

BICUSPID AORTIC VALVE: WHEN AN ANATOMICAL VARIANT BECOMES A SURGICAL PROBLEM¹Shupyk National Healthcare University of Ukraine (Kyiv, Ukraine)²Donetsk National Medical University (Kropyvnytskyi, Ukraine)³Irpin Central City Hospital (Irpin, Ukraine)

konyshevskaya63@gmail.com

Bicuspid aortic valve is a congenital heart defect that occurs in 0.5–1.3% of the population. Bicuspid aortic valve should be regarded as a complex valvulo-aortic phenotype encompassing a broad spectrum of morphological abnormalities, valvular dysfunction, and aortic pathology and may be associated with other congenital cardiovascular anomalies. Comprehensive assessment of all these characteristics has important prognostic implications. Particular attention should be paid to the identification of the partial-fusion (forme fruste) phenotype, which is often difficult to diagnose by routine echocardiography. A stepwise and comprehensive approach is essential for the echocardiographer. The initial evaluation should be based on the recently introduced international nomenclature and classification to ensure a comprehensive understanding of this condition and its natural history. Understanding the relationships among different bicuspid aortic valve phenotypes, the type of valvular dysfunction, aortic dimensions, and the pattern of aortopathy is important for individualized decision-making in patients with this congenital heart defect. The management strategy should be based not only on aortic dimensions but also on changes in these dimensions over time and associated factors, necessitating lifelong surveillance. Our clinical case highlights the importance of consistent multimodality follow-up after surgical intervention. Although bicuspid aortic valve is considered a relatively isolated congenital malformation, our hypothesis regarding the potential value of further investigating its association with features of connective tissue dysplasia, particularly the MASS phenotype, provides a rationale for patient screening aimed at the early detection of this condition.

Key words: bicuspid aortic valve, aortopathy, associated defects, echocardiographic screening, surgical treatment.

Connection of the publication with planned research works.

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Introduction.

Bicuspid aortic valve (BAV) has remained a subject of continuous scientific interest for more than five centuries. The earliest known description of this anatomical variation is associated with the studies of Leonardo da Vinci. Since then, the understanding of BAV has evolved from that of an isolated anatomical feature to that of a complex congenital phenotype [1].

Despite the substantial body of accumulated evidence, questions regarding its natural history, the mechanisms underlying the development of associated lesions, and the identification of patients who require particular attention during early initial diagnosis remain a matter of debate.

The current understanding extends beyond the concept of an isolated congenital anomaly of the aortic valve. Its development is thought to involve a complex interplay of genetic, molecular, and embryogenetic mechanisms, while its phenotypic variability is attributed to the multifactorial nature of the pathological process. Particular attention has been focused on the role of structural and functional alterations in the connective tissue matrix, which are relevant to both the development of the valvular apparatus and remodeling of the aortic wall. Of particular interest is the concept of BAV not merely as a localized aortic valve anomaly but as a potentially broader phenotype involving abnormalities in the development and remodeling of connective tissue structures. Mutations in the *FBN1* gene, which are associated with Marfan

syndrome, have also been described in patients with the MASS phenotype of connective tissue dysplasia and have been implicated in the development of BAV [2, 3].

In this context, the phenotypic features of MASS (M – myopia, A – aortic root dilatation, S – skin manifestations, including striae and increased skin extensibility, and S – skeletal features, such as chest wall deformities, scoliosis, or joint hypermobility) may be considered potential clinical indicators for the targeted evaluation for this aortic anomaly. This approach represents a clinical hypothesis and requires further confirmation. Timely recognition of phenotypic markers, combined with medical history, clinical examination, and cardiovascular imaging findings, may facilitate the early diagnosis of BAV and its associated lesions [3].

The aim of the study.

To analyze the current state of the BAV problem, identify algorithms for its timely and differential diagnosis, and provide a rationale for an individualized approach to treatment.

Object and research methods.

Data on BAV published over the past 10 years and available in the public domain on the official websites of peer-reviewed medical journals were analyzed. The authors' own clinical case is also presented.

Main part.

Definition. BAV is a common congenital cardiac malformation, with a prevalence in the general population ranging from 0.5% to 1.3% [4, 5]. BAV accounts for a substantial proportion of aortic valve replacements performed over a patient's lifetime and is associated with the early development of calcific heart disease in adults [6]. Early valvular degeneration in BAV has been well documented, with rapidly progressive fibrosis occurring

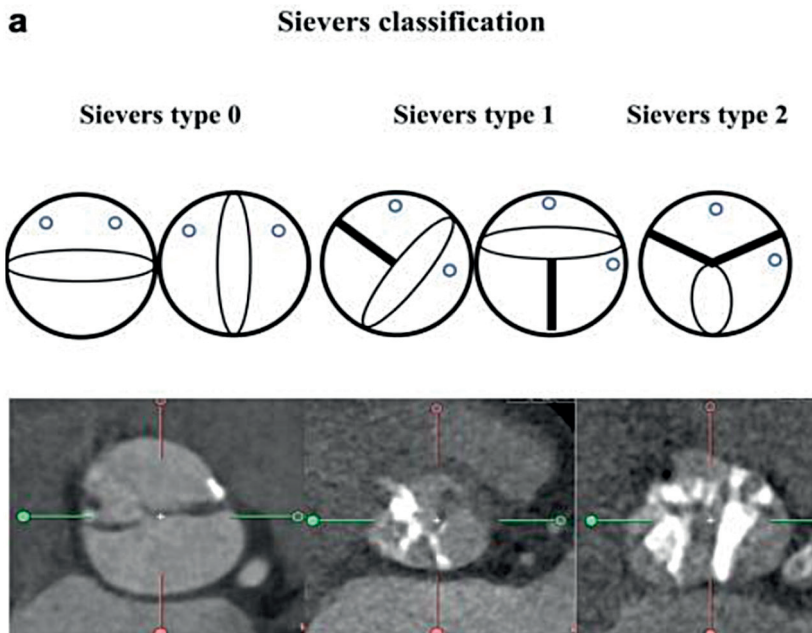


Figure 1 – Classification system for BAV: schematic representations (upper panel) and computed tomography images (lower panel) of each Sievers classification type [9].

during the second decade of life and leading to irreversible calcification by the fourth decade [7]. Valvulo-aortopathy associated with BAV develops almost inevitably by the age of 90 years. BAV-related valvulo-aortic pathology is characterized by considerable heterogeneity in anatomical phenotypes, associated structural abnormalities, and clinical course, resulting in variability in long-term prognosis [5].

History. BAV was first described by Leonardo da Vinci in 1500, when he sketched the geometry of the valve leaflets while investigating blood flow through the heart [1, 6]. During the 19th century, the understanding of BAV gradually expanded: in 1844, J. Paget described it as a rare anomaly; in 1866, T. Peacock noted its propensity to develop calcific stenosis; and in 1886, W. Osler was the first to demonstrate its association with infective endocarditis [8]. Despite more than a century of clinical and

scientific investigation, BAV remains one of the most common congenital cardiac anomalies and continues to be a subject of sustained interest among clinicians and researchers.

Classification. For many years, the Sievers–Schmidtke classification, which is based primarily on the number of raphe, has remained the most widely used system for the morphological characterization of BAV (fig. 1).

However, in 2021, an international consensus proposed a more comprehensive approach to BAV classification that takes into account valve morphological type and phenotype, the presence and characteristics of raphe, leaflet symmetry and morphology, valve functional status, as well as the presence of associated aortopathy and aortic coarctation [9, 10]. In the new international classification, Michelena H. I. et al. (2021) proposed three BAV types with their

respective subphenotypes. The most common is the fused BAV type, characterized by 3 aortic sinuses, 2 leaflets, 2 commissures, and 1 raphe (raphe fusion) [10]. Leaflet symmetry was assessed separately and determined according to the commissural angle: at an angle of 160–180°, the leaflets were considered symmetrical, whereas at an angle of less than 160°, they were considered asymmetrical [11] (fig. 2).

In this classification, the partially fused BAV phenotype was formally introduced as partial-fusion (forme fruste) BAV. This form is difficult to identify by transthoracic echocardiography (TTE), because partial leaflet fusion gives the aortic valve a morphology resembling that of a tricuspid aortic valve. This is particularly challenging to differentiate during routine imaging in the presence of a mini-raphe.

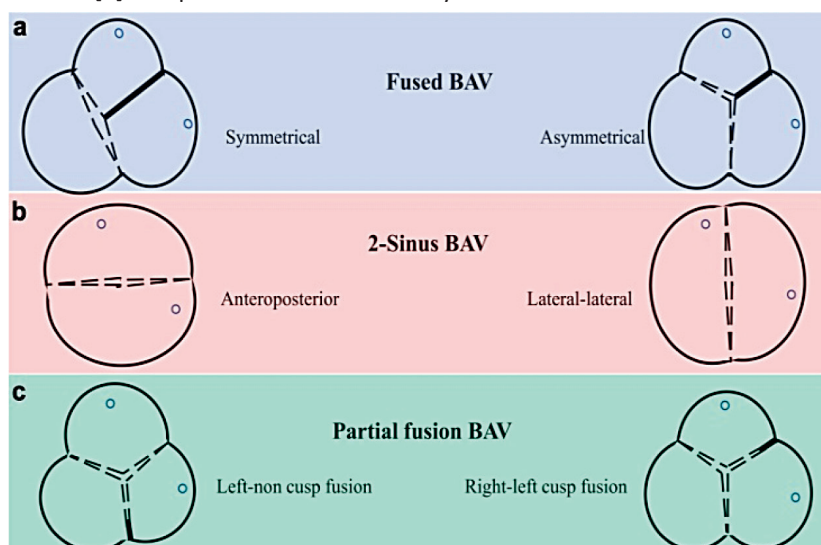


Figure 2 – New international consensus classification of bicuspid aortic valve: (a) fused BAV type with a symmetrical phenotype characterized by a wide angle of the nonfused noncoronary leaflet, or an asymmetrical phenotype with a commissural angle of <160°; (b) 2-sinus BAV type with its 2 phenotypes: anteroposterior and laterolateral; (c) partial-fusion BAV type, in which 2 leaflets are fused along <50% of the commissural length [10–12].

Computed tomography and magnetic resonance imaging (CT/MRI) facilitate the identification of this specific phenotype, which has attracted increasing attention from cardiac surgeons in recent years [13, 14]. The identification of this BAV phenotype predominantly during TAVR procedures suggests that its prevalence and potential contribution to the development of aortic complications may have been underestimated. Further prospective multicenter studies are required to clarify its clinical and prognostic significance [15, 16].

Pathogenesis. **Genetic Predisposition.** BAV has a strong hereditary component; however, its genetic basis is heterogeneous. Current genetic studies support the concept of an inherited predisposition to BAV development. There is no single universal gene responsible for the development of this defect. Instead,

BAV may result from the interplay of rare pathogenic variants, common genetic variants, and other factors affecting the development of the valve and aorta [17]. NOTCH1 remains the most extensively studied gene and plays an important role in the embryonic development of the aortic valve and the formation of valvular structures. Rare NOTCH1 variants have been identified in familial forms of BAV; however, their pathogenic role has not been confirmed for all reported variants. In addition to impaired valvular morphogenesis, NOTCH1 dysregulation may be associated with aortic valve calcification [18]. Genes involved in the regulation of cardiogenesis and valve development also play an important role. Genes associated with BAV include GATA4, GATA5, GATA6, NKX2-5, and TBX20. These genes are involved in the regulation of early cardiac development, cell differentiation, and aortic valve formation. Variants in GATA5 and GATA6 have been reported in association with familial cases of BAV; however, the strength of evidence for individual genes and variants remains variable [17]. A separate group comprises genes associated with aortopathy. Genetic predisposition in BAV may involve not only valve development but also the structure of the aortic wall. In particular, SMAD6, ROBO4, and genes involved in the TGF- β signaling pathway have been investigated in relation to BAV phenotypes and aortopathy. These findings support the current concept of BAV as a disorder that may involve concomitant abnormalities of both the valve and the aorta [19]. Genetic determinants are not limited to the presence of BAV itself. Particularly interesting findings were reported in a 2022 family study: the morphological BAV phenotype did not show a simple pattern of concordance among first-degree relatives, suggesting a more complex genetic basis underlying different patterns of valve morphology [20]. Causal mutations in the *FBN1* gene, which encodes fibrillin-1 and typically cause Marfan syndrome and are frequently associated with the MASS phenotype, may also be considered in the context of syndromic aortopathy and overlapping BAV/Marfan syndrome phenotypes. Thus, genetic factors may influence not only the development of BAV itself but potentially also its phenotypic variability [21, 22]. At the same time, the precise pathogenic and prognostic significance of most identified genetic variants remains insufficiently defined.

Epidemiology. BAV is one of the most common congenital cardiac anomalies; however, its actual prevalence varies depending on the age of the population studied, the imaging modality used, and the study design. Most epidemiological studies report a BAV prevalence ranging from 0.5% to 1.3% [5, 6, 10]. According to a population-based study of 25,556 newborns, the prevalence of BAV was 0.77%, with a male-to-female ratio of 2.1:1. In the same cohort, aortopathy was diagnosed in 33.2% of children with BAV [5, 23]. Given its clinical and morphological heterogeneity, the distribution of BAV according to the Sievers classification among newborns was as follows: type 1, 90.8%; type 0, 8.7%; and type 2, 0.5%. Thus, BAV should be regarded not as a single anatomical anomaly but as a spectrum of phenotypes associated with different risks of valvular dysfunction and aortopathy [23]. The current international consensus classification recognizes three major morphological types of BAV: fused, two-sinus, and partial-fusion (*forme fruste*) [10]. In a contemporary clinical cohort of 302 patients classified

according to this system, the fused phenotype accounted for 81.1%, the two-sinus phenotype for 13.6%, and the partial-fusion (*forme fruste*) phenotype for 5.3%. Aortopathy was identified in 33.6% of patients and was most frequently associated with the fused phenotype [24]. Overall, our current understanding of the prevalence of BAV in the general population may underestimate its true prevalence because many patients with BAV are asymptomatic [10].

Clinical Presentation. Diagnostic Criteria. Differential Diagnosis. The clinical course of BAV ranges from a prolonged asymptomatic period, with the condition often detected incidentally, to the development of serious complications, including valvular dysfunction, aortopathy, infective endocarditis, or acute aortic syndromes [10, 25]. BAV may be diagnosed at any stage of life, from the neonatal period to older age, and under highly heterogeneous clinical circumstances [26]. The current approach defines BAV as a heterogeneous disorder in which the clinical presentation depends not only on the morphological characteristics of the valve but also on its functional status and associated aortic abnormalities. Over time, BAV pathology may progress, resulting in stenosis or regurgitation. In aortic stenosis (AS), narrowing of the valve orifice occurs predominantly due to calcification, leading to left ventricular (LV) pressure overload and hypertrophy. Aortic regurgitation is usually associated with anatomical abnormalities of the leaflets or dilatation of the aortic root. Therefore, when evaluating patients with BAV, simply confirming the diagnosis is insufficient; the functional status of the valve and the severity of hemodynamic impairment must also be assessed [25]. A key aspect of BAV diagnosis is the shift from viewing this condition as an isolated anatomical defect toward a comprehensive assessment of its phenotypic variability. Accordingly, confirmation of the defect should be accompanied by detailed BAV phenotyping, thorough assessment of the thoracic aorta, and active screening for associated congenital anomalies. This approach is of fundamental clinical importance because valve morphology may be associated with the pattern of valvular dysfunction and the characteristics of aortic remodeling [10, 27]. The clinical significance of the morphological BAV phenotype may differ according to patient sex. In a large study, Kong WKF et al. (2021) demonstrated significant sex-related differences in the clinical associations of BAV phenotypes, which should be taken into account in future studies investigating the role of these phenotypes in individualized patient management [27]. In a large two-center surgical cohort of 1,045 patients, the most common phenotype was right-left coronary cusp fusion (RL), accounting for 73.6% of cases, followed by right-noncoronary cusp fusion (RN) at 16.2%, the two-sinus (2-sinus) phenotype at 9.2%, and left-noncoronary cusp fusion (LN) at 1.1%. No clear association was identified between a specific BAV phenotype and AS; however, the pattern of aortic regurgitation (AR) differed according to phenotype. In men, AR was most frequently observed in the RL and LN phenotypes, whereas in women, it was most frequently observed in the RN phenotype. In men, the RL phenotype was also associated with larger aortic root dimensions, while the 2-sinus BAV phenotype was associated with a higher prevalence of aortic root dilatation. In contrast, the 2-sinus BAV phenotype was not associated with aortic

root dilatation in women. The authors also demonstrated that patients with AR had larger aortic root dimensions than those with AS, with this difference being particularly pronounced in women. Thus, the morphological BAV phenotype may be associated with the pattern of valvular dysfunction and the aortopathy phenotype; however, these relationships are sex-dependent and cannot be automatically extrapolated to all patients with BAV [27]. These findings are partially complemented by the study by Choi BH et al. (2021), in which 312 patients underwent transthoracic echocardiography (TTE) and cardiac CT. The authors found no independent association between cusp orientation or the presence of a raphe and dilatation of the aortic root or ascending aorta. Instead, age, sex, and AS severity were significant predictors of aortic dilatation. The most common pattern in this cohort was combined dilatation of the aortic root and the mid-ascending aorta, observed in 62.5% of patients [28]. Thus, current evidence does not support considering valve morphology as an independent and universal predictor of aortopathy; rather, its clinical significance should be interpreted in conjunction with age, sex, and the functional status of the valve.

BAV may also coexist with other congenital cardiovascular anomalies. In the study by Szöcs K et al. (2022), which included 200 patients with so-called isolated BAV, aortic coarctation was identified in 4.2% of patients, coronary artery anomalies in 3.6%, and mitral valve prolapse (MVP) in 1.5% [29]. The correlation between the morphological characteristics of BAV and the rate of disease progression remains a critically important issue. The findings reported by Shen M et al. (2020) demonstrate that the cusp fusion pattern is not the sole determinant of the rate of aortic stenosis progression. These data emphasize that valve morphology represents only one aspect of the overall clinical phenotype; therefore, the diagnostic approach should be comprehensive and should take into account the patient's age, baseline degree of calcification, and severity of the lesion [30]. At the same time, the phenotype is relevant not only to the natural history of the disease but also to cardiac surgical and transcatheter interventions. In an international registry of 1,034 patients with CT-confirmed BAV who underwent TAVR, the combination of a calcified raphe and extensive leaflet calcification was associated with an increased risk of aortic injury, moderate-to-severe paravalvular regurgitation, and higher 2-year mortality. Among patients with both morphological features, 2-year mortality was 25.7%, compared with 9.5% in those with one of these features and 5.9% in those with neither feature [31].

Particular attention should be paid to the partial-fusion (*forme fruste*) phenotype, which is often difficult to diagnose by routine TTE because of its atypical morphology. The inclusion of this variant in the international consensus classification reflects the evolving understanding of this condition: it has become evident that a substantial proportion of patients with limited leaflet fusion were previously misclassified as having a tricuspid aortic valve. An analysis of patients who had not undergone surgical intervention demonstrated that the *forme fruste* phenotype was a predictor of the most pronounced thoracic aortic dilatation over the mean follow-up period [10, 24].

Infective endocarditis represents another critical condition associated with BAV. According to a meta-analysis of eight cohort studies ($n=5,351$), the incidence of this

complication was 48.13 per 10,000 patient-years, which was 12-fold higher than that in the general population. Therefore, any clinical manifestation suggestive of an infectious process, including fever, systemic infection, or embolic events, or the development of a new cardiac murmur in these patients warrants prompt evaluation to exclude infective endocarditis [32].

In some patients with BAV-associated aortic dilatation, phenotypic manifestations of inherited connective tissue disorders may also be present. Clinical and genetic overlap between Marfan syndrome and BAV has been reported [33], suggesting that early identification of underlying syndromic connective tissue disorders associated with aortic ectasia in patients with BAV may help guide these patients toward different decision-making algorithms for aortic surgery [33]. Recognition of such features is critically important because it determines the subsequent surveillance strategy, the extent of diagnostic evaluation, and the need for referral to specialized centers. In particular, Pepe G et al. (2021) developed a specific scoring system to assess the likelihood of Marfan syndrome in patients with BAV. The score is based on simple clinical and TTE criteria readily assessable by general practitioners and cardiologists: myopia (≥ 3 D), pectus carinatum, pes planus, positive wrist/thumb signs, MVP, and aortic root dilatation relative to the ascending aorta (≥ 4 mm). Each feature is assigned 1 point. The presence of three or more of these markers was found to increase the likelihood of Marfan syndrome [34]. Thus, BAV morphology and phenotypes may be associated with the type of valvular dysfunction, the pattern of aortopathy, hemodynamic abnormalities, and characteristics of the subsequent clinical course and treatment; however, these associations are not universal and may depend on age, sex, and concomitant functional valve impairment [10, 24, 25–34].

Diagnosis. The diagnostic approach to BAV is based on imaging of the anatomical structure of the valve, assessment of its functional status, and evaluation of ascending aortic dimensions. Transthoracic echocardiography (TTE) is the primary and preferred diagnostic modality, providing a comprehensive assessment that includes determination of valve morphotype and phenotype, evaluation of the severity of AS or regurgitation, measurement of aortic diameter, and screening for associated congenital abnormalities, including coarctation. The key echocardiographic features of BAV are the presence of 2 leaflets and 2 commissures instead of 3. During systole, the valve orifice assumes a characteristic elliptical configuration ("fish-mouth" or "handball" appearance), whereas during diastole, the leaflets can be directly counted. Particular attention during diagnostic evaluation is also given to identification of the raphe, which is a key determinant in the classification of the morphological BAV phenotype according to the current classification system [10, 35, 36]. TTE can accurately diagnose BAV in 80–90% of cases, with estimated sensitivity, specificity, and accuracy of 77%, 97%, and 99%, respectively, with the best diagnostic performance observed in patients without stenosis. Kim J et al. (2023) demonstrated that the sensitivity of TTE decreased with increasing aortic valve calcification and was 75%, compared with 97% for cardiac CT [37].

Even in patients with AS, TTE can identify aortic valve morphology in up to 80% of patients, with a sensitivity

and specificity of 77% and 61%, respectively; these values increase to 94% and 100%, respectively, when ECG-gated contrast-enhanced cardiac CT is used [38]. Thus, the echocardiographer should address six major clinical objectives: 1) confirmation of the diagnosis of BAV; 2) determination of the morphological valve phenotype; 3) assessment of valve functional status; 4) measurement of thoracic aortic dimensions to identify associated aortopathy, including dilatation; 5) differential diagnosis of aortic coarctation and associated congenital abnormalities; and 6) surveillance for rare but critical complications, such as infective endocarditis and aortic dissection [10, 35, 39–41]. It is important to recognize that TTE diagnosis of BAV is not always unequivocal. Diagnostic errors may occur in the presence of extensive leaflet calcification, severe valve deformation, a poor acoustic window, eccentric valve orientation, or minimal leaflet fusion. Particular diagnostic difficulties may arise with the partial-fusion (forme fruste) phenotype, in which the extent of leaflet fusion is minimal and the valve may more closely resemble a tricuspid aortic valve [39–41]. According to the current consensus, when valve morphology cannot be reliably determined by TTE, transesophageal echocardiography (TEE), ECG-gated CT, or cardiac MRI should be considered [42]. TEE also provides excellent diagnostic accuracy for aortic dissection [43, 44] and is mandatory in the evaluation of infective endocarditis [45], regardless of whether the native or prosthetic valve is involved. At the same time, as a semi-invasive modality, TEE does not always provide complete visualization of the mid and distal portions of the ascending aorta.

Cardiac CT and CT angiography (CTA) provide high spatial resolution and allow detailed assessment of the number of leaflets, the presence of a raphe, the degree of calcification, and the geometry of the aortic root and ascending aorta. Of particular importance is the ability to perform multiplanar reconstructions, enabling highly

precise measurement of the aortic diameter perpendicular to its longitudinal axis. The diagnostic value of CT for the preoperative identification of BAV is important for determining the treatment strategy and is of particular interest to clinicians involved in the management of AS. In a study of 212 patients with severe AS, agreement between CT-based diagnosis of BAV and surgical verification was high ($\kappa=0.90$) for the identification of BAV and good ($\kappa=0.69$) for the determination of the BAV phenotype. CT can also identify the shape of the valve orifice and the leaflet balance angle during systole, as well as the number of ridges during diastole, which substantially contributes to the diagnostic accuracy of BAV [46].

Recently, Sylivris A, Liu ZF, Theuerle J, and Lim RP (2025) conducted a systematic review and meta-analysis in which ECG-gated CT was proposed as a second-line diagnostic modality for BAV after inconclusive TTE. The 16 studies included in the meta-analysis demonstrated a sensitivity of 95.5% for CT compared with 79.9% for TTE. Specificity was high for both modalities and did not differ significantly between CT and TTE [47].

Cardiac magnetic resonance imaging (MRI) is an effective alternative, particularly for patients who require serial follow-up of the aorta without exposure to ionizing radiation. This modality provides a comprehensive assessment of valve morphology, ventricular systolic function, thoracic aortic dimensions, and hemodynamic characteristics. According to current clinical guidelines, MRI or CT is preferred when TTE does not provide complete diagnostic information. In particular, international experts recommend supplementing TTE with CT or MRI when aortic dilatation (≥ 45 mm) is detected, coarctation is suspected, or certain segments of the aorta are not adequately visualized [10, 48, 49].

Thus, the diagnosis of BAV cannot be limited to a description of its anatomical structure alone. To establish a comprehensive clinical profile of the patient, it is

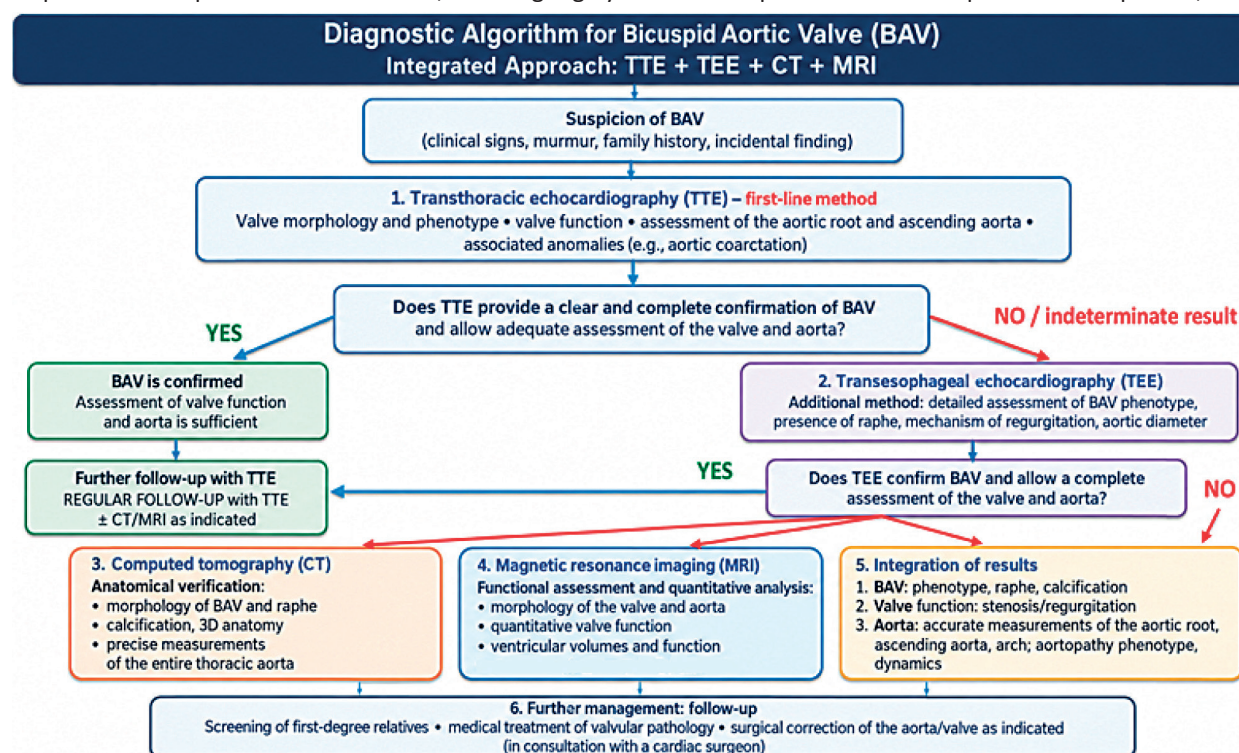


Figure 3 – Diagnostic algorithm for BAV (TTE, TEE, CT, MRI) [10, 36–41, 48].

necessary to determine the BAV phenotype, identify the presence of a raphe or leaflet fusion, assess valve function and the severity of aortic stenosis/regurgitation, measure aortic dimensions (aortic root, ascending aorta, and aortic arch), exclude associated congenital abnormalities, including coarctation, and assess overall structural changes in the cardiovascular system. This comprehensive approach allows the diagnostic process to move beyond the identification of an anatomical variant toward characterization of the individual valvulo-aortic phenotype, which is critically important for prognostic assessment and selection of an appropriate treatment strategy [10, 36–41, 48]. Based on the above, we propose an algorithm for an integrated multimodality approach to the diagnosis of BAV and subsequent follow-up of these patients (fig. 3).

Treatment. The presence of BAV alone does not require specific pharmacological treatment. Management is determined by valve functional status, the severity of AS or regurgitation, LV status, and the presence and progression of aortopathy. Pharmacological therapy cannot correct the morphological defect of BAV or replace timely valvular or aortic intervention. In patients with BAV who have no indications for interventional treatment, management is based on regular clinical and TTE follow-up, with monitoring of blood pressure and cardiovascular risk factors [10, 50]. This aspect is particularly relevant in the presence of aortic dilatation, as adequate control of hemodynamic parameters is an integral component of the management protocol for patients with aortic disease [50].

In patients with concomitant cardiovascular disease, particularly heart failure or arterial hypertension, pharmacotherapy should be administered in accordance with current clinical guidelines [50]. It should be emphasized, however, that pharmacological treatment should not serve as a reason to delay surgical intervention in patients with severe AS, aortic regurgitation (AR), or clinically significant aortopathy [51].

The most common complication of BAV, occurring in nearly 50% of patients, is the development of AS. Surgical aortic valve replacement (SAVR) remains the gold standard for the surgical treatment of aortic valve disease. At the same time, in patients with BAV and AR, which occurs considerably less frequently than AS (30% vs. 70%), aortic valve repair should be considered in the absence of extensive calcification. The success of reconstructive surgery directly depends on the anatomical characteristics of the valvular apparatus, including leaflet morphology and the condition of the commissures and aortic root, as well as on the expertise of the surgical team [10, 52, 53]. In appropriately selected patients with concomitant aortic root pathology and a valve suitable for reconstruction, valve-sparing aortic root surgery may be performed [52].

TAVI in Bicuspid Aortic Valve. Because of the complex annular geometry, uneven calcification, leaflet asymmetry, and the risk of concomitant aortopathy, BAV has long been considered an unfavorable anatomical setting for transcatheter aortic valve implantation (TAVI). However, the current ESC/EACTS guidelines (2025) no longer consider BAV an absolute contraindication to TAVI. The choice of intervention should be determined by a multidisciplinary Heart Team based on an individualized assessment of anatomical characteristics. In particular, in patients with stenosis or severe regurgitation, TAVI

is recommended for those at high surgical risk, provided that the anatomy is favorable. At the same time, the presence of aortopathy often becomes a decisive factor in favor of open surgery, allowing concomitant repair of the ascending aorta or aortic root [50]. Aortopathy is a fundamentally important component of BAV. The international consensus recommends considering BAV and its associated aortopathy as a single clinical entity requiring standardized phenotyping and lifelong surveillance [10]. Aortic diameters and the identification of risk factors for dissection are of major importance. An aortic root or ascending aortic diameter of ≥ 5.5 cm is an indication for surgical replacement of the affected aortic segment. An aortic diameter of 5.5 cm warrants referral to a cardiac surgeon. In patients with BAV and an aortic root or ascending aortic diameter of 5.0–5.4 cm, surgical intervention is considered reasonable in the presence of additional risk factors for dissection [54]. These criteria include a family history of aortic dissection, progressive aortic dilatation, the presence of coarctation, or a specific “root phenotype” of aortopathy [54]. Therefore, a diameter of 52 mm cannot be considered a sufficient standalone criterion for clinical decision-making. The critical threshold is a diameter of ≥ 45 mm. According to the ACC/AHA guidelines (2020, 2022), if a patient with BAV has an indication for aortic valve replacement and the diameter of the aortic root or ascending aorta is ≥ 45 mm, concomitant replacement of the affected aortic segment should be considered at a specialized cardiac surgical center. There is evidence that the so-called root phenotype may represent a more severe form of aortopathy, as recently reviewed [55]. The root phenotype has been found to be associated with acute aortic events after isolated aortic valve replacement, as well as with genetic variants potentially associated with aortopathy [22, 56]. Accordingly, the root phenotype has recently been included among the additional risk factors that should be considered when determining the indication for early elective surgery for BAV-associated aortopathy [57, 58]. For the echocardiographer, this represents a key marker: identification of these parameters is a direct indication for consultation with a cardiac surgeon regarding the need for a more extensive surgical procedure [53, 54]. However, assessment based exclusively on absolute aortic diameter values is insufficient for comprehensive clinical evaluation. The rate of aortic growth is a critically important parameter that requires careful monitoring. Therefore, in patients with BAV-associated aortic dilatation, several parameters should be considered together, including comparison of previous and current measurements, the time interval between examinations, and the calculated rate of progression. According to the ACC/AHA guidelines, an aortic root or ascending aortic growth rate of ≥ 0.3 cm/year is classified as rapid and warrants reconsideration of the management strategy in favor of more intensive surveillance or surgical intervention [48, 52, 54]. For a more accurate assessment of aortic dimensions in patients who are significantly shorter or taller than average, the ACC/AHA recommends, in certain circumstances, indexing aortic dimensions to body surface area or height. In patients with BAV, one criterion for which surgical treatment is considered reasonable at an experienced cardiac surgical center is a cross-sectional aortic area-to-height ratio of ≥ 10 cm²/m [54]. Based on this framework, we developed an algorithm in which the

TTE protocol is transformed from a simple descriptive report into an effective tool for optimizing patient referral pathways. The use of standardized approaches to aortic measurement and a consistent measurement methodology is fully aligned with current clinical guidelines for the management of aortic disease (fig. 4).

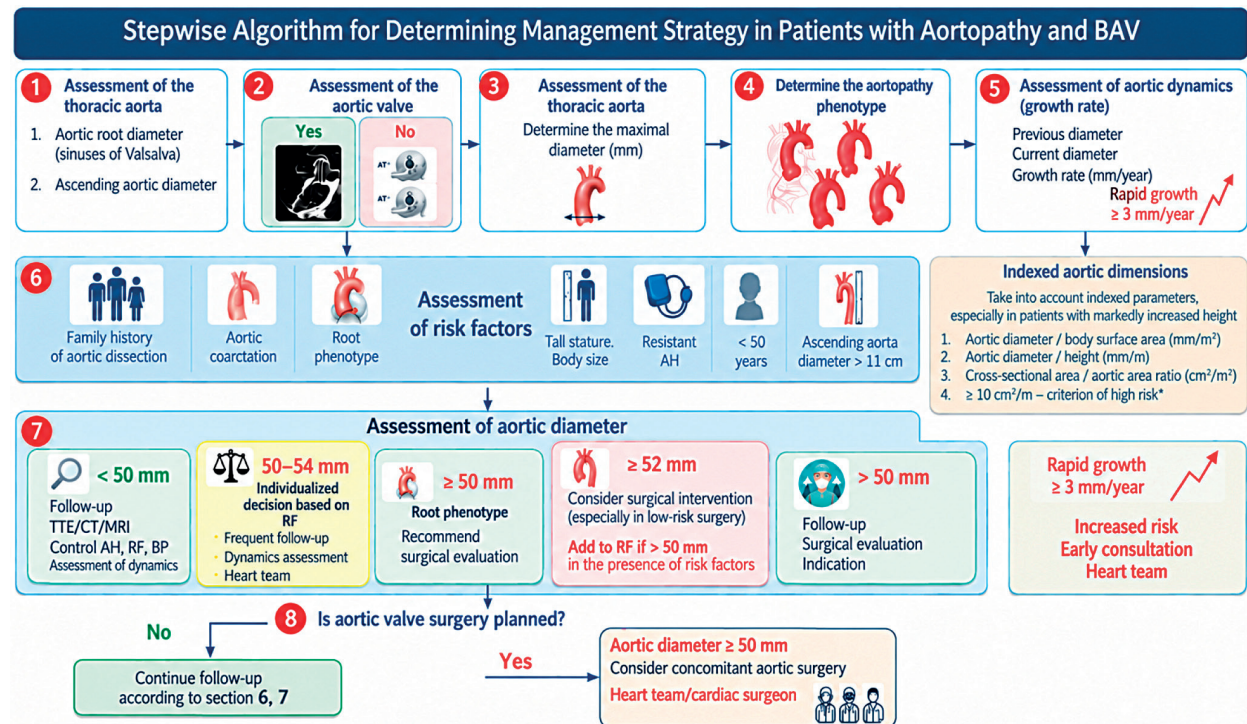
We present our own clinical case. Patient D., a 68-year-old woman born in 1956, presented on April 26, 2024, for scheduled TTE at the Central District Hospital in Bucha, with complaints of weakness, exertional dyspnea, and chest discomfort. These symptoms had been present since April 2024. She had been under the care of her family physician for hypertension. Following TTE, she was referred and admitted to the Amosov National Institute of Cardiovascular Surgery of the National Academy of Medical Sciences of Ukraine for further evaluation and determination of the subsequent treatment strategy.

Diagnosis: Severe paravalvular aortic regurgitation. Status post aortic valve replacement with a No. 19 On-X mechanical prosthetic valve on March 12, 2024, performed with cardiopulmonary bypass for congenital heart disease: bicuspid aortic valve with severe combined aortic valve disease, predominantly stenotic, Ca 3+. Moderate mitral and tricuspid regurgitation. Paroxysmal atrial fibrillation, tachysystolic form; CHA₂DS₂-VA score, 4; EHRA class 3. Pharmacological cardioversion performed on March 14, 2024, with restoration of sinus rhythm. Pulmonary hypertension, stage II, group 2, functional class II. Heart failure, stage IIA, with preserved LV ejection fraction (57%). Hypertension, stage II, grade 3, risk 4. Nonstenotic atherosclerosis of the brachiocephalic arteries. Stenotic atherosclerosis of the lower-extremity arteries.

History of Present Illness. The patient reported a long-standing history of illness. Arterial hypertension had been present since 2011, when an increase in blood pressure to a maximum of 175/105 mmHg was first documented. Beginning in 2022, she noted a deterioration in her condition, with the onset of exertional dyspnea. She periodically received outpatient treatment at her place of residence. In February 2024, critical AS was detected during a routine examination, and she was referred to the M.M. Amosov National Institute of Cardiovascular Surgery. On February 28, 2024, she was evaluated at the Institute and diagnosed with aortic valve stenosis: severe AS, Ca 3+; minimal mitral regurgitation; mild tricuspid regurgitation; heart failure, stage IIA, with preserved LV ejection fraction of 69%, functional class II; and hypertension, stage I, grade 3, risk 4.

The patient was hospitalized at the Amosov National Institute of Cardiovascular Surgery from March 11 to March 21, 2024. On March 11, 2024, coronary angiography was performed and demonstrated an intramyocardial course of the mid left anterior descending artery (LAD) without systolic obstruction. A left-dominant coronary circulation was identified, with 30% stenosis of the distal third of the anterior interventricular branch (AIV).

On March 11, 2024, ultrasound examination of the lower extremities was performed in accordance with current recommendations. Stenotic atherosclerosis of the lower-extremity arteries was identified. On the right, stenosis of the common femoral artery (CFA) of up to 20%, popliteal artery (PA) of up to 20%, and anterior tibial artery (ATA) of up to 45% was detected. On the left, stenosis of the CFA of up to 15%, anterior femoral artery (AFA) of up to 20%, PA of up to 20%, and ATA of up to 40% was



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Figure 4 – Stepwise algorithm for determining the management strategy for BAV-associated aortopathy.

Notes: Root phenotype – aortic root phenotype; Ascending phenotype – ascending aortic phenotype; AH – arterial hypertension; RF – risk factors; BP – blood pressure [10, 51, 54].

detected. Duplex ultrasonography of the major vessels of the neck was performed and demonstrated nonstenotic atherosclerosis of the brachiocephalic arteries. A small diameter of the right vertebral artery (VA) with blood flow asymmetry ($S > D$) was noted. The following stenoses were identified: 20% stenosis of the right common carotid artery (CCA) bifurcation, 20% stenosis at the origin of the right internal carotid artery (ICA), and 20% stenosis of the left CCA bifurcation according to the European Carotid Surgery Trial (ECST) method for grading the degree of vascular stenosis [59].

On March 12, 2024, aortic valve replacement was performed with implantation of a No. 19 On-X mechanical prosthetic valve under cardiopulmonary bypass. Intraoperative transesophageal echocardiography revealed a Sievers type 0 bicuspid aortic valve with severe leaflet calcification and extension of calcific changes to the mitral–aortic junction. The aortic annular diameter was 20 mm. Follow-up control transesophageal echocardiography after completion of the surgical procedure demonstrated satisfactory prosthetic valve function, with no evidence of paravalvular regurgitation.

In the early postoperative period, on March 14, 2024, the patient developed an episode of atrial fibrillation with a tachysystolic ventricular response. Pharmacological cardioversion was performed, resulting in restoration of sinus rhythm. Because of the presence of a mechanical aortic valve prosthesis, anticoagulant therapy with warfarin was initiated.

In June 2024, a new complication following valve replacement, paravalvular AR, was identified during follow-up examination. TEE performed on June 27, 2024, demonstrated an abnormal regurgitant jet in the region of the mitral–aortic junction, with a paravalvular defect measuring approximately 5.5 mm. Moderate mitral and tricuspid regurgitation was additionally identified.

To further characterize the anatomy of the paravalvular defect, CTA was performed on August 27, 2024. A paravalvular fistula measuring approximately 6 mm was identified in the region of the left coronary sinus. The ascending aorta measured 35×38 mm. No evidence of significant stenotic coronary artery disease was identified on the examination.

In September 2024, the patient was referred again and evaluated at the Amosov National Institute of Cardiovascular Surgery. The following diagnosis was established: severe paravalvular AR. Status post aortic valve replacement with a No. 19 On-X mechanical prosthetic valve on March 12, 2024, performed under cardiopulmonary bypass. Moderate mitral and tricuspid regurgitation. Paroxysmal atrial fibrillation with a tachysystolic ventricular response; CHA₂DS₂-VASC score, 4; HAS-BLED score, 3; pharmacological cardioversion performed on March 14, 2024. Pulmonary hypertension, stage II, group 2, functional class II. Heart failure, stage IIA, with preserved LV ejection fraction (59%), functional class II. Hypertension, stage II, grade 3, risk 4.

Holter ECG monitoring (September 3, 2024): A brief episode of atrial flutter was detected.

The patient was electively admitted to the M.M. Amosov National Institute of Cardiovascular Surgery for further diagnostic evaluation and treatment. She remained hospitalized from September 18 to September 23, 2024.

The family history was notable for hypertension in her mother, a first-degree relative. The patient's general condition was satisfactory. Height was 160 cm and body weight was 62 kg. Lung boundaries were unchanged, and breath sounds were vesicular. The cardiac borders were displaced to the left. Heart sounds were regular, with an accentuated second heart sound over the aortic area and a systolic murmur at the apex. Peripheral oxygen saturation was 97%. Heart rate was 89 beats/min, and blood pressure was 165/86 mmHg. The abdomen was soft on palpation; the liver and spleen were not palpable below the costal margins. Bowel movements and urine output were within normal limits.

Investigations. Complete blood count: RBC, $4.1 \times 10^{12}/L$; Hb, 122 g/L; color index, 0.9; Hct, 40%; WBC, $4.7 \times 10^9/L$; platelets, $227 \times 10^9/L$; neutrophils, 43% (band neutrophils, 2%; segmented neutrophils, 41%); lymphocytes, 45%; monocytes, 8%; eosinophils, 4%. ESR was 5 mm/h. Blood biochemical parameters, including creatinine, urea, uric acid, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin and its fractions, total protein, and glycated hemoglobin, were within normal limits. Urinalysis findings were also within normal limits.

ECG (September 23, 2024): Regular sinus rhythm with a heart rate of 71 beats/min. Normal cardiac electrical axis. LV hypertrophy. Left atrial hypertrophy.

The following medications were prescribed: bisoprolol 2.5 mg once daily; rosuvastatin 40 mg once daily; Valsacor 80 mg twice daily with blood pressure monitoring; Jardiance 10 mg once daily with NT-proBNP monitoring; warfarin 7.5 mg once daily with INR monitoring (target INR, 2–3) and dose adjustment; Clexane 0.4 mL subcutaneously twice daily until the target INR of 2–3 was achieved; Kaldyum, 1 capsule twice daily for 14 days with monitoring of serum potassium levels; Indalen 1.5 mg once daily; and Nolpaza 40 mg once daily for 14 days.

On September 19, 2024, an endovascular procedure was performed to close the defect of the aortomitral fibrous continuity (AMFC) using a 10-mm Cera Vascular Plug delivered through a 5-Fr system. Follow-up angiography demonstrated appropriate device positioning.

All TTE examinations were performed by experienced sonographers in accordance with the recommendations of the American Society of Echocardiography for the assessment of AS [60]. Data from serial TTE examinations are presented in **table**.

TTE performed on February 26, 2024, demonstrated severe AS with grade 3 calcification (**fig. 5**). Hemodynamic parameters were as follows: AV Vmax, 5.10 m/s; maximum/mean pressure gradients, 104/78 mmHg. LV systolic function was preserved (LVEF, 66%) in the presence of concentric LV hypertrophy. In addition, LA dilatation, an increased LA volume index, and dilatation of the ascending aorta were documented, with values of 4.3 cm, 43 mL/m², and 4.05 cm, respectively. Post-AV replacement TTE performed on April 22, 2024, demonstrated the following hemodynamic parameters: Vmax across the AV prosthesis, 2.50 m/s, and a maximum pressure gradient of 25 mmHg.

LV systolic function remained preserved (LVEF, 60%), with concentric LV hypertrophy. LA diameter and LA volume index decreased to 4.0 cm and 33 mL/m², respectively. Notably, TTE findings obtained 5 months after AV replacement demonstrated changes associated

Table – Changes in the Main TTE Parameters Over Time

Parameter	Reference range	Feb 26, 2024	Apr 22, 2024	Sep 18, 2024	Oct 2, 2024	Jan 8, 2025
AV status		AV stenosis	AV prosthesis	AV prosthesis	AV prosthesis, AMFC occluder	AV prosthesis, AMFC occluder
BSA, m ²		1.67	1.65	1.6	1.65	1.67
Aortic diameter, cm	<3.7	2.75	–	–	2.8	2.8
Ascending aorta, cm		4.05	3.3	3.3	3.5	3.7
LA, cm	<4.0	4.30	4.00	3.8	4.0	3.6
LA volume index, mL/m ²	22±6	43	34	40.6	34	33
LVEDD, cm	3.9–5.3	4.72	–	5.45	5.2	5.2
LVEDD/BSA index, cm/m ²	2.4–3.2					
LVEDV, mL		103.38	109	145	130	135
IVSd, cm	0.6–1.1	1.36	1.50	1.1	1.1	1.0
LVPWd, cm	0.6–1.1	1.4	1.50	1.0	1.07	1.0
LV mass, g	67–162	274.6	–	216.9	256	240
LV mass index, g/m ²	43–95	164.43	–	135.6	150.2	145
LVEF, %	53–70	66	59	57	65	66
Vmax across AV/prosthesis, m/s		5.10				2.6
Maximum AV gradient, mmHg		104	25	33	24	27
Mean AV gradient, mmHg		78				
Aortic regurgitation		None	+	Severe	Mild paravalvular	Mild paravalvular
Mitral regurgitation		Mild	Mild	Mild	Minimal	Minimal
Tricuspid regurgitation		Mild	Mild	Mild	Minimal	Minimal
Systolic PA pressure, mmHg		47	45	32	25	20

Notes: LVEDD – left ventricular end-diastolic diameter; IVSd – interventricular septal thickness at end-diastole; LVPWd – left ventricular posterior wall thickness at end-diastole; LV mass – left ventricular myocardial mass; LVEF – left ventricular ejection fraction; PA – pulmonary artery; AR – aortic regurgitation; VC – vena contracta; AMFC – aortomitral fibrous continuity; LA – left atrium; BSA – body surface area; AV – aortic valve; LVEDV – left ventricular end-diastolic volume.

with the development of a defect of the mitral–aortic fibrous continuity. LVEDD and LVEDV increased to 5.45 cm and 145 mL, respectively. The LA volume index increased again to 40.6 mL/m². The pattern of LV hypertrophy changed from concentric to eccentric. LV systolic function also showed some variation, although it remained within the normal range, with an LVEF of 57%. Following endovascular closure of the paravalvular fistula with an occluder on October 8, 2025, the TTE parameters showed further changes (fig. 6).

An increase in LVEF to 66% was observed, while eccentric LV hypertrophy persisted. In addition, the LA diameter, LA volume index, and ascending aortic diameter decreased to 3.7 cm, 33 mL/m², and 3.6 cm, respectively. The maximum velocity across the AV prosthesis remained unchanged at 2.60 m/s, with a maximum pressure gradient of 27 mmHg.

The patient's clinical condition improved. During the prescribed therapy, blood pressure stabilized at 130/80 mmHg, exercise tolerance increased, and dyspnea decreased. For further follow-up, regular use of the prescribed medications, INR monitoring, serial TTE follow-up, continued cardiology follow-up at the patient's place of residence, blood pressure monitoring, and adherence to an appropriate physical activity regimen were recommended.

This clinical case clearly demonstrates the complexity of the diagnostic process, the challenges of determining valve morphology, and the diverse clinical manifestations and progression patterns of congenital BAV. A key objective remains the identification of clinical markers that would allow patients at risk to be recognized before the development of hemodynamic abnormalities or potentially dangerous aortic changes, ranging from dilatation to dissection, thereby facilitating the timely

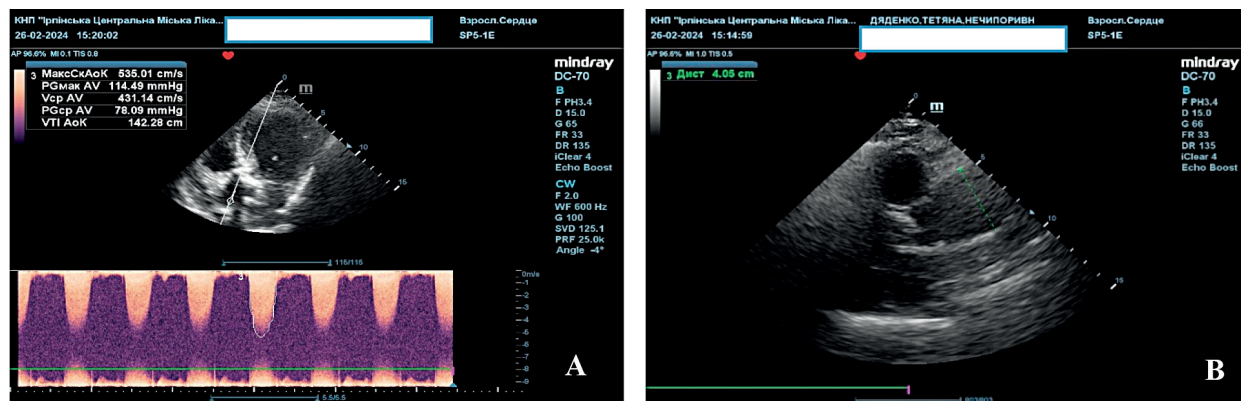


Figure 5 – Patient D., 68 years old.

Aortic valve stenosis: A – apical five-chamber view; B – dilatation of the ascending aorta, parasternal long-axis view.

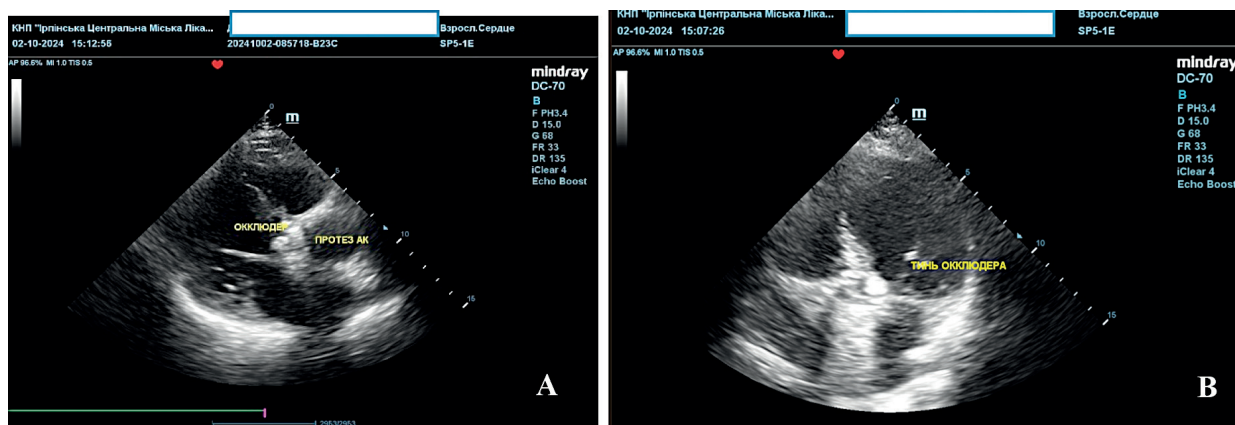


Figure 6 – Aortic valve prosthesis and occluder of the aortomitral fibrous continuity (AMFC) in patient D., 68 years old: A – parasternal long-axis view; B – apical five-chamber view.

and early diagnosis of BAV. Analysis of the initial manifestations of the disease in our patient, including elevated blood pressure, exertional dyspnea, and reduced exercise tolerance, indicates that these symptoms are common and nonspecific for BAV. However, the coexistence of several abnormalities should always raise the possibility that they represent manifestations of a single complex disorder requiring a multidisciplinary approach, particularly at the stage of early diagnosis, rather than only after congenital aortic valve disease is diagnosed, as occurred in this patient at the age of 68 years. Analysis of LV remodeling over time confirms a direct relationship between hemodynamic changes and myocardial structural alterations during the postoperative period. Before surgical intervention (February 26, 2024), the findings were consistent with severe AS. The development of paravalvular regurgitation after aortic valve replacement (September 18, 2024) resulted in LV dilatation (LVEDV, 145 mL; LVEDD, 5.45 cm) and a decrease in LVEF to 57%. Endovascular correction of the fistula in October 2024 was followed by favorable changes: LV volumes decreased and systolic function recovered, with LVEF increasing to 65% and subsequently remaining within the normal range. Thus, this case demonstrates the reversibility of pathological LV remodeling following successful correction of the hemodynamic defect. Given that structural and functional alterations in the connective tissue matrix are relevant to both the development of the valvular apparatus and remodeling of the aortic wall, it may be appropriate to consider the potential coexistence of BAV, mitral valve abnormalities, and aortopathy in patients with the MASS phenotype. We hypothesize that phenotypic features of MASS, including myopia, aortic root dilatation, skin manifestations, and skeletal abnormalities, may serve as clinical markers prompting targeted evaluation for BAV and facilitating its early diagnosis. This hypothesis requires future validation and more comprehensive investigation in clinical studies. Thus, the identification of such markers in combination with the patient's medical history may improve the early diagnosis of BAV, which is critically important for preventing disease progression, particularly early valve calcification. Implementation of a multidisciplinary management strategy may be an important factor in limiting the progression of AS. Furthermore, recognition of potential concomitant aortopathy in these patients may facilitate a more individualized approach to the surgical correction of AS, particularly in view of the poten-

tial structural vulnerability of the aortic wall associated with BAV. Therefore, timely and more comprehensive diagnostic evaluation using TTE, TEE, CT, or MRI, together with a more thorough diagnostic assessment at the primary care level, may facilitate surveillance of the natural history of BAV and help identify early valve dysfunction and its progression with age. This clinical case also highlights the important role of the family physician as the principal clinician responsible for coordinating the patient's diagnostic pathway and longitudinal follow-up. Unfortunately, such coordinated care is not consistently available across clinical settings, particularly in district-level healthcare facilities.

Conclusions.

Bicuspid aortic valve is an important challenge in contemporary medicine. Clear and well-defined diagnostic criteria, effective collaboration among physicians of different specialties, and the involvement of a multidisciplinary team in the diagnostic process are essential for timely diagnosis, appropriate treatment, and prevention of complications. An improved understanding of the diversity of BAV phenotypes and the potential relationship between the natural history of the disease and specific phenotypes highlights the need for continued investigation of criteria for early diagnosis.

The hypothesis of a potentially more frequent association between BAV and various manifestations of connective tissue dysplasia, particularly the MASS phenotype, requires further comprehensive investigation. Early aortic valve calcification and initial signs of aortopathy, including an increase in thoracic aortic diameter, should prompt clinicians to consider the possibility of BAV and undertake targeted diagnostic evaluation. Patients with BAV require lifelong surveillance, particularly following cardiac surgical intervention.

Prospects for further research.

Given that BAV is a diagnostically challenging congenital condition characterized by diverse valvular and aortopathy phenotypes and associated with an increased risk of early surgical intervention and aortic dissection, further comprehensive investigation of this condition is warranted. Future research will focus on optimizing diagnostic and differential diagnostic algorithms and developing more individualized approaches to treatment.

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ДВОСТУЛКОВИЙ АОРТАЛЬНИЙ КЛАПАН: КОЛИ АНАТОМІЧНА ОСОБЛИВІСТЬ СТАЄ ХІРУРГІЧНОЮ ПРОБЛЕМОЮ

Кузеванова М. В., Конюшевська А. А., Козаренко Т. М., Сторожчук Ю. О., Смирнова Г. С.

Резюме. Згідно з сучасними даними у більшості людей з ДАК розвиваються клапанні та/або аортальні ускладнення, які зустрічається приблизно в 50% випадків. Визнаний зв'язок між природним перебігом та фенотипом ДАК, розуміння розвитку самої аномалії та механізмів ускладненого захворювання досі є непевним. Чому один ДАК стає стенозуючим, інший – регургітуючим, ще один – пов'язаний з дилатацією аорти, а ще один залишається функціонально не порушений протягом усього життя, залишається принципово невідомим і непередбачуваним. Пошук шляхів для ранньої діагностики та подальшого позитивного спостереження робить ДАК клінічним викликом для лікарів і по сьогодні. Алгоритмічне підсумовування багаточисельних даних, припущення корекції кута клінічного погляду на пацієнта з ознаками дисплазії сполучної тканини, як можливий крок раннього діагностичного скринінгу на ДАК, передчасна дегенерація клапана, пов'язана з ранньою кальцифікацією і пошуку шляхів кардіохірургічної корекції особливо на тлі розвитку в майбутньому аортопатії, яка дає більшу ймовірність розвитку післяопераційних ускладнень ще вимагають подальшого дослідження.

Пацієнт з ДАК – це пацієнт мультидисциплінарної команди з послідовним використанням клапаних, аортальних та генетичних систем класифікації як у клінічній практиці, так і в дослідженнях. Саме так може сприяти кращому розумінню моделей захворювання, які мають як прогностичне, так і терапевтичне значення.

Ключові слова: двостулковий аортальний клапан, аортопатія, супутні вади, ехокардіографічний скринінг, хірургічне лікування.

BICUSPID AORTIC VALVE: WHEN AN ANATOMICAL VARIANT BECOMES A SURGICAL PROBLEM

Kuzevanova M. V., Koniushchevska A. A., Kozarenko T. M., Storozhchuk Y. O., Smyrnova G. S.

Abstract. According to current evidence, most individuals with BAV develop valvular and/or aortic complications, which occur in approximately 50% of cases. Although an association between the natural history and phenotype of BAV has been recognized, our understanding of the development of the anomaly itself and the mechanisms underlying its complications remains incomplete. Why one BAV becomes stenotic, another becomes regurgitant, another is associated with aortic dilatation, while yet another remains functionally unaffected throughout life remains fundamentally unknown and unpredictable. The search for approaches to early diagnosis and subsequent lifelong surveillance continues to make BAV a clinical challenge for physicians. The systematic integration of the extensive available evidence, together with a potential shift in the clinical perspective on patients with features of connective tissue dysplasia as a possible step toward early diagnostic screening for BAV, requires further investigation. Premature valve degeneration associated with early calcification and the search for optimal approaches to cardiac surgical correction, particularly in the context of the potential future development of aortopathy and its associated increased risk of postoperative complications, also warrant further study. A patient with BAV requires multidisciplinary management, with consistent application of valvular, aortic, and genetic classification systems in both clinical practice and research. Such an approach may contribute to a better understanding of disease patterns that have both prognostic and therapeutic significance.

Key words: bicuspid aortic valve, aortopathy, associated defects, echocardiographic screening, surgical treatment.

ORCID and contributionship:

Kuzevanova M. V.: <https://orcid.org/0000-0002-1383-5555> ^{ABDF}

Koniushchevska A. A.: <https://orcid.org/0000-0002-1056-7137> ^{BDEF}

Kozarenko T.M.: <https://orcid.org/0000-0002-0838-9773> ^{BEF}

Storozhchuk Y. O.: <https://orcid.org/0000-0002-3186-6654> ^{ABEF}

Smyrnova G. S.: <https://orcid.org/0000-0001-8788-7975> ^{BEF}

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The authors declare no conflict of interest.

Corresponding author

Koniushchevska Alla Anatoliyivna
Donetsk National Medical University
Ukraine, 25000, Kropyvnytskyi, 4A Yuria Kovalenka str.
Tel.: +380965664385
E-mail: konyshchevska63@gmail.com

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

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