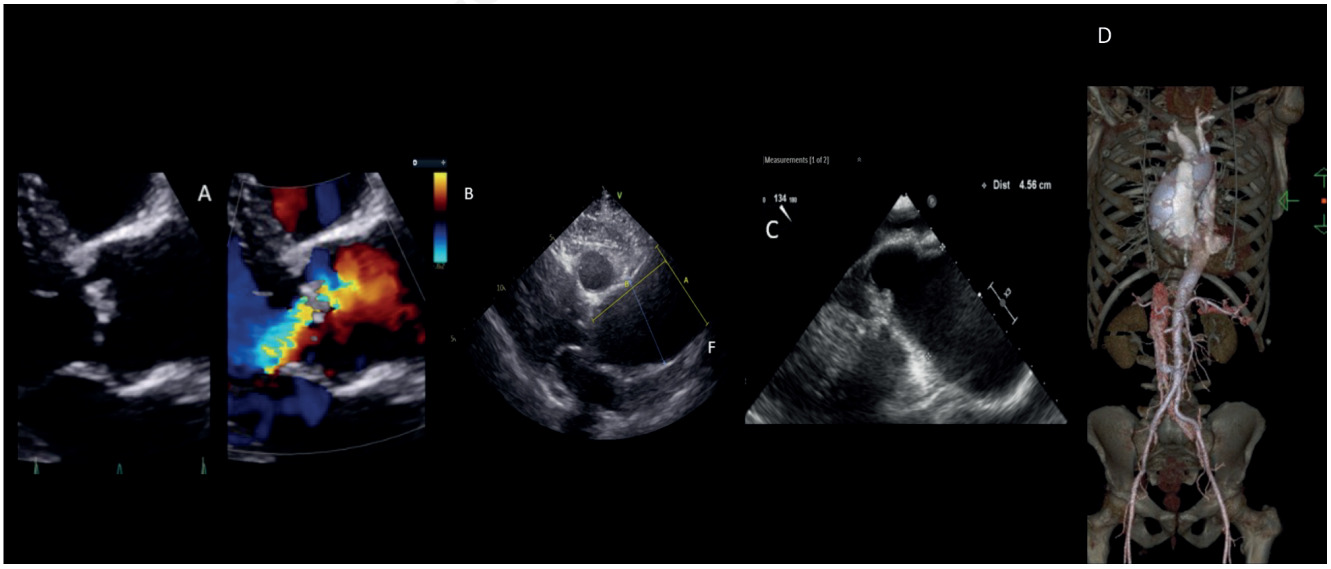


**Figure 3.** Bicuspid aortic valve. A) 2D transthoracic echocardiography, bicuspid aortic valve with aortic regurgitation; B) 2D transthoracic echocardiography ascending aorta dilatation; C) 2D transthoracic echocardiography bicuspid aortic valve, dilatation of ascending aorta; D) 3D cardiac computerized tomography: aneurysmal dilatation of the ascending aorta.

mechanical stress across the cardiac cycle. This uneven stress distribution incites regions of escalated mechanical strain, subsequently triggering inflammation and fibrosis within the valvular tissue [9]. As fibrotic processes advance, the cusps stiffen and lose their pliancy. This rigidity constrains their capacity to fully open during systole, leading to a reduction in the effective orifice area for blood passage. Consequently, an obstruction to blood outflow from the left ventricle to the aorta emerges, culminating in heightened pressure gradients across the valve. This obstruction imposes an augmented workload on the heart and can eventually give rise to symptoms such as angina, fatigue, and dyspnea [8].

Regurgitation represents another sequela of BAV. The mechanism behind regurgitation involves cusp dysfunction and incomplete leaflet coaptation [3]. The non-uniform cuspal fusion and modified hemodynamics contribute to cusp thickening, fibrosis, and impaired mobility. This malfunction impedes the cusps from achieving complete closure during diastole, thereby permitting retrograde blood flow into the left ventricle. Furthermore, the turbulent flow patterns engendered by the irregular cuspal configuration further disrupt the proper coaptation of the valve leaflets, intensifying the regurgitant flow. The antegrade blood flow compromise not only curtails the heart's pumping efficacy but also fosters volume overload and eventual dilation of the left ventricle over time.

## Imaging and clinical implications

The pathophysiological mechanisms underlying stenosis and regurgitation in the context of BAV underscore the imperative nature of early detection and suitable therapeutic strategies. Notable diagnostic modalities, including echocardiography, magnetic resonance imaging (MRI), and computerized tomography (CT) imaging, hold pivotal roles in evaluating valvular function and the severity of associated complications [10-12].

A study by Santarpia *et al*. revealed significant insights into aortic and left ventricular (LV) remodeling patterns among BAV patients, even in the absence of marked valvular dysfunction [12].

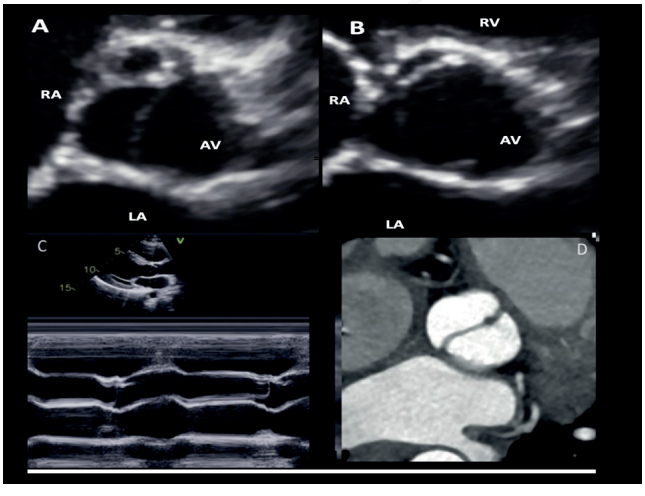


**Figure 4.** A,B) 2D transthoracic echocardiography, type 2 bicuspid aortic valve, diastole and systole; C) M mode transthoracic echocardiography on aortic valve shows eccentric valve closure in diastole; D) cardiac computerized tomography imaging: type 2 bicuspid aortic valve. RV, right ventricular; LA, left atrium; RA, right atrium; AV, aortic valve.

Despite seemingly insignificant valvular impairment, individuals with BAV demonstrated distinctive trends in aortic dilation and LV alterations. Enlarged aortic dimensions, particularly within the aortic root, were observed in BAV patients compared to healthy controls. Furthermore, LV hypertrophy manifested as an adaptive response to altered hemodynamics.

An intricate classification system, derived from comprehensive cardiac MRI assessment, enhances the comprehension of BAV morphology, as demonstrated by another study [13]. The researchers proposed a 4-stage categorization system to classify the diverse morphological patterns of BAV leaflets. This classification aimed to capture the intricate variations in the fusion and structure of the valve leaflets, providing a more nuanced and detailed characterization of BAV morphology. This enhanced classification system could aid in predicting potential complications, guiding surgical decision-making, and tailoring treatment strategies to the specific characteristics of each BAV morphology.

Another study using echocardiography and cardiac CT investigated the relationship between BAV phenotype and cardiovascular anomalies correlations [14]. The research unveiled distinct valvular dysfunction patterns associated with specific BAV phenotypes, shedding light on the interplay between morphological characteristics and varying degrees of valvular impairment. Furthermore, the study highlighted a significant association between BAV phenotype and the presence of aortopathy, illustrating the intricate relationships between these components.

The link between BAV and aortic coarctation has been extensively explored [12,15]. Although the mechanisms intertwining BAV and aortic coarctation remain complex and not fully elucidated, both conditions are linked to aortic vasculopathy, which is a significant cause of morbidity and mortality in young individuals with congenital heart disease. The natural progression of aortic dimensions in individuals with BAV demonstrates considerable variability, with reported diameter increments of 1-2 mm annually [16]. However, an important subset of patients experience accelerated aortopathy progression, marked by an annual diameter increase of up to 5 mm, heightening the risk of aortic dissection [16,17]. Surgical intervention concerning the ascending aorta becomes necessary under these conditions, particularly when the aortic root or ascending aorta reaches a diameter exceeding 45 mm, especially in cases concurrently requiring surgical aortic valve replacement [18]. Addressing both stenosis and regurgitation holds the potential to mitigate aortopathy progression [19].

A retrospective single-center study centered around patients with native BAV sought to unravel associations between aortic morphology and cardiovascular function [20]. Analyzing a 3D- cardiovascular MRI dataset, the study encompassed subgroups with repaired coarctation, unrepaired coarctation, and no coarctation. Notably, patients with coarctation displayed distinctive aortic architectures and dimensions, with those in the unrepaired coarctation subgroup exhibiting ascending aorta dilation. Morphological features were linked to reduced ejection fraction, elevated end-diastolic volume, and increased ventricular mass among patients with repaired coarctation.

Individuals with BAV demonstrate an elevated propensity for aortic aneurysm formation, emphasizing the necessity for vigilant monitoring [21]. The correlation between BAV and aortic dilation underscores the critical importance of a precise assessment of aortic dimensions and morphology. Surgical intervention becomes imperative when aneurysmal expansion jeopardizes aorta integrity, necessitating preemptive measures to avert catastrophic rupture.

While the elevated risk remains subtle, BAV is associated with an increased susceptibility to infective endocarditis [22]. This

nuanced risk underscores the significance of rigorous infection prevention and swift management strategies. Surgical considerations extend to instances where infective endocarditis jeopardizes the compromised valve structure, necessitating repair or replacement.

Furthermore, research has illuminated a substantial link between LV diastolic function and arterial stiffness in BAV patients, highlighting the potential impact of altered aortic elasticity on cardiac mechanics [22-24]. Diastolic dysfunction, a recognized mortality risk factor, further underscores the multifaceted nature of BAV-related implications [25].

## The significance of regular follow-up in bicuspid aortic valve

Frequent follow-up holds a pivotal role in overseeing patients with BAV due to potential complications and the progressive nature of the condition [7,12,22]. Consistent follow-up holds immense importance in the management of BAV patients due to potential complications and the dynamic nature of the condition [7,12,22]. Regular medical evaluations, echocardiograms, and subsequent scans during follow-up enable the early detection of any alterations in valve structure, function, or aortic measurements [14,23-26]. This early identification of complications allows for timely intervention, thwarting the progression of conditions like aortic stenosis or aneurysms. Regular follow-up serves as an effective means of preventing severe issues like aortic dissection, which can arise due to untreated aortic enlargement. Complications associated with BAV tend to develop gradually over time [13]. BAV management is not a one-size-fits-all approach. Follow-up appointments provide an avenue for medical experts to tailor treatment plans based on each patient's individual condition, complications, and risk profile [1]. This personalized approach to monitoring aortic measurements and other relevant risk indicators permits timely surgical intervention when necessary, effectively reducing the risk of life-threatening events [27].

A recent study based on MRI findings indicated that after 10-year follow-up of patients with isolated BAV, indexed aortic diameters remained stable in patients with lower wall shear stress values in the later assessment, and the decrease in wall shear stress could potentially serve as an indicator of a favorable long-term prognosis [28].

Another study [29], spanning over a retrospective analysis of 227 ambulatory adults with BAV over 13±9 years, found that nearly 29% of the participants exhibited severe aortic valve dysfunction, underlining the significance of valvular issues in the BAV population. Concurrently, 12.3% of the cohort showcased ascending thoracic aorta dimensions exceeding 45 mm. Cardiovascular events proved to be a prevalent theme, as about 38.8% of patients encountered at least one cardiac outcome during the follow-up period. An intriguing aspect came to light in the incidence rate of these cardiac events, spanning 20 years of follow-up, which stood at 47±4%. This statistic highlighted the continual risk that individuals with BAV face over extended periods, emphasizing the importance of vigilant monitoring and appropriate interventions. The interventions themselves were a significant facet, with approximately 33% of patients undergoing aortic valve or thoracic aorta interventions. Despite these challenges, the study revealed encouraging survival rates, with a 94±2% survival rate noted 20 years post-diagnosis. The study's significance was rooted in its ability to identify two prominent predictors of cardiac events: baseline moderate-severe aortic valve dysfunction and aortic valve leaflet calcification.

Utilizing a range of imaging techniques is fundamental for diagnosing, monitoring, and managing BAV patients. Transthoracic echocardiography (TTE) serves as the initial choice for BAV diagnosis, valve function assessment, and aorta measurement, while CT and cardiovascular magnetic resonance (CMR) excel at accurately evaluating aortic segments beyond TTE's scope. CT offers superior spatial resolution for valve morphology and aorta size, including coronary arteries, while CMR's capabilities encompass aortic functional properties and blood flow patterns, potentially aided by innovative sequences like 4D-flow. Integrating these imaging modalities provides a comprehensive understanding of BAV's morphological and dynamic aspects, enabling risk stratification and informed therapy decisions for patients [30,31]. Echocardiographic follow-up is of utmost importance as it has been demonstrated that in BAV patients with normal LV ejection fraction, impaired LV global longitudinal strain (LVGLS), determined by a cut-off value of -13.6%, was associated with a higher risk of aortic valve intervention or all-cause mortality [32].

Another prospective cohort study [33] evaluated a novel technique to measure LVGLS using feature-tracking software on the magnitude dataset of 4D flow CMR. The study involved 59 adult patients with BAV, comparing this new approach with dynamic CT and speckle-tracking TTE. The results demonstrated strong correlations between LVGLS measurements obtained through CMR, CT, and TTE, indicating the feasibility and reliability of this novel method using 4D flow CMR for assessing myocardial deformation and function in BAV patients.

## Surgical options

The surgical management of BAV varies depending on the extent of valvular and aortic involvement. Individualized treatment plans are crucial to strike a balance between addressing valvular dysfunction and managing aortic complications [7]. Surgical interventions may include aortic valve repair or replacement, each tailored to the patient's condition [12]. Aortic valve repair aims to restore the function of the native valve, often beneficial for patients with early-stage valvular degeneration or regurgitation [1]. On the other hand, aortic valve replacement involves removing the diseased valve and replacing it with a mechanical or biological prosthetic valve [3]. The choice between repair and replacement is determined by factors such as patient age, health status, and preferences.

One notable surgical procedure for BAV is the Ross procedure, also known as the pulmonary autograft procedure [34]. This approach involves transferring the patient's pulmonary valve to the aortic position and replacing the pulmonary valve with a cadaveric human donor valve [35]. The Ross procedure offers unique advantages, particularly for younger patients. These advantages include reduced thrombogenicity, potential for growth with the patient, excellent hemodynamic performance, and a lower risk of valve degeneration over time [36].

Multimodality imaging plays a pivotal role in the diagnosis, follow-up, and surgical management of BAV patients [14]. While TTE serves as a first-line imaging tool for BAV diagnosis and initial assessment, CT and CMR offer superior spatial resolution for evaluating aortic segments and assessing aortic size and morphology [8,37]. Multimodality imaging techniques play a crucial role in diagnosis, follow-up, and treatment planning for BAV patients.

The surgical indications for BAV encompass a spectrum of complexities, including valvular dysfunction, aortic aneurysm, infective endocarditis risk, and symptomatic presentation [37]. Decisions regarding surgical interventions are evidence-based and guided by authoritative sources [14]. A study by Kang *et al*. highlighted the association between BAV phenotypes and patterns of valvular dys-

function and aortopathy, providing insights critical for surgical decision-making [14]. The DA VINCI pilot study focused on optimizing valve orientation in transcatheter aortic valve implantation (TAVI) for BAV patients, aiming to enhance procedural outcomes and long-term results [8].

The surgical management of BAV is a nuanced process that considers the balance between valvular dysfunction and aortic complications. The choice of intervention is guided by patient characteristics, anatomical considerations, and surgical risks. Advancements in imaging and research contribute to evidence-based surgical decision-making and improved patient outcomes.

## Post-surgical surveillance

The management of patients with BAV presents unique challenges, necessitating a comprehensive approach that extends beyond surgical interventions to encompass vigilant post-operative care.

Current literature offers valuable insights into various aspects of BAV management and treatment outcomes. However, when considering the specific role of imaging in post-surgical management, there is a lack of in-depth analysis. Instead, the emphasis remains largely on surgical techniques, procedural outcomes, and clinical characteristics.

A review by Hardikar and Marwick [36] underscores the importance of surgical intervention thresholds for BAV patients. This study delves into the significance of proper timing for surgery, emphasizing the role of imaging in the post-surgical phase.

Similarly, the BAVARD Multicenter Registry [37] centers around sizing considerations for TAVI in BAV patients. It acknowledges pre- and post-TAVI imaging data on the interaction between BAV anatomy and device selection.

Patients with infective endocarditis related to BAV exhibit a notably heightened susceptibility to perivalvular abscess formation. Swift diagnosis and timely surgical intervention in cases of BAV infective endocarditis are crucial to mitigate the development and expansion of perivalvular abscesses [4].

In BAV patients undergoing TAVI, the outcomes at both the 30-day and 1-year marks, encompassing mortality, stroke incidence, and new pacemaker insertions, closely resembled those of their counterparts who had tricuspid AV. Nevertheless, BAV recipients exhibited an elevated propensity for encountering challenges, including moderate/severe paravalvular peak [38], necessitating conversion to surgical intervention, and device malfunction. Notably, the adoption of novel-generation devices led to a marked reduction in adverse events.

## Conclusions

As we delve into the realm of BAV morphology, it becomes evident that a one-size-fits-all approach is inadequate. The varied types of BAV morphology, characterized by different cusp fusions, require nuanced considerations for optimal management. The BAV presents a unique set of challenges in clinical management, necessitating a nuanced approach to surgical indications. While many individuals with BAV remain asymptomatic, a subset faces an array of complications that warrant surgical intervention guided by robust clinical assessments. The integration of mechanistic insights, advanced imaging modalities, and clinical expertise forms the cornerstone of effective surgical management for BAV-related valvular dysfunction. Ultimately, understanding the association between BAV and aortopathy emphasizes the importance of a holistic approach to patient care, addressing not only the valvular abnormalities but also potential coexisting cardiovascular challenges.

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