

## CONTEMPORARY REVIEW

# Contemporary Overview of Aortic Regurgitation in Young Individuals: Insights From Real-Life Evidence

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**ABSTRACT:** Aortic regurgitation (AR) in young adults (aged 18–44 years) is often under- or misdiagnosed and is not always benign. As in older populations, prognosis depends on the severity of regurgitation, early left ventricular dysfunction, cause of, and the chosen intervention strategy. Prompt diagnosis and timely treatment improve outcomes, yet the optimal timing for surgery in asymptomatic chronic AR remains uncertain. Recent studies have proposed new thresholds for left ventricular structural and functional assessment to better evaluate the impact of AR on prognosis and guide intervention timing. Echocardiography remains the primary imaging modality, but a multimodality approach is essential to accurately assess AR severity and subtle left ventricular changes. Transesophageal echocardiography with 3-dimensional imaging is crucial for evaluating valve repair feasibility, particularly when valve-sparing root repair, reintervention, or transcatheter procedures are considered. Additional tools such as cardiac magnetic resonance, global longitudinal strain, and biomarkers may further enhance disease monitoring. Assessment can be challenging, especially with eccentric jets or complex valve anatomy, and current surgical cut-offs remain debated. Aortic valve repair is preferred in young patients, including those with concomitant proximal aortic aneurysm, but it remains underutilized. Here, we propose a treatment algorithm for severe AR in young adults, integrating cause of, valve anatomy, and left ventricular function, with a special focus on multimodality imaging to guide monitoring and therapeutic strategies.

**Key Words:** aortic regurgitation ■ cardiac magnetic resonance ■ echocardiography ■ prognosis ■ surgical repair ■ young patients

**A**ortic regurgitation (AR) can progress to severe complications such as left ventricular (LV) volume overload, dilatation and, if left untreated, LV dysfunction. Young adults were recently defined as individuals aged 18 to 44 years.<sup>1</sup> This age range represents a period of life that precedes the development of degenerative calcific valvular disease, which is typically associated with aging and traditional coronary risk factors that may influence the process. However, an earlier age of onset may occur with congenital valve abnormalities, especially bicuspid aortic valve (BAV).<sup>2–4</sup>

The cause includes congenital, inflammatory, infectious and connective tissue diseases. The most

common etiologies observed in the elderly, as well as AR associated with complex congenital heart diseases, are not addressed in this review. AR in younger adults is typically because of congenital heart disease, especially BAV, and the clinical presentation and natural history can differ from that of older individuals with acquired aortic valve (AV) disease. Timing of surgical intervention for severe AR is critical but may be challenging, especially for asymptomatic young adults, to minimize long-term sequelae and potential repeat surgeries in their lifetime. This is where a validated risk analysis that incorporates the benefits of early intervention, the risks of surgery, and the likelihood of complications would be

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## Nonstandard Abbreviations and Acronyms

<b>AR</b>	aorta regurgitation
<b>AV</b>	aortic valve
<b>BAV</b>	bicuspid aortic valve
<b>TAVR</b>	transcatheter aortic valve replacement

helpful. A clear advantage and class I recommendation for intervention is recognized by the current guidelines based on the presence of symptoms, LV dysfunction, and severe chamber dilatation.<sup>5,6</sup> These indications are based largely on survival analyses conducted in predominantly adult male cohorts and therefore do not account for sex- and age-related differences in prognosis.<sup>7</sup> The prerequisites to successful AV surgery need to have a clear understanding of the mechanisms of the valve dysfunction and a suboptimal diagnostic precision justify the surgical under-treatment, despite the true prevalence of those not offered surgery in young patients affected by AR remains unknown.

In this review, we examine AR in young adults, with a focus on the key aspects of noninvasive imaging and the clinical markers for detecting the severity and progression of AR in the young. Inconsideration for women in childbearing age, and the crucial role of multimodality imaging in monitoring the disease progression and guiding treatment decisions in a real-life perspective are discussed.

## CAUSE OF AORTIC REGURGITATION IN THE YOUNG

The main etiologies of AR in young adults are listed in Table 1,<sup>3,4,8–22</sup> along with the prevalence of significant AR for each cause when available. In individuals younger than 50 years, trace AR is present in 3% of the population, whereas moderate or severe AR is identified in only 0.3% of cases.<sup>23</sup> It results from diseases affecting the aortic valve leaflets (primary) and/or abnormalities of the aortic root and ascending aorta (secondary).

Primary AR in young individuals arises from a variety of conditions, including congenital abnormalities of the AV, connective tissue disorders, rheumatic heart disease, infective endocarditis, trauma, or autoimmune diseases. In developed countries, the most common causes are congenital disorders such as BAV and aortic annular ectasia, whereas rheumatic heart disease remains the leading cause in developing regions.<sup>24</sup> Secondary AR, on the other hand is attributable to a consequence of structural abnormalities in the aortic annulus and ascending aorta or surrounding structures that affect the

AV leaflets coaptation, leading to blood backflow into the LV.<sup>25</sup> Notably, congenital valve anomalies such as BAV and unicuspid AV are frequently associated with concomitant aortopathy with root dilatation, which may further contribute to the development or progression of secondary AR.<sup>2</sup> According to the EURObservational Research Programme Valvular Heart Disease II Survey, the prevalence of AR is estimated as 5.3%.<sup>26</sup>

## Bicuspid Aortic Valve and Other Abnormalities With Multiple Etiologies

BAV is the most frequent congenital heart defect, with an estimated prevalence of 1% to 2% in the general population.<sup>27</sup> It is defined by the presence of only 2 functional commissures instead of the usual 3. Notably, men with BAV are more prone to AR, while women more commonly develop aortic stenosis.<sup>28</sup> Congenital BAV is best described as a part of the spectrum of valvulo-aortopathy, given the frequent coexistence of valvular and aortic abnormalities. It exhibits marked heterogeneity in both valve and aortic phenotypes, associated conditions, complications, and clinical outcomes.<sup>2</sup> In the Olmsted County series of asymptomatic patients with BAV 47% had some degree of AR at baseline.<sup>29</sup> AR in BAV occurs independently of aortic stenosis, and the mechanism includes prolapse of the larger of unequal cusps, myxoid degeneration of the valve, or may be the result of a former infective endocarditis. Numerous and heterogeneous classification systems have been proposed for BAV, but their variability can lead to confusion in clinical practice, particularly when trying to identify phenotypes that predict outcomes or provide essential anatomical information for surgical and transcatheter AV replacement (TAVR). Michelena et al. proposed a unified nomenclature and classification system including 3 phenotypes<sup>30–35</sup> as presented in Figure 1. Although patients with BAV typically do not experience complications during infancy and childhood, they are at risk of developing AV stenosis and insufficiency as they age. Later in life, they may develop root dilatation, rupture, and dissection and AR is commonly seen. In fact, 30% of patients with BAV are diagnosed with moderate to severe AR at their initial presentation. Despite not having a high mortality risk per individual, its high prevalence makes BAV responsible for the greatest absolute number of deaths among congenital heart defects, mainly attributable to aortic complications such as dissection.<sup>34</sup> Two main aortopathy phenotypes are described: the root phenotype, where dilatation is predominantly located at the proximal aortic root, potentially involving the ventriculo-aortic junction (about 20% of cases and typical of younger patients with BAV, usually males with AR) and the ascending phenotype (approximately 70% of cases, affecting older patients with BAV with AV sclerosis/stenosis), where dilatation primarily occurs

**Table 1. Epidemiology of Aortic Regurgitation by Cause**

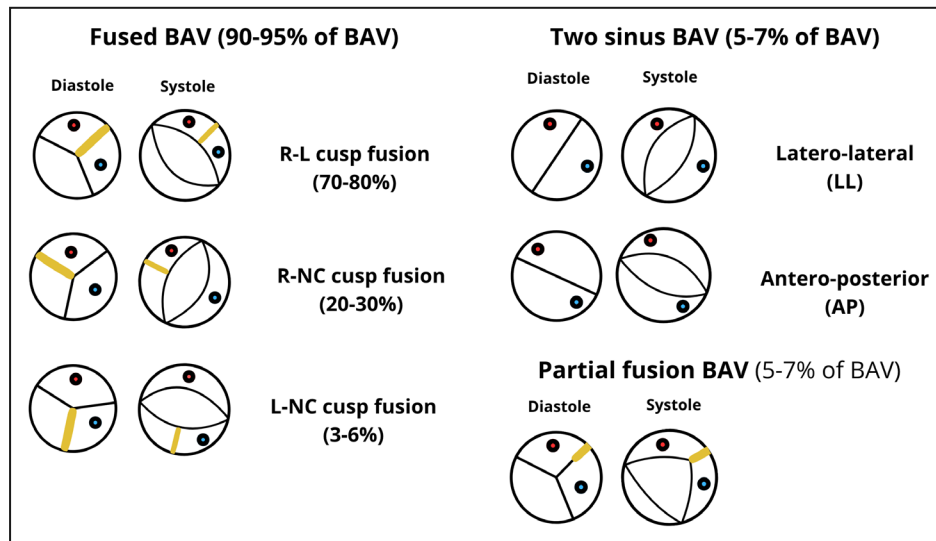
Cause	Presence of AR	Population studied	References
Congenital abnormalities			
BAV	Significant AR*: 12%	Population screening study. 20946 young men; 167 with BAV	Nistri et al. <sup>8</sup>
Unicuspid AV	AR of any grade 93%	75 pts, mean age 37 y	Slostad et al. <sup>3</sup>
Quadricuspid AV	Significant AR 26%	50 pts, mean age 47 y	Tsang et al. <sup>4</sup>
Multiple etiologies			
Fenestrations	Autoptic studies: 43% Significant AR*: rare (unknown)	400 autopsied human hearts (formalin-fixed)	Dudkiewicz et al. <sup>9</sup>
Connective tissue disorders			
Marfan syndrome	Significant AR*: 6%	Cross-sectional observational study, 160 young patients with Marfan syndrome	Aburawi and O'Sullivan <sup>10</sup>
Vascular Ehlers-Danlos syndrome	Significant AR*: rare (unknown)		Morris et al. <sup>11</sup>
Loeys-Dietz syndrome	Significant AR*: 43%	Cross-sectional observational study	Nabi et al. <sup>12</sup>
Acquired causes			
Infective endocarditis	Involvement of the aortic valve in IE: 43.9%	Cross-sectional observational study, 867 cases with definite IE with >18 yo	Erdem et al. <sup>13</sup>
Rheumatic fever	Aortic valve involvement: 29%	Cross-sectional observational study, 13289 patients with primary valvular heart disease	Manjunath et al. <sup>14</sup>
Acute type A aortic dissection	Significant AR*: 38%	Multicenter Cross-sectional observational study; 951 patients with aortic dissection	Januzzi et al. <sup>15</sup>
Thoracic trauma	Significant AR*: 12%	Multicenter retrospective study. 17 major trauma patients with traumatic aortic injury	Mosquera et al. <sup>16</sup>
Inflammatory and autoimmune disorders			
Rheumatic fever	Aortic valve involvement: 29%	Cross-sectional observational study, 13289 patients with primary valvular heart disease	Manjunath et al. <sup>14</sup>
Ankylosing spondylitis	Significant AR*: 5%	Cross-sectional observational study, 187 patients.	Klingberg et al. <sup>17</sup>
Libman-Sacks endocarditis	Significant AR*: rare, unknown (mainly mild)		Moysakis et al. <sup>18</sup>
RA	Incidence rate of AR (any grade): 1%/y	Prospective cohort study, 6673 patients with RA	Wang et al. <sup>19</sup>
BD	Prevalence of AR in BD: 51% Prevalence of Severe AR: 41% (mainly form cusp prolapse)	Cross-sectional observational study, 121 patients	Fu et al. <sup>20</sup>
APLA	Significant AR*: 5%	Cross-sectional observational study, 144 patients	Pons et al. <sup>21</sup>
Takayasu arteritis	Significant AR*: 12%	Cross-sectional observational study 252 patients with Takayasu arteritis	Yağmur et al. <sup>22</sup>

APLA indicates antiphospholipid antibodies; AR, aortic regurgitation; AV aortic valve; BAV bicuspid aortic valve; BD, Behçet's disease; and RA, rheumatoid arthritis.

\*Moderate or severe AR.

in the tubular ascending aorta beyond the sinotubular junction.<sup>29,35</sup> The traditional Sievers classification bases the categorization on the number with arrangement of the cusps and fused areas (raphes), having the type 0 as the "true" BAV with 2 leaflets and no raphe (fusion line), the type 1 with 1 raphe, formed by the fusion of 2 underdeveloped cusps (the most common type) and the type 2, with 2 raphe.<sup>36</sup> While this system remains useful for identifying raphe patterns, it does not fully capture the functional relevance of commissural orientation and cusp fusion. The classification proposed by de Kerchove et al.<sup>37</sup> provides a contemporary,

repair-oriented framework for the anatomical characterization of BAV, describing valve morphology as a continuum rather than discrete phenotypes. This unified spectrum is based on commissural orientation, extent of cusp fusion and raphe height, categorizing BAVs into 3 phenotypes according to the intercommissural angle: Type A (near-symmetric, 160°–180°), Type B (asymmetric, 140°–159°), and Type C (markedly asymmetric, 120°–139°). It is designed to be clinically applicable and surgically relevant, linking valve geometry to repair strategies and functional outcomes including both bicuspid and unicuspid AV morphologies. There



**Figure 1.** Bicuspid aortic valve classification according to the current International consensus statement by Michelena et al.

Three distinct types of bicuspid valve are shown: (1) Fused type: most common, characterized by fusion of 2 cusps with a raphe, resulting in 3 phenotypes: right-left (R-L), right non-coronary (R-NC), and left non-coronary (L-NC) fusion; (2) Two-sinus type: less common, characterized by the presence of 2 cusps formed within only 2 aortic sinuses; each cusp occupies 180° of the annular circumferences, and results in a 2-sinus/2-cusps valve, without any raphe; (3) Partial-fusion type or form fruste: resembling a tricuspid valve with incomplete cusp fusion forming a small raphe.

are concomitant or associated disorders which may result in complex valvulo-aortopathy and portend particularly poor prognosis, as in Turner syndrome, Loeys-Dietz syndrome, Shone complex, and severe aortic coarctation, which cause accelerated valve dysfunction and aortopathy in the pediatric adolescent and young adult population.<sup>38,39</sup>

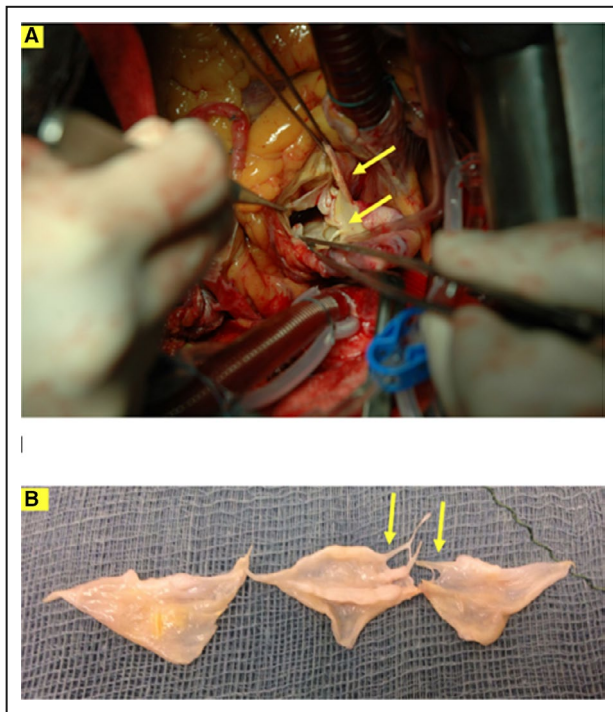
A clinically relevant defect is AV fenestration, in which the thin marginal strand representing the free cusp border elongates or ruptures causing small perforations or gaps in the valve leaflets that can degenerate to prolapse and impairing coaptation with AR (Figure 2A and 2B). This condition can be secondary to congenital cause, but also to infective endocarditis and/or aortic root enlargement. While fenestrations may be asymptomatic early in life, they can progressively worsen, contributing to significant AR as the patient ages. Studies have shown that the presence of valve fenestrations, although less common than BAV, can significantly impact valve function, particularly when associated with other structural anomalies such as aortic root dilation.<sup>40</sup> These defects underline the importance of early detection and monitoring in young individuals to prevent the progression of AR and to manage the condition effectively before it leads to significant complications. In a study that retrospectively reviewed congenital abnormalities in patients undergoing surgery for moderate to severe and severe AR, isolated mechanisms were noted in 30% of patients. Fenestrations by surgical or pathological report

were present in 7% of patients, especially in those with tricuspid AV. Other mechanisms of pure native AR were prolapse (11%) and restriction/retraction (9%), especially in patients with BAV.<sup>41</sup>

### Acquired Causes

Acquired causes of primary AR in the young include infective endocarditis, rheumatic, connective, and inflammatory disorders. Endocarditis is a significant cause of primary AR, accounting for about 10% to 20% of cases of acute AR in young adults, especially in those with congenital heart defects or those who engage in high-risk behaviors, such as intravenous drug use.<sup>9</sup> The pathogenesis of AR in the context of endocarditis is typically attributable to the destructive effects of the infection on the valve structure with formation of vegetations, that can damage the valve cusps, leading to fenestration, perforation, erosion, rupture, periannular abscess, and fistulization in the adjacent cardiac chambers. The risk of developing AR as a complication of infective endocarditis (IE) is particularly high in cases involving virulent organisms such as *Staphylococcus aureus* or *Streptococcus* species as these pathogens can rapidly invade and destroy the valve tissue. The clinical course of endocarditis-induced AR is often fulminant, requiring prompt surgical intervention to prevent life-threatening complications.<sup>42,43</sup>

Rheumatic heart disease is the only long-term consequence of acute rheumatic fever from single or repetitive episodes leading to chronic valvular disease.



**Figure 2. Intraoperative surgical findings of a trileaflet aortic valve visualized during surgery.**

**A**, The yellow arrows indicate the right and non-coronary cusp of the aortic valve. **B**, Close-up image of the 3 leaflets after surgery reveals multiple fenestrations in the right and non-coronary cusp (yellow arrows).

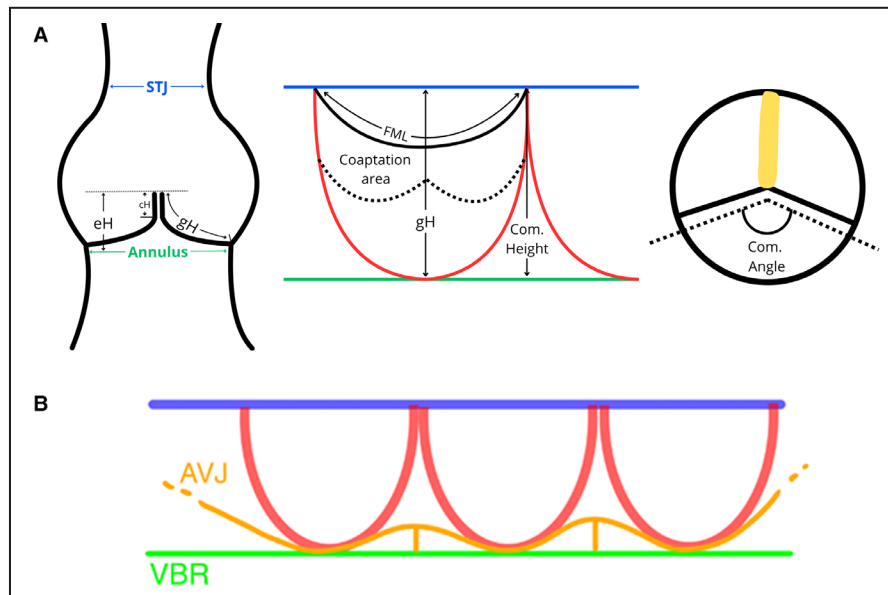
Rheumatic heart disease is the leading cause of cardiovascular death in children and young adults, particularly affecting women, in low-income countries, where Streptococcal infections are still endemic and ineffectively treated. The time interval between the initial episode of rheumatic fever and the clinical evidence of valve disease ranges from a few years to over 20 years,<sup>44,45</sup> having the AV being the second most involved valve after mitral valve. Rheumatic disease causes primary AV pathology with the infiltration of fibrous tissue into the cusps, resulting in leaflet retraction and inability in the coaptation leaflets.<sup>14</sup>

Connective tissue disorders represent genetic conditions including Marfan, Ehlers-Danlos, and Loeys-Dietz syndrome. In young patients with Marfan syndrome, AR is a common cardiovascular manifestation due to aortic root dilation (approximately 40%–50% of individuals affected).<sup>46</sup> In patients with Ehlers-Danlos syndrome, approximately 28% have aortic root dilation; however, there are no robust data on the prevalence of AR in this population.<sup>47</sup> Loeys-Dietz syndrome is associated with a high risk of AR attributable to aggressive aortic root dilation, often occurring at a younger age than in Marfan syndrome.<sup>48</sup> The inflammatory and autoimmune disorders include ankylosing spondylitis, which is most frequently associated with AR in young

adults (approximately 10%–30% of patients, particularly in those with longstanding disease and aortitis).<sup>49</sup> Systemic lupus erythematosus has a prevalence of AR estimated to be around 2% to 3%, usually associated with Libman-Sacks endocarditis. In juvenile rheumatoid arthritis AR is less common and usually occurs in patients with systemic-onset disease.<sup>50</sup>

## ANATOMY OF THE AORTIC VALVE APPARATUS AND MECHANISM OF REGURGITATION

The AV apparatus is a geometric structure composed of the AV and the aortic root in close relationships. The aortic root constitutes the native stent of the AV and can also be described as the 3-dimensional (3D) functional aortic annulus. It is composed of the anatomic ventriculo-aortic junction, which is the transition zone from the LV outflow tract to the aortic wall, the sino-tubular junction, and the hemodynamic ventriculo-aortic junction (a crown-like 3D structure that corresponds to the AV cusps insertion line). Loss of integrity of any of these components leads to AV dysfunction and AR.<sup>51</sup> The true aortic annulus is not the virtual basal ring, which is projected at the most basal leaflet insertion, but rather the hemodynamic ventriculo-aortic junction (Figure 3A). The virtual basal ring is the plane passing through the AV leaflet nadirs, which is deeper and more proximal than some parts of the ventriculo-aortic junction. The latter aligns with the virtual basal ring along the fibrous portion of coronary cusps (at the level of the mitro-aortic curtain) but is up to half a centimeter above the virtual basal ring along the muscular portion and membranous septum<sup>51</sup> (Figure 3B). In valve-sparing reimplantation surgery, the ventriculo-aortic junction is the limit of dissection and is well-delineated externally. The different anatomical structure could explain why prolapse is more frequently observed in the leaflet supported by the dilated muscular portion (right coronary leaflet or the fused left/right leaflet in BAV). Ventriculo-aortic junction dilatation has been recognized as a structural factor contributing to the development of AR in both tricuspid and BAV, with BAVs generally exhibiting larger ventriculo-aortic junction dimensions compared with tricuspid valves. In surgical series of valve repair, larger preoperative ventriculo-aortic junction diameters have been associated with a higher likelihood of recurrent AR or need for reintervention when simple annuloplasty alone is performed, underscoring the importance of appropriate annular and root stabilization in achieving durable outcomes.<sup>52</sup> However, the severity of AR does not consistently correlate with the absolute size of the ventriculo-aortic junction, as isolated AR may occur in the absence of significant root



**Figure 3. Echocardiographic measurements in the functional aortic valve apparatus.** FAA encompassing the entire aortic root. It includes the STJ, the aortic leaflets attachment, the VAJ, and the VBR, which collectively define the anatomical and hemodynamic boundaries within the aortic root. **A**, gH; eH; cH; com height; com angle; FML. **B**, Leaflet insertion line in tricuspid aortic valve (red line); STJ is represented by the blue line; VAJ is the yellow line and VBR is the green line. cH indicates coaptation high; com angle, commissural angle; com height, commissural height; FAA, functional aortic annulus; FML, free margin leaflet; eH, effective height; gH, geometric height; STJ sinotubular junction; VAJ, ventriculo-aortic junction; and VBR, virtual basal ring.

or junctional dilatation. In this context, dilatation of the sinotubular junction also plays a relevant role in impairing leaflet coaptation.<sup>53,54</sup>

In addition to root dynamics, intrinsic cusp abnormalities are major determinants of AR. In patients with a trileaflet AV and root aneurysm, cusp prolapse and retraction are the most frequent findings. As highlighted by Ehrlich et al.,<sup>55</sup> nearly 90% of these patients exhibit cusp pathologies, where prolapse often results from a relative excess of tissue and retraction from chronic fibrotic changes. These findings underscore the importance of assessing the leaflets and the aortic root as a single functional unit, as cusp morphology significantly impacts both the mechanism of AR and the feasibility of surgical repair.

The El Khoury functional classification for AR<sup>56</sup> can be helpful not only to appraise the mechanism of AR and guide valve repair technique but also to predict recurrence of regurgitation during follow-up. It includes type I AR with the dilation of the functional aortic annulus. The dilatation can be limited to the distal portion of the functional annulus, (type Ia if localized at the sinotubular junction, type Ib when extended to the entire functional annulus) or be limited to the proximal portion of the functional annulus, the ventriculo-aortic junction (type Ic). In this case AR is secondary to the disproportionate functional annulus dilatation relative to leaflet size, with a loss of central coaptation,

because the leaflets are pulled outward. In most patients with this form, and to a certain extent of functional annulus dilatation, compensatory mechanisms exist at the level of the leaflets so that the AV-leaflets can stretch and thus increase in size to accommodate for the functional annulus dilatation and remain functional and competent. In functional annulus dilatation, especially type Ia and Ib, the leaflets are stretched up- and outward, so that the coaptation height is abnormally increased and the leaflet motion is restricted. This functional restriction (with “normal” AV leaflet tissues) needs to be differentiated from the organic restriction caused by leaflet thickening and retraction of the type III AR. Type II AR corresponds to an excess of leaflet motion (prolapse of 1 or more leaflets) with a disproportionate elongation of the leaflet free margins relative to the functional annulus diameter, and in comparison, to the other 2 leaflet’s free margins. The consequence is that the elongated leaflet free edge drops below the level of the others, with a loss of coaptation and resultant eccentric AR. Type III AR occurs due to restricted leaflet motion and fibrous thickening, calcification or leaflet retraction. These lesions, if severe or diffuse, can certainly also induce AV stenosis. The different mechanisms of AR can be isolated or can occur simultaneously, especially in cases of long-standing severe AR, large aneurysmal disease or congenital AV disease. Type Ic AR is almost always associated with type II, because the outward pulling of the leaflets, which

decreases coaptation high, increases stress on the leaflets, and favors the appearance of a leaflet prolapse.<sup>57</sup>

## INTEGRATIVE DIAGNOSTIC APPROACH

An integrated approach combining multiple methodologies for AR evaluation is recommended especially for optimal timing of surgical intervention. The decision to intervene in patients with AR hinges on evaluating clinical symptoms, AR severity, and LV remodeling.<sup>5,6</sup> Patients often adapt slowly to the hemodynamic burden of AR, which may mask their awareness of physical limitations. Exercise treadmill stress testing can help assess effort tolerance. The optimal timing of intervention in asymptomatic patients with significant AR depends on evaluating the regurgitation severity and detecting early indicators of LV dysfunction or chamber enlargement. While echocardiography remains the primary imaging method for assessing AR patients, employing multiple imaging techniques is essential for a comprehensive evaluation of AR severity and subtle LV changes in many cases (39). Echocardiography and cardiac magnetic resonance (CMR) are central for assessing LV response. LV dimensions and volumes inform on intervention timing, while deformation imaging and myocardial fibrosis markers provide additional prognostic value. Cardiac computed tomography (CT) complements these tools, particularly for anatomical assessments. Both European and American guidelines recommend cardiac catheterization to evaluate hemodynamics and the severity of AR when there is a discrepancy between clinical symptoms and echocardiographic findings.<sup>5,6</sup>

### Echocardiography

A comprehensive transthoracic echocardiography examination reveals the mechanism and severity of the valve lesion, its hemodynamic impact on cardiac chambers, and the presence of other cardiac pathologies. Quantitative, semi-quantitative, and qualitative approaches using 2D echocardiography and Doppler techniques for assessing the severity of AR are described in Table 2 and are similar in young adults as in aged population. Quantification of regurgitant volume and effective regurgitant orifice area (EROA) is likewise recommended, in addition to assessing jet density, vena contracta, and pressure half-time.<sup>58</sup> Additionally, end-systolic size, EF, and, when feasible, volumes and global longitudinal strain have a crucial role. LV end-systolic diameter is the historical predictor of survival because it reflects both dilation severity and systolic dysfunction. A LV end-diastolic dimension index of  $\geq 25$  mm/m<sup>2</sup> indicates high mortality risk and a threshold  $\geq 20$  mm/m<sup>2</sup> is recently shown to be better.<sup>59,60</sup> LV volumes offer a comprehensive

**Table 2. Threshold Values for Severe Regurgitation as Assessed by Echocardiography, Cardiac Magnetic Resonance, and Computed Tomography**

Parameters	Severe grade
Echocardiography	
Qualitative	
Aortic valve morphology	Abnormal/prolapse/flail/coaptation defect
Color flow aortic regurgitation jet width	Large in central jet, variable in eccentric jets
Color flow convergence	Large
Continuous wave spectral Doppler intensity	Dense
Semi-quantitative	
Diastolic flow reversal in descending aorta	Holodiastolic flow reversal: end-diastolic vel. $>20$ cm/s
Diastolic flow reversal in abdominal aorta	Present
Jet CSA/LVOT CSA (%)	$>60$
Jet width/LVOT diameter (%)	$>65$
Quantitative	
Vena contracta width (mm)	$>6$
Vena contracta area (mm <sup>2</sup> )	$>32$
Pressure half time (ms)	$<200$
EROA (mm <sup>2</sup> )	$>30$
Regurgitant volume (mL)	$>60$
Regurgitant fraction (%)	$>50$
Cardiac magnetic resonance	
Flow reversal in proximal descending aorta	Positive
Regurgitant fraction (%)	$>50$
Computed tomography	
Regurgitant area (mm <sup>2</sup> )	$>23$

CSA indicates cross-sectional area; EROA, effective regurgitant orifice area; and LVOT, left ventricular outflow tract.

dilation assessment. A threshold LV end-systolic volume index of  $\geq 45$  mL/m<sup>2</sup> is associated with increased mortality in asymptomatic severe AR.<sup>61</sup> LV deformation imaging, particularly global longitudinal strain, helps identify early LV dysfunction. Reduced global longitudinal strain values measured both by echocardiography and by CMR are linked to worse outcomes and guide surgical decisions<sup>62</sup> (Table 2). Global longitudinal strain is influenced by loading conditions, so alternative measures like myocardial work parameters are emerging as potential assessment tools.<sup>62</sup> LV remodeling in AR is influenced by age and sex, with older and/or female patients often showing a blunted response compared with younger and/or male patients.<sup>63</sup> This discrepancy highlights the need for sex and age-based thresholds for intervention, which are areas of future research.

Transesophageal echocardiography with the 3D approach, allowing for biplane imaging and multiplanar

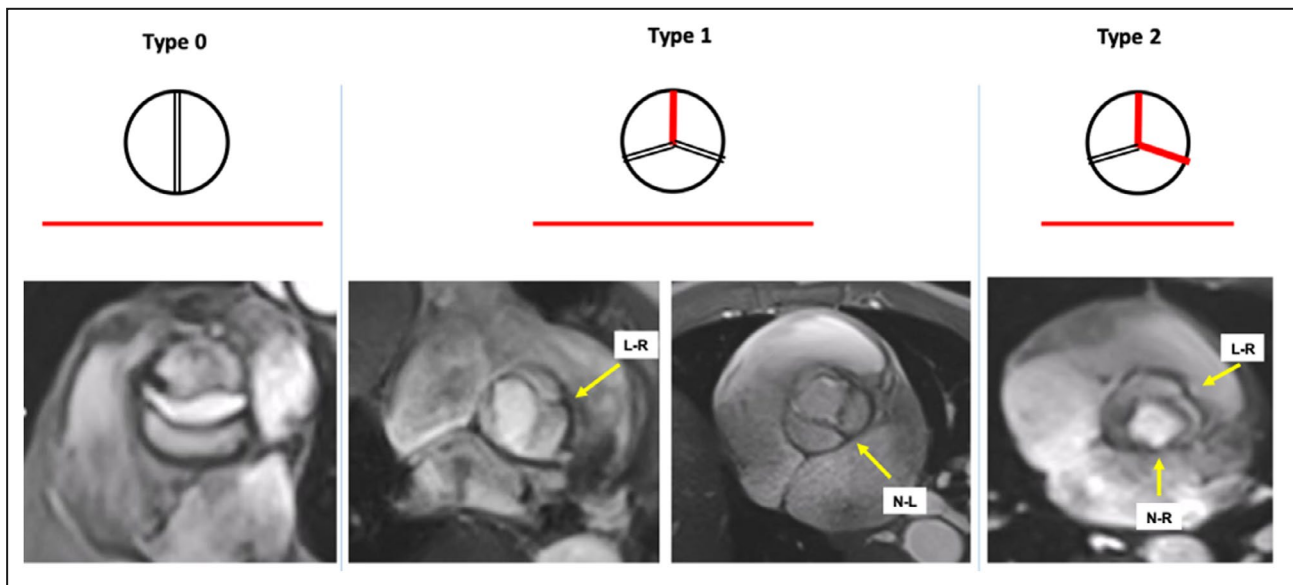
reconstruction, is relevant to assess the feasibility of AV surgical repair and is essential when further surgical AV repair, valve-sparing root repair, or transcatheter treatment options are considered. The 3D acquisition of the valve with and without color Doppler, processed in multiplanar reconstruction, allows for en-face view and direct sizing of vena contracta area or regurgitant orifice area, regardless of the regurgitant jet eccentricity, thus confirming the severity of AR. High resolution 2D imaging reveals the AV anatomical detail that may not be apparent in transthoracic echocardiography. Multiplane views of the orthogonal or cross-sectioning planes reveal the complex structural relationships of the AV with the surrounding anatomy. Familiarity and application of 3D transesophageal echocardiography multiplanar imaging is particularly important in delineating the mechanism behind AR, as recent data from Ehrlich et al. demonstrated that preoperative 2D transesophageal echocardiography alone has a low sensitivity in detecting cusp prolapse in patients with trileaflet aortic valves and root aneurysms.<sup>55</sup>

The parameters used to define severe AR are listed in Table 2.<sup>58,62</sup> Recent studies show that aortic root size is strongly associated with age, body size, and gender, being larger in men and increasing with body size and age.<sup>64</sup> The shape and size of the AV leaflets can be easily characterized using 3 key measurements (Figure 3): (1) leaflet height or geometric height, (2) effective height defined as the vertical distance between the aortic annular plane and the free edge of the coapting leaflets, and (3) commissural height. These measurements are well-established parameter for assessing cusp configuration. The geometric height is a straightforward measurement taken from the leaflet's lowest point (nadir) to the middle of the leaflet's free edge. It is often used as a surrogate for leaflet size or surface area and serves as a criterion for deciding whether to preserve or replace the valve. During valve-sparing procedures, geometric height is also used as a reference for graft sizing. An adequate geometric height is essential for considering a durable AV-sparing or AV-repair approach, and this measurement must never be reduced during AV repair. The free edge length is measured between 2 commissures. Given the 3D thin and mobile nature of the free edge, obtaining a precise measurement can be challenging. Nonetheless, this measurement is a good indicator of leaflet mobility and coaptation height. While the free edge length cannot be increased, it can be easily shortened through plication to correct prolapse, thereby enhancing leaflet coaptation height.<sup>65</sup> The commissural height is not a direct measurement of the leaflets but rather represents the valve configuration that needs to be preserved during valve-sparing procedures. Commissural height is measured from the base of the interleaflet triangle to the tip of the commissure near the sinotubular junction. While commissural

height should ideally not be shortened, as this could induce prolapse, it is important to recognize that a relative reduction of commissural height is common during the suturing process of valve-sparing reimplantation. Consequently, the intraoperative measurement of effective height becomes mandatory after the procedure to ensure adequate coaptation and to exclude residual prolapse. The commissural height also serves as a reference for graft sizing in valve-sparing procedures.<sup>65</sup>

## Cardiac Magnetic Resonance

There is a growing role of CMR in assessing AR severity and LV dysfunction. The American<sup>5</sup> and European Society<sup>6</sup> guidelines recommend CMR as an additional diagnostic tool when echocardiography results are inconclusive or when further evaluation of AR severity is needed. When clinical symptoms and LV parameters at echocardiography do not align with severity of AR, further evaluation with CMR is recommended. This can happen with eccentric regurgitation jets. CMR is accurate in assessing the chamber volumes and function and the aortic dimensions. Phase contrast CMR sequences, at the sino-tubular junction level, allow for direct quantification of forward volume, regurgitant volume, and regurgitant fraction. Both CMR-regurgitant fraction and regurgitant volume offer higher reproducibility than the transthoracic echo derived.<sup>66</sup> Although formal cut-off values for hemodynamically significant AR are not yet defined, literature indicates that CMR-regurgitant fraction cut-offs ranging from 26% to 48% correspond with severe AR determined by echocardiography.<sup>67</sup> Moreover, higher AR severity by CMR is associated with increased symptom progression and a higher likelihood of requiring surgery. For example, a CMR-regurgitant fraction cut-off of 33% was found to predict surgery in 85% of cases, compared with 8% for those with a CMR-regurgitant fraction <33%.<sup>68</sup> Another parameter assessed by CMR is holodiastolic retrograde flow at the proximal descending thoracic aorta, which has shown to predict risk of death or heart failure hospitalization.<sup>69</sup> It is important to remember that lower thresholds of regurgitant fraction by CMR, compared with echocardiography, are linked to the progression of symptoms and adverse cardiovascular outcomes. CMR is the gold standard for LV volumetric assessment, offering precise and reproducible measurements. It helps monitor LV dilation and guides early intervention. CMR-derived LV end-diastolic diameter and LV end-systolic diameter thresholds predict symptom development and surgical needs. Recently an LV end-diastolic volume index of 155 mL/m<sup>2</sup> was found to be associated with incomplete reverse remodeling.<sup>70</sup> Myocardial fibrosis assessment via late gadolinium enhancement and extracellular volume predicts clinical outcomes, with fibrosis markers (quantification of fibrosis with T1 mapping



**Figure 4. Bicuspid aortic valve at magnetic resonance imaging including commissural orientation and variation of aortic annulus morphology in relation to the leaflet insertion line.**

Comparison between “on valve plane” cine-MR images and schemes of valve anatomy based on Sievers classification. Type 0 with antero-posterior and horizontal orientation; type 1 (1 raphe): L-R (left–right) and N-L (non-coronary/left); type 2 (2 raphe): N-R (non-coronary/right) and L-R.

and extracellular volume indicating increased mortality risk).<sup>71</sup> CMR has also a high resolution for the evaluation of the AV anatomy, therefore in defining trileaflet, bicuspid or unicuspid AV (Figure 4). In addition, CMR is equivalent to cardiac CT angiography for trans-aortic valvular implantation and surgical AV replacement planning. Therefore, CMR has the unique capability to evaluate in an “all-in-one technique” the principal severity parameters of AR (valve anatomy, valve hemodynamics, aortic remodeling, LV remodeling) and is able to provide pre-repair assessment and prognostic information.

### Cardiac CT

Cardiac CT is not the main tool for assessing AR severity as it does not measure flow directly. However, it can accurately evaluate aortic valve/root morphology, exclude dissection in the setting of acute AR and help quantify AR severity through geometric measurements of the anatomic regurgitant orifice area. CT planimetry for AR severity correlates well with CMR assessments. Regurgitant orifice area cut-off values of 15 and 23 mm<sup>2</sup> by CT effectively discriminate between mild, moderate, and severe AR as defined by CMR.<sup>72</sup> Cardiac CT is valuable for evaluating aortic root and ascending aorta dimensions. It accurately defines the aortic wall, and multiplanar reconstruction corrects shape distortions. Measurements of the aortic root and ascending aorta are highly reproducible, and indexing these dimensions to body size improves risk stratification.<sup>73</sup> From a surgical planning perspective, preoperative CT is essential for identifying coronary artery abnormalities. This is

particularly critical when a Ross procedure is contemplated, as precise knowledge of coronary anatomy is required for successful reimplantation.<sup>74</sup> Furthermore, in patients with BAV, coronary ostia are frequently more cranially displaced<sup>75</sup> and identifying these higher take-offs is crucial during valve-sparing procedures to prevent accidental injury to the coronary arteries during graft fixation.

### INDICATIONS FOR INTERVENTION AND PROGNOSIS

Determining the appropriate timing of surgical intervention for AR in young adults is particularly challenging because a large part of the major society guidelines is based on survival analyses conducted mainly in older adults with AV degeneration and a higher incidence of comorbidities with an increased perioperative risk.<sup>76</sup> Younger patients with congenital valve disorder often adapt their lifestyles to their limitations and may not report symptoms despite having objective exercise limitations, such as those revealed by abnormal cardiopulmonary exercise tests. Although young patients have fewer comorbidities, they frequently have a history of previous surgical or percutaneous interventions. When considering surgery for these young adults, the timing of intervention is crucial to prevent long-term complications and to reduce the number of surgeries needed throughout their lives.<sup>76</sup> Following an integrated approach, the timing of intervention should be guided by the presence of adverse prognostic factors. Key

**Table 3. Ventricular Parameters Associated with Adverse Outcomes, Including the Respective Threshold Values (Cut-Offs)**

Method	Parameter	Cut-off
Echocardiography/ CMR	LV ejection fraction	<55%–60%
Echocardiography	LVESVi	>45 mL/m <sup>2</sup>
	LVESDi	>20–25 mm/m <sup>2</sup>
	Global longitudinal strain %	From –15% to –19%
CMR	LVEDV	>246 mL
	LVEDVi	>129 mL/m <sup>2</sup>
	Global longitudinal strain	<–16%
	Extracellular volume index	>24 mL/m <sup>2</sup>

CMR indicates cardiac magnetic resonance; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVEDVi, left ventricular end-diastolic volume indexed; LVESDi, left ventricular end-systolic diameter indexed; and LVESVi, left ventricular end-systolic volume indexed.

indicators for surgical intervention include the development of symptoms or reduced exercise tolerance, as well as LV dilation or impaired LV function (see Table 3 where the ventricular parameters associated with adverse outcomes are listed).

Recent evidence and expert consensus have refined recommendations for the timing of intervention in young adults with AR, highlighting the importance of preventing irreversible myocardial damage and optimizing long-term outcomes.<sup>77</sup> Registry analyses indicate that earlier surgical intervention—before the onset of symptoms or advanced LV dysfunction—leads to better postoperative survival compared with waiting for the traditional class I triggers outlined in previous guidelines. Specifically, patients operated on when the LV end-systolic diameter index was 20 to 25 mm/m<sup>2</sup> or when LVEF declined to 50% to 55% had outcomes comparable with those with normal LV function, whereas postponing surgery until more advanced thresholds (LV end-systolic diameter >50 mm or LVEF <50%) was associated with a significant adverse impact on prognosis.<sup>78</sup>

Current guidelines indicate that surgery for severe AR is recommended in all symptomatic patients, and in asymptomatic individuals with LV dilation (end-systolic diameter >50 mm or LV index >25 mm/m<sup>2</sup>) or reduced EF (≤50%). In addition, in asymptomatic patients with severe AR, surgery may be considered (Class IIb) when LV end-systolic diameter index exceeds 22 mm/m<sup>2</sup> or when LV end-systolic volume index is >45 mL/m<sup>2</sup> or when resting LVEF is ≤55% and surgical risk is low.<sup>2</sup>

Beyond current guideline recommendations, emerging evidence suggests that reliance on

symptoms and conventional volumetric or functional thresholds alone may underestimate early myocardial and geometric remodeling in chronic aortic regurgitation. Persistent pressure and volume overload may lead to progressive myocardial injury that can become only partially reversible once overt LV dysfunction or symptoms develop. In this context, additional parameters such as myocardial strain, fibrosis markers assessed by cardiac magnetic resonance, and circulating biomarkers of subclinical heart failure may provide incremental prognostic information. In particular, the presence of focal or diffuse myocardial fibrosis and elevated B-type natriuretic peptide levels—values ≥130 pg/mL being associated with adverse outcomes—may identify patients at increased risk of irreversible remodeling and shift the risk–benefit balance toward earlier surgical intervention.<sup>77</sup> Overall, a myocardial biology–informed approach to timing may help maximize postoperative ventricular recovery and reduce late referral with established irreversible LV damage.<sup>77</sup>

Moreover, progressive LV dilatation may lead to secondary aortic annular dilatation, a well-established predictor of suboptimal outcomes after aortic valve repair<sup>79</sup> and valve-sparing root replacement.<sup>80</sup> Annular dilatation may also preclude the feasibility of other surgical strategies, including the Ross procedure<sup>81</sup> and the Ozaki procedure.<sup>80</sup> Therefore, appropriate timing of intervention is crucial not only to preserve myocardial function but also to avoid limiting future surgical options.

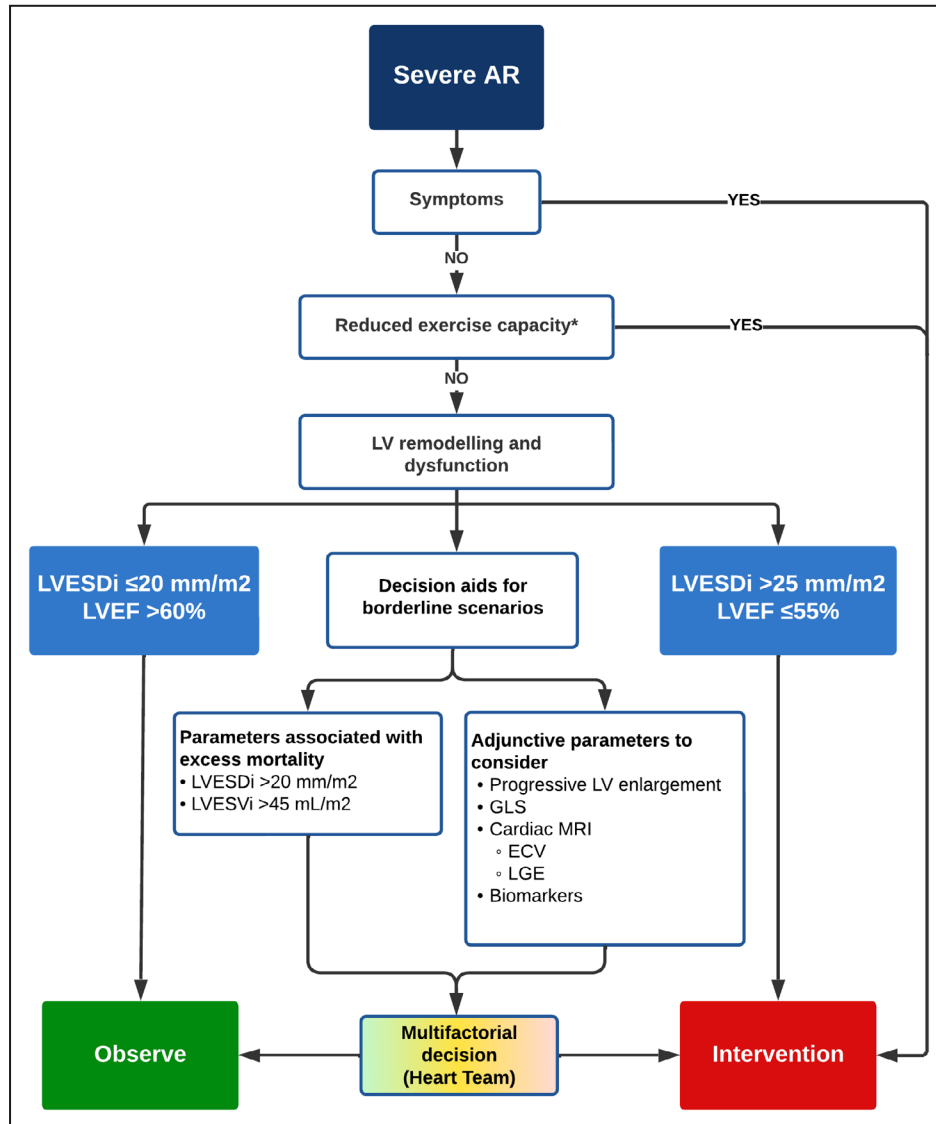
All major guidelines emphasize the importance of clinical decision-making through a multidisciplinary heart valve team. The assessment includes considerations of comorbidities, frailty, mobility, and any specific procedure-related limitations. Patients with severe asymptomatic AR should have follow-ups every 6 to 12 months. If there is a decline in LVEF or an increase in LV size, imaging should be repeated more frequently, at intervals of 3 to 6 months. For mild to moderate AR, follow-ups should occur every 1 to 2 years, and for mild AR, every 3 to 5 years.

Based on the clinical experience of the authors, a proposed flowchart is shown in Figure 5.

## TREATMENT STRATEGIES

The choice of the optimal surgical strategy for aortic regurgitation should be guided by the underlying mechanism of valve dysfunction.<sup>82</sup>

In Type I aortic regurgitation, characterized by normal cusp motion, treatment is directed at correcting annular, root, or ascending aortic dilatation. Isolated replacement of the ascending aorta may be sufficient



**Figure 5. Decision-making algorithm for severe aortic regurgitation.**

ECV indicates extracellular volume; LGE, late gadolinium enhancement; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVEDVi, left ventricular end-diastolic volume indexed; LVESDi, left ventricular end-systolic diameter indexed; LVESVi, left ventricular end-systolic volume indexed; and MRI, magnetic resonance imaging. \*Evaluated with an exercise test.

in Type Ia regurgitation, whereas Type Ib regurgitation due to aortic root dilatation is typically managed with valve-sparing root replacement or root remodeling procedures. In Type Ic regurgitation, caused by annular dilatation, sub-commissural or ring-based annuloplasty techniques have emerged as effective strategies to stabilize the annulus and improve repair durability. Leaflet perforation (Type Id) is usually addressed with patch repair.

In Type II aortic regurgitation, excessive cusp motion because of leaflet prolapse represents the predominant mechanism and is managed with leaflet repair techniques aimed at restoring effective

coaptation, including free-margin plication, triangular resection, or leaflet resuspension, often combined with annuloplasty.

In Type III aortic regurgitation, restricted cusp motion because of fibrosis or calcification may be addressed with cusp mobilization or limited decalcification; however, repair durability is often limited compared with type I and II,<sup>83</sup> and valve replacement may therefore represent a more appropriate option in selected patients.

In patients with bicuspid aortic valves, similar repair principles apply, but operative complexity is increased and outcomes depend on valve phenotype, with more

symmetrical configurations associated with better durability. When valve anatomy is unfavorable or leaflet tissue quality precludes a durable repair, surgical aortic valve replacement is generally preferred, with the Ozaki procedure or the Ross procedure representing potential alternatives in carefully selected patients.

One of the major challenges for physicians caring for patients with AR is optimizing long-term outcomes while minimizing the number of interventions throughout the patients' lifetime, especially in young patients. Traditionally, the primary treatment for severe AR has been surgical AV replacement. However, modern techniques now include surgical repair and TAVR. Surgical AV replacement in patients with isolated AR (no aorta dilatation) has been the gold standard for many years and is considered a safe, reproducible procedure. However, prosthetic valve replacement has significant limitations, especially in the young population, including thromboembolism, bleeding, limited long-term durability and eventually reduced life expectancy compared with the general matched population.<sup>84</sup>

The longevity of a valve prosthesis is related to the type of valve chosen; despite mechanical prostheses being considerably more durable, most young patients opt for bioprosthetic valves.

In addition to classical indications, there are less common but clinically relevant scenarios in which intervention may be appropriate, particularly when discussed within the Heart Team framework. These special situations in young adults include severe AR in patients planning future pregnancy or with imminent exposure to extreme altitudes/intense activity. Indeed, young individuals who want to remain active or become pregnant often choose biological prostheses. The Ross procedure, which involves replacing the diseased AV with the patient's own pulmonary autograft, is an excellent option for young patients seeking to avoid lifelong anticoagulation. While pure AR and aortic root dilatation were historically viewed as potential contraindications because of the risk of autograft failure, contemporary surgical techniques have challenged this paradigm. Recent evidence demonstrates that the Ross procedure yields excellent long-term outcomes in patients with AR, provided that the autograft is adequately supported to prevent late dilatation.<sup>85,86</sup> Specifically, Poh et al. reported an 85% freedom from reoperation at 20 years in adults with BAVs and pure AR.<sup>86</sup> Thus, rather than being a contraindication, the presence of AR necessitates a tailored surgical approach—such as autograft reinforcement—to ensure durability comparable to that seen in aortic stenosis patients.

Regarding pregnancy, current guidelines recommend surgical intervention before pregnancy in women with severe AR who present with symptoms, impaired LV function, or significant LV dilatation (Class I, level

of evidence C). Surgery during pregnancy should be reserved for situations where maternal mortality risk is high, and all other treatment options have been exhausted (Class IIa, level of evidence C). In women of childbearing age who require valve replacement, careful planning is essential. Whenever possible, valve repair or the use of bioprosthetic/non-mechanical valves is preferred to minimize or avoid the need for long-term anticoagulation. Decisions on the valve type should be individualized, ideally involving a multidisciplinary cardio-obstetric heart team, to balance maternal and fetal risks while considering future pregnancies.<sup>87</sup>

Although AV repair versus replacement has never been compared head-to-head in a prospectively randomized trial, recent data in the literature suggest that AV repair can offer prolonged durability compared with a bioprosthesis and a better survival rate and a better quality of life with fewer valve-related events compared with a mechanical valve.<sup>88</sup> AV repair, therefore, may be a viable alternative to valve replacement in selected patients with AR. Recent advancements, such as improved stabilization through circumferential annuloplasty and systematic assessment of valve configuration using the effective height concept at transesophageal echo and intraoperatively by the dedicated caliper, have significantly contributed to its broader adoption. This standardized approach, pioneered by Schäfers et al., allows for objective verification of cusp geometry to ensure optimal coaptation and long-term durability.<sup>89</sup> The goal of AV-sparing surgery and repair is to restore the geometric relationship between the different components of the AV and root, and to stabilize the repair, with annuloplasty or an aortic graft, which improves long-term durability. The 2025 European guidelines<sup>5</sup> classify aortic valve repair with an oral anticoagulant indication as Class IIa, Level B in selected patients at experienced centers when durable results are expected. When considering repair, the aorta phenotype and the mechanism of AR are the most important factors. It is important to accurately characterize proximal aortic dilation, when present.<sup>2</sup> Based on the different phenotype of proximal aortic dilation, a specific surgical approach is considered. As for the mechanism of AR, AV repair is generally more durable in patients with El Khoury classification type I and type II than in type III AR. Therefore, AV repair is generally performed in the first 2 types. The one exception in which pure type III AR is considered for AV repair is in pediatric and adolescent patients.<sup>90</sup> The feasibility of AV repair is heavily dependent on the quality and quantity of available cusp tissue. Standardized cut-off values for geometric height have been established by leading centers in Homburg and Brussels to identify cusp retraction, a condition that significantly compromises repair durability.<sup>65,91</sup>

For tricuspid AV, a gH <16 mm is generally considered indicative of retraction, while in BAV, the threshold

is typically <19 to 20mm (because of the larger dimensions of BAV leaflets). As synthesized by Abeln et al.,<sup>92</sup> valves falling below these thresholds may not be suitable for reconstruction and might require replacement.

Furthermore, a recent systematic analysis by Almaghrabi et al. emphasizes that while most mechanisms of AR in tricuspid AV are potentially repairable (such as prolapse or root aneurysm), severe cusp retraction or extensive calcification remain the primary reasons for choosing replacement over repair.<sup>93</sup> This highlights the necessity of systematic assessment to tailor the surgical strategy to the specific valve pathology. Additional factors to consider are patient's age, LV function, lesion complexity, experience of the center and other intraoperative parameters. The repair should be considered satisfactory when residual AR is mild (grade I) or less. Cusp prolapse is a common issue in AR, typically managed by shortening the free margin of the cusp to ensure proper coaptation. For cases involving cusp fenestrations or other specific lesions, patch repair might be necessary, although this can impact long-term durability. Advances in annuloplasty techniques, such as double sub- and supra-annular annuloplasty, have improved repair stability and outcomes, making AV repair a viable alternative to replacement, particularly in younger or growing patients.<sup>90</sup> AV repair is an appealing alternative to replacement, especially in younger patients. Advances in understanding BAV and surgical techniques over the last 2 decades have improved repair outcomes. BAVs show a spectrum of phenotypes, from symmetrical to asymmetrical, with varying repair stability based on commissure orientation.<sup>37</sup> Cusp prolapse is an important cause of AR in tricuspid AV and can be caused by myxomatous degeneration or cusp fenestration. Giebels reports that AV repair in patients with AV prolapse in tricuspid morphology causing AR with preserved root dimensions is related to an acceptable durability.<sup>94</sup>

Successful BAV reconstruction requires a systematic approach that addresses both the valve and the aortic root components. The primary surgical goals include restoring optimal cusp configuration and coaptation, stabilizing the aortic annulus, and reducing the sinotubular junction when necessary to ensure an adequate fit for the geometric high and effective high. Furthermore, achieving a symmetrical commissural orientation is critical for long-term stability. These objectives can be accomplished through various surgical techniques, such as cusp plication for prolapse correction, circumferential annuloplasty, sinotubular junction reduction via ascending aortic replacement or dedicated sutures, sinus plication, and valve-sparing root replacement. Achieving a favorable commissure orientation, typically >160°, improves valve geometry and durability, with leading centers reporting over 90% freedom from reoperation after nearly a decade.<sup>95</sup> Aortic

repair techniques showed good mid- and long-term clinical results in both tricuspid AV and BAV with some authors reporting a higher incidence of reintervention in patients with BAV.<sup>96</sup> Some recent published data suggest that AV repair surgery, whenever intraoperatively feasible, is associated with a significantly better 1-year survival and 1-year cardiac event-free survival compared with AV replacement.<sup>97</sup>

## Ozaki Procedure

The Ozaki procedure, first introduced in 2007, is a technically demanding but attractive alternative to conventional AV replacement and repair. The technique involves resection of the diseased aortic leaflets followed by individual leaflet reconstruction using autologous pericardium or a tissue substitute, a process known as neocuspidization.<sup>98</sup> The primary goal is to create a large coaptation zone, thereby minimizing cusp strain and stress while ensuring a large effective orifice area. By preserving native aortic valve geometry, the Ozaki procedure allows physiological adaptation of the aortic root throughout the cardiac cycle, closely reproducing the function of a native tricuspid aortic valve.<sup>99</sup> One of the main advantages of the Ozaki procedure is its excellent hemodynamic performance with very low transvalvular gradients and a low incidence of patient-prosthesis mismatch. Long-term data from the Ozaki series report a mean AV gradient of approximately 8mmHg at 10years.<sup>98</sup> In addition, the technique permits preservation of native aortic root dynamics and artificial augmentation of valve coaptation height, a feature that may be particularly relevant in pediatric and younger patients.<sup>99</sup> Another major advantage is the avoidance of long-term anticoagulation, making this approach especially appealing in women of childbearing age and patients with contraindications to anticoagulant therapy. Furthermore, low rates of permanent pacemaker implantation (1.5% in large series) have been consistently reported.<sup>98</sup>

The Ozaki procedure has been applied across a broad spectrum of AV pathologies, including stenotic, regurgitant, and mixed lesions of congenital, degenerative, infective, and rheumatic origin, and in both tricuspid and bicuspid valve morphologies. Compared with surgical bioprosthesis, the Ozaki procedure is associated with lower transvalvular gradients, albeit at the expense of higher rates of recurrent AR.<sup>100</sup> In the pioneering cohort of 1196 patients reported by Ozaki and colleagues, 10-year follow-up demonstrated 93.4% freedom from moderate or greater AR, 91.2% freedom from reoperation, and a survival rate of 75%.<sup>98</sup> In light of these considerations, the Ozaki procedure represents a valuable option in the aortic surgeon's armamentarium, particularly for patients in whom lifelong anticoagulation is undesirable, those at

increased risk of patient–prosthesis mismatch or early degeneration with a bioprosthetic valve, or when the Ross procedure may be suboptimal, such as in cases of predominant AR with annular or root dilatation.<sup>81</sup> Likewise, valve-sparing root replacement may yield suboptimal outcomes in patients with BAVs, those undergoing complex valve repair,<sup>101</sup> or with significant annular dilatation.<sup>80</sup> In addition, the Ozaki procedure may represent a valuable alternative to AV repair in selected patients in whom repair is technically not feasible or unlikely to provide durable results, further highlighting its potential role in this challenging subset. The procedure has recently been updated with the introduction of new dedicated tools and leaflet templates. Vital to successful outcome is a meticulous and highly standardized surgical approach, with strict adherence to each procedural step and systematic use of dedicated instrumentation. Despite these favorable outcomes, several considerations should be acknowledged when interpreting the broader applicability of the Ozaki procedure. Compared with standard surgical valve replacement, the operation is associated with longer cardiopulmonary bypass and aortic cross-clamp times, underscoring the importance of surgical experience and procedural standardization. The development of late AR remains a potential concern, with reported rates of approximately 7% at mid- to long-term follow-up. Infective endocarditis represents a relevant cause of late valve reoperation.<sup>98</sup> In addition, although mid- and long-term outcomes are encouraging, durability beyond the second decade has yet to be fully established, a consideration of particular relevance in very young patients. Finally, despite the initial uncertainty about the feasibility of TAVR for structural valve degeneration after the Ozaki procedure—because of the presence of tall reconstructed cusps and the potential risk of coronary obstruction—a recent study involving 11 patients reported no cases of coronary obstruction and a technical success rate of 91%. Therefore, TAVR appears to be a feasible option and may be considered in selected cases when performed in experienced centers.<sup>102</sup>

### Transcatheter Alternatives

While surgical intervention remains the gold standard for severe AR, especially in young patients, TAVR has emerged as an alternative for those deemed unsuitable for surgery. However, its use in isolated AR is challenging because of the absence of leaflet calcification and the presence of root dilation, which hinder stable device anchoring. Current guidelines reflect this uncertainty, with the European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) providing a Class IIb recommendation

for inoperable cases, while the American College of Cardiology/American Heart Association guidelines generally do not recommend TAVR for isolated AR (Class III). First- and second-generation devices were not specifically designed for AR, and often required significant oversizing to ensure device stability in the absence of calcification, leading to higher rates of aortic root injury and conduction disturbances, reported in large series to reach 1.5% and 22%, respectively.<sup>103</sup> In addition, conventional valves carry a non-negligible risk of device embolization and moderate-to-severe residual AR, observed in 12.4% and 9.5% of cases, respectively.<sup>104</sup> Although newer-generation systems with dedicated anchoring mechanisms, such as the JenaValve Trilogy and J-Valve, have shown improved procedural success and favorable short-term outcomes in observational studies,<sup>105</sup> their role in the young population remains extremely limited. A major limitation in this field is the lack of randomized controlled trials directly comparing TAVR and surgical AV replacement in patients with isolated AR. Current evidence mainly comes from observational registries and meta-analyses, which report conflicting results, some indicating improved mortality outcomes with TAVR, while others show worse outcomes. High-quality randomized control trials are urgently needed to clarify whether expanding TAVR indications to patients with native AR beyond those at high surgical risk is appropriate.

### CONCLUSIONS

Management of severe AR is challenging, especially for young adults, not only to avoid long-term sequelae but also to minimize the number of surgeries across their lifespan. The accurate diagnosis and severity assessment is crucial for addressing the best management. Evaluation of AR entails assessing valve morphology, severity, aortic root and LV remodeling, and should entail comprehensive multi-modality imaging. There is a growing role in assessing AR severity and LV dysfunction with CMR. Clinicians should carefully balance the long-term benefits of AV surgery against procedural risks and future interventions, especially in younger patients. Evidence-based criteria for AV replacement, repair or TAVR in severe AR in young adults are to be weighed carefully to improve outcomes. Because younger patients tend to prefer biological valves because of lifestyle considerations, vigilance is required to promptly detect and manage prosthetic valve complications. Repair is the preferred surgical treatment in young patients with AR and/or proximal aorta aneurysm. Many of the favorable surgical outcomes discussed in the review reflect the experience of centers of excellence. It is important to consider the learning curve effects. Repair

durability and complex reconstructive strategies are dependent on the experience of the surgeon and the center. Further studies are needed to identify the optimal timing and strategies for AV surgery.

## ARTICLE INFORMATION

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### Disclosures

None.

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