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# ANMCO position paper: 2022 focused update of appropriate use criteria for multimodality imaging: aortic valve disease

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# **KEYWORDS**

Multimodality imaging; Appropriateness use criteria; Aortic valve disease This document addresses the evaluation of the Appropriate Use Criteria (AUC) of multimodality imaging in the diagnosis and management of aortic valve disease. The goal of this AUC document is to provide a comprehensive resource for multimodality imaging in the context of aortic valve disease, encompassing multiple imaging modalities. Clinical scenarios are developed in a simple way to illustrate patient presentations encountered in everyday practice.

These updated Appropriate Use Criteria (AUC) are focused on valvular heart disease (VHD) and reflect a thorough review of recent American and European Guidelines for the management of VHD. The method applied in our previous work<sup>1</sup> is briefly reported.

The concept of appropriateness as applied to health care includes consideration of benefits and risks. Appropriate Use balances the risks and benefits of a treatment, diagnostic test, or procedure within the resources available for a given patient with specific characteristics.

The basic definition states: 'An appropriate diagnostic or therapeutic procedure is one in which the expected clinical benefit exceeds the risks of the procedure by a sufficiently wide margin such that the procedure is generally considered acceptable or reasonable care'.<sup>2</sup>

When applied to diagnostic imaging procedures, benefits consist of incremental information at each stage of the process model proposed by Douglas to optimize patient treatment and improve health outcomes.<sup>3</sup>

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The benefits of incremental information of imaging are weighed against the expected negative consequences (risks include the possibility of missed diagnoses, the use of radiation, contrast agents, and/or unnecessary downstream procedures).

In more recent documents, the term 'appropriateness criteria' has been replaced by the term AUC. This change reflects the more active function of the AUC in promoting evidence based, effective use of cardiovascular technologies.

The publication of AUC reflects the growing effort of the Scientific Societies to 'create review, and systematize in a creative and organic manner all those clinical situations in which diagnostic tests and procedures are used by clinicians also for patients with cardiovascular disease'.<sup>4</sup>

The process is based on the current knowledge of techniques and their application in several imaging methods. AUCs of the various cardioimaging methods should be formulated for all diseases.

The updated terms and definitions of AUCs reflect their application in practice, including an expected distribution between each AUC category for every population, methods for documenting exceptions, and proper application to individual patients.

The AUCs are classified into three groups:

- (1) Appropriate (A): score 7-9;
- (2) May be appropriate (M): score 4-6; and
- (3) Rarely appropriate (*R*): score 1-3.

The terms inappropriate and uncertain are no more used.

The AUC Development is based on the four-step process revision: Step 1: topic selection, nomination process, and writing group composition; Step 2: indication development and literature review; Step 3: external review of clinical indications; and Step 4: panel rating.

The attribution of a diagnostic test to one of the three groups is a very articulated process divided into different stages. Usually, a panel of experts evaluates the test by assigning a score based on scientific evidence (guidelines, recommendations, etc.). In addition to imaging technicians and experts, the panel includes clinicians to assess the possibility that one method might be preferred over another or to avoid that strategies that do not involve the use of diagnostic tests are not taken into due consideration.

The drafting and the verification of AUCs are created through a flow of activities that can feature diverse mechanisms depending on the methods and Societies.<sup>5</sup> AUCs can be applied through two different methods. The first method starting from each imaging test considers its appropriateness in different clinical scenarios. The second method starting from each clinical scenario considers the appropriateness of the different imaging tests. This latter method seems the most suitable to highlight the performance of multimodal imaging.

The previous consensus document<sup>1</sup> was developed taking into account the international guidelines and published scientific papers, as well as the clinical and legislative setting in Italy and the many professional profiles involved in the management of patients. The availability of imaging Lab throughout the whole national territory was also considered. In drafting and elaborating the document, we decided to implement the following methodology that involved 48 writers, 12 reviewers, and 24 professionals for rating:

- (1) Writing panel. The writing panel consisted of 48 writers. For each chapter at least one clinician and one imaging expert were considered. They referred to the most recent and appropriate guidelines, recommendations, and of course, if already present in the literature, to publications on AUCs. The authors then drew up a grid as the first proposal of appropriateness grading.
- (2) Review panel. Individual chapters were reviewed by the 5 coordinators of the document.
- (3) Rating panel round 1. All chapters were presented by the writing panel, discussed jointly with the authors of the document and with a panel of imaging and clinical experts, composed of 24 professionals belonging to the Scientific Societies involved in the document, and voted concomitantly. The level of appropriateness is directly proportional to the score given.
- (4) Rating panel round 2. Each chapter was subsequently re-evaluated by the individual authors with the Review Panel, by integrating comments and changes that had been approved during the first round of panel rating, and then underwent final revision.
- (5) Writing panel. All chapters were finalized in the same format.

The most critical and discussed/shared issue was the choice of the clinical scenarios that are the field of use of the diagnostic tests. In general, for each of the main pathologies we considered 'the majority of clinical scenarios, avoiding excessive lists', using a practical approach common to the most important scientific works on criteria of appropriateness of imaging tests 3, as proposed, for example, by Garbi *et al.*<sup>6</sup>

The present document does not aim to explain how methods work nor to illustrate the disease aspects detectable in a given pathology. If it is necessary to indicate the choice of an imaging test over another in the case of the same appropriateness rating, this information is given in the text.

We focused our interest to native chronic valve disease and starting from our previous experience, AUCs were reevaluated and updated considering recent specific Guidelines.<sup>7-11</sup>

# Chronic valvular heart disease

Multimodality Imaging plays a pivotal role in the different diagnostic steps of VHD assessment, confirming diagnosis, assessing aetiology, physiopathology, severity and prognosis of VHD. The haemodynamic consequences of valve obstruction or valve regurgitation on the cardiac chambers, on the left and right ventricle function, and on pulmonary vasculature are exhaustively characterized by Multimodality Imaging.

Aortopathy (abnormalities of the aortic root and ascending aortic geometry and dimension), myocardial involvement (scar, fibrosis, viability), coronary artery disease, and pericardial disease are well assessed by multimodality imaging.

Multimodality imaging helps to decide the medical, interventional, or surgical treatments. Transcatheter therapy for VHD was initially limited to balloon valvuloplasty but afterwards many different devices were introduced for catheter-based approaches of regurgitant as well as stenotic valvular disease. Multimodality imaging plays an essential role in identifying patients suitable for transcatheter procedures and transesophageal echocardiography is now routinely used for intra-procedural and intra-operative monitoring.

Stenosis and regurgitation can be found on the same valve and disease of multiple valves may be present in the same patient not only in rheumatic and congenital heart disease but also in degenerative and actinic valve disease. There is a lack of data on combined or multiple-valve diseases and evidence-based recommendations are not as many as for the management of single valve disease.

In this complex picture, each patient should be meticulously evaluated in the different stages of his VHD. Decisions about treatment are based on the symptoms that patients may not recognize because they have gradually limited physical activities to avoid symptoms. In these patients, dynamic components of valve heart disease influenced by loading conditions and ventriculo-arterial coupling and subclinical myocardial dysfunction, could be missed at rest. Modifying loading conditions, flow states and ventricular performance with exercise testing or with pharmacological stress<sup>12,13</sup> the dynamic changes in valvular and ventricular function can unmask the symptoms of patients and the severity of valve heart disease.<sup>14</sup>

Decisions concerning treatment and intervention should not be made by Cardiac Imagers alone but by all physicians experienced on management of different aspects of VHD. Clinical cardiologists, cardiovascular multimodality imaging cardiologists, interventional cardiologists, cardiac surgeons, cardiovascular anaesthesiologists, and other specialists if necessary (psychologists, geriatrics, electrophysiologists) are comprised in the Heart Team that is one of the requirements to define the Heart Valve Centre, centre of excellence in the treatment of the heart valve disease.

# Scenario 1: patient with suspected valvular heart disease

Patients with suspected VHD may present with auscultatory finding of a heart murmur, atypical symptoms, incidental findings of ECG abnormalities or valvular abnormalities on non-invasive testing. Some patients with familiarity with valvular disease (bicuspid aortic valve, Barlow's disease) are at risk for VHD. Irrespective of the presentation, all patients with known or suspected VHD should undergo an initial meticulous history and physical examination. A careful history is of great importance in the evaluation of patients with VHD because decisions about treatment are based on the presence or absence of symptoms. A detailed physical examination should be performed to diagnose and assess the severity of valve lesions based on a compilation of all findings made by inspection, palpation, and auscultation. The use of an electrocardiogram (ECG) to confirm heart rhythm and use of a chest X-ray to assess the presence or absence of pulmonary congestion and other lung pathology may be helpful in the initial assessment of patients with known or suspected VHD. Following clinical evaluation, a comprehensive transthoracic echocardiogram with two-dimensional imaging and Doppler interrogation should be performed for diagnosis and complete evaluation of VHD. TTE-2D and Doppler are mostly sufficient to rule out VHD diagnosis or to confirm and define the diagnosis of VHD by assessing its anatomy and possibly its aetiology, mechanisms and valve haemodynamics, grading its severity and assessing the compensatory adaptation of cardiac chambers and vasculature (Table 1).

Patients with VHD, who underwent appropriately ordered TTE,<sup>15</sup> were significantly more likely to have a better management undergoing appropriately subsequent cardiac testing within 90 days and valve intervention within 1 year than patients who rarely underwent TTE, suggesting that appropriate TTE is more likely to influence clinical decision-making.

Bidimensional transoesophageal echocardiography with Doppler interrogation is considered if TTE is suboptimal or inconclusive and clinical suspicion of VHD is high or in case of discrepancy on some data.

Other non-invasive investigations are not appropriate in this scenario.

If a VHD is diagnosed, the subsequent decisional steps are considered in specific scenarios.

#### Scenario 2: aortic stenosis

Once aortic stenosis (AS) has been diagnosed, imaging is used to assess anatomy and possibly aetiology (bicuspid aortic valve) evaluating the morphology and the number of the cusps, the presence and extent of calcifications, to assess the severity of obstruction, left ventricle (LV) function, and wall thickness, to detect other valve diseases or aorta pathology. Chronic pressure overload results in concentric LV hypertrophy and in left atrial enlargement. Left atrial function plays an important role to prevent rising of the pulmonary venous and capillary pressures (*Table 2*).

All these information can be mostly obtained with TTE. TTE is the clinical imaging modality of choice allowing direct visualization of aortic valve anatomy, function, and haemodynamics, also making possible measurement of the left ventricular wall thickness, internal chamber dimensions, and both systolic and diastolic function.

The measures of AS severity that are appropriate for all patients with AS are based on 2D-TTE and Doppler. The primary haemodynamic parameters recommended for the clinical evaluation of AS severity are: AS peak jet velocity, mean transvalvular pressure gradient, and effective aortic valve area by continuity equation (functional area). If TTE is unable to assess AS severity,<sup>16</sup> in patients with poor acoustic windows, flow alignment difficulties or inaccurate aortic annulus diameter measurement, or mostly discordant or

| Table 1 Patient with suspected valvular heat | rt disease        |       |             |       |        |       |
|--|-------------------|-------|-------------|-------|--------|-------|
|  | TTE               | TEE   | Stress echo | СТ    | CT COR | MRI   |
| Scenario 1                                   |                   |       |             |       |        |       |
| Suspected VHD (rule out)                     |                   |       |             |       |        |       |
| Heart murmur, atypical symptoms, famili      | arity for valvulo | pathy |             |       |        |       |
| Diagnosis (anatomy, aetiology)               | A (9)             | M (4) | R (1)       | R (1) | R (1)  | R (1) |
|  |                   |       |             |       |        |       |

CT, computed tomography; CT COR, computed tomography coronary; MRI, Magnetic Resonance Imaging; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography echocardiogram; VHD, valvular heart disease.

### Table 2 Aortic stenosis

|                                     | TTE   | TEE   | Stress echo | СТ    | CT COR | MRI   |
|-------------------------------------|-------|-------|-------------|-------|--------|-------|
| Scenario 2. Aortic stenosis. Stages |       |       |             |       |        |       |
| Asymptomatic (follow-up)            |       |       |             |       |        |       |
| Diagnosis (anatomy, aetiology)      | A (9) | M (4) | R (1)       | A (7) | R (1)  | M (4) |
| Number of cusps                     | A (7) | A (9) | R (1)       | A (7) | R (1)  | A (9) |
| Calcification                       | M (6) | A (8) | R (1)       | A (9) | R (1)  | A (7) |
| Severity (grading)                  |       |       |             |       |        |       |
| Primary measures                    | A (9) | M (4) | A (9)       | R (1) | R (1)  | M (4) |
| Alternative measures                | A (7) | A (9) | A (9)       | A (7) | R (1)  | A (9) |
| Symptomatic                         |       |       |             |       |        |       |
| Diagnosis (anatomy, aetiology)      |       |       |             |       |        |       |
| Number of cusps                     | A (7) | A (9) | R (1)       | A (7) | R (1)  | A (9) |
| Calcification                       | M (6) | A (8) | R (1)       | A (9) | R (1)  | A (7) |
| Severity (grading)                  | A (9) | M (4) | A (9)       | A (7) | R (1)  | M (4) |
| Primary measures                    | A (9) | M (4) | A (9)       | R (1) | R (1)  | M (4) |
| Alternative measures                | A (7) | A (9) | A (9)       | A (7) | R (1)  | A (9) |
| Associated heart disease            |       |       |             |       |        |       |
| Valvular                            | A (9) | A (7) | R (1)       | A (7) | R (1)  | A (7) |
| Aorta                               | A (9) | A (7) | R (1)       | A (9) | R (1)  | A (7) |
| Pulmonary pressure                  | A (9) | R (1) | R (1)       | R (1) | R (1)  | R (1) |
| LV dimension and function           | A (9) | M (4) | R (1)       | R (1) | R (1)  | A (9) |
| Pericardial                         | A (9) | R (1) | R (1)       | M (6) | R (1)  | M (4) |
| Coronary artery disease             | R (3) | R (1) | A (7)       | R (1) | A (7)  | M(4)  |
| Indication to SAVR                  | A (9) | A (7) | A (7)       | M (6) | M (6)  | M (6) |
| Indication to TAVI                  | A (9) | A (7) | A (7)       | A (9) | A (7)  | M (6) |

CT, computed tomography; CT COR, computed tomography coronary; MRI, Magnetic Resonance Imaging; LV, left ventricle; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography echocardiogram.

inconclusive findings in the grading of AS severity, other options can be considered. These alternative measures of stenosis severity include aortic valve planimetry (anatomic area) using 3D-TEE that overcomes the limit of 2D-TTE and 2D-TEE for properly detecting non-planar structures.<sup>17</sup> Cardiac magnetic resonance imaging (MRI) is a good and reliable alternative to echocardiography<sup>18</sup> for a better definition of the anatomy and the area of aortic orifice.<sup>19</sup>

Other alternative or experimental measures can be used by expert and trained cardiac imagers in Heart Valve Centre.

Valvular calcification is strong predictor of aortic valve replacement and mortality<sup>20</sup> and significant valve calcification is also associated with faster disease progression predicting clinical events.<sup>21</sup> The extent and distribution of valve calcification can be accurately quantified on ECG

gated non-contrast computed tomography (CT). The calcium score can be measured using the Agatston score that correlates with primary echocardiographic measures of severity of AS.

Increased wall thickness develops as response to chronic pressure overload and assessment of LV mass, geometry and function is critical for the management of patient with AS. Development of hypertrophy may be heterogeneous and the degree of increased wall thickness may be not proportionate to the severity of AS.

LV fibrosis in AS is part of the hypertrophic response and Cardiac MRI is the only non-invasive technique that allows direct global assessment of focal and diffuse fibrosis.

Degenerative AS and age-related transthyretin cardiac amyloidosis<sup>22</sup> share common demographic and clinical

characteristics. Many patients undergoing transcatheter aortic valve replacement have occult cardiac amyloidosis. Even though TTE (2D, Doppler, Strain) may be helpful to diagnosis confirmation by Cardiac MRI is required to confirm diagnosis.<sup>23</sup>

The assessment of left ventricular function based on Echocardiographic LV ejection fraction (LVEF) is used in clinical guidelines to reflect LV systolic function. LVEF is an insensitive measure of LV systolic dysfunction in hypertrophied ventricle. LVEF remains preserved for long time in patients with AS and LV structural and functional abnormalities as demonstrated using cardiac magnetic resonance.

Other LV quantification measurements better than LVEF to more accurately assess the consequences of AS are now available. Speckle-tracking echocardiographic (STE) imaging is a novel imaging technique that enables the quantification of LV myocardial deformation. STE imaging is the more widely used technique and can be applied for studying myocardial deformation<sup>24</sup> so that subclinical myocardial dysfunction can be easily identified (Global Longitudinal strain).<sup>25,26</sup>

In patients with severe AS without symptoms tests eliciting symptoms are needed to identify the patients eligible for aortic valve replacement (surgical or transcatheter replacement). Exercise test performed by trained cardiologist is safe and exercise stress echo provide incremental prognostic value.<sup>27</sup>

In non-severe valve disease with symptoms many stress tests can be used to evaluate the actual severity of AS analysing stress-induced changes of different severity parameters.

In AS with low flow, the aim of the test is to determine severity of the valve disease analysing flow dependent changes in severity parameters with stress.<sup>28</sup>

The European Guidelines<sup>11</sup> define four categories of AS based on mean transvalvular pressure gradient, effective aortic valve area by continuity equation and indexed stroke volume.

In high-gradient AS, severe AS, can be assumed irrespective of LV function and flow conditions.

In low-flow, low-gradient AS with reduced ejection fraction (EF), low-dose dobutamine stress echocardiography is recommended to distinguish between true severe and pseudo-severe AS<sup>29</sup> and identify patients with no flow (or contractile) reserve.<sup>30</sup>

In low-flow, low-gradient AS with preserved EF, diagnosis of severe AS is challenging<sup>31</sup> and requires CT assessment of the degree of valve calcification that provides important additional information.<sup>32</sup>

Various combinations of cardiac diseases may be encountered. Combined VHD, aortopathy, myocardial involvement, coronary artery disease, pericardial disease, and pulmonary hypertension may be associated with AS.

In these cases, the most appropriate method based on specific AUC will be chosen for each of them. For example, in patients with AS and associated coronary artery disease, echo-stress, Single Photon Emission Computed Tomography (SPECT), coronary CT, coronary angiography are usually appropriate.

Indications for interventions [surgical aortic valve replacement (SAVR) or transcatheter aortic valve In Symptomatic patients with severe AS documented by Multimodality Imaging, intervention is recommended regardless of LVEF.

Management of patients with low-gradient AS is more challenging and intervention is recommended if severe AS is unmasked by stress echocardiography (true severe AS vs. pseudo-severe AS).

In asymptomatic patients with severe AS and impaired LV function of no other cause as documented by Multimodality Imaging, intervention is recommended.

In other asymptomatic patients with severe AS exercise testing is helpful in unmasking symptom status. When symptoms are provoked by exercise testing, the patient is considered symptomatic. 'Symptoms are symptoms, whether reported spontaneously by the patient or provoked on exercise testing'.<sup>10</sup>

In TAVI diagnostic workup, CT is the preferred imaging tool to assess aortic valve anatomy, annular size and shape, extent and distribution of valve calcifications, and aortic root dimensions.

CT-guided assessment of aortic valve anatomy is an integral part of procedural planning and is important because of its ability to recognize the different morphological patterns particularly in case of bicuspid aortic valve that has significant potential to influence outcome.<sup>33</sup>

Careful quantification of annular dimensions and description of annular and sub-annular calcification (landing zone) can be obtained with CT.

CT provides greater predictive value for vascular complications than invasive angiography analysing iliofemoral vessel size, calcification, and tortuosity. This information is required to determine if transfemoral access can be achieved or whether an alternative access route is required (subclavian, axillary, carotid, transcaval, or transapical).<sup>34</sup>

CAC detected with Coronary CT can rule out significant coronary stenosis with high negative predictive value. Assessment of coronary stenosis severity is difficult due to a high prevalence of coronary calcification in elderly patients. Coronary CT disease can be considered in appropriately selected patients, if the image quality is of diagnostic quality, to avoid coronary angiography.

Coronary occlusion is a relatively rare complication of TAVI but is associated with a poor clinical outcome and with high mortality. CT is well established as the pre-procedural imaging gold standard for the determination of the risk of coronary occlusion allowing the precise measurement of coronary ostial height.<sup>35</sup>

#### Scenario 3: aortic regurgitation

Once aortic regurgitation has been diagnosed, imaging is used to assess anatomy and when possible aetiology and mechanism of regurgitation, to assess the severity of regurgitation, LV dimension and function, to detect other valve diseases (*Table 3*).<sup>9-11</sup>

TTE is the clinical imaging modality of choice to obtain the first general and comprehensive assessment of valvular

|                                   | TTE   | TEE   | Stress echo | СТ    | CT COR | MRI   |
|-----------------------------------|-------|-------|-------------|-------|--------|-------|
| Scenario 3. Aortic regurgitation  |       |       |             |       |        |       |
| Asymptomatic                      |       |       |             |       |        |       |
| Diagnosis and follow-up           |       |       |             |       |        |       |
| Anatomy, aetiology                | A (9) | M (6) | R (1)       | M (4) | R (1)  | M (4) |
| Severity (grading)                | A (9) | M (4) | R (1)       | M (4) | R (1)  | M (4) |
| Severity (LV Dimensions/Function) | A (9) | R (1) | M (6)       | R (1) | R (1)  | A (7) |
| Symptomatic                       |       | ( )   |             | ( )   | ( )    | ( )   |
| Anatomy, aetiology                | A (9) | A (7) | R (1)       | M (6) | R (1)  | M (6) |
| Severity (grading)                | A (9) | M (4) | R (1)       | M (6) | R (1)  | A (7) |
| Severity (LV dimensions/function) | A (9) | R (1) | M (6)       | R (1) | R (1)  | A (7) |
| Associated heart disease          |       |       |             |       |        |       |
| Valvular                          | A (9) | A (7) | R (1)       | A (7) | R (1)  | A (7) |
| Aorta                             | A (9) | A (7) | R (1)       | A (9) | R (1)  | A (7) |
| Pulmonary pressure                | A (9) | R (1) | R (1)       | R (1) | R (1)  | R (1) |
| LV dimension and function         | A (9) | M (4) | R (1)       | R (1) | R (1)  | A (9) |
| Pericardial                       | A (9) | R (1) | R (1)       | M (6) | R (1)  | M (4) |
| Coronary artery disease           | R (3) | R (1) | A (7)       | R (1) | A (7)  | M (4) |
| Indication to SAVR                | A (9) | A (7) | M (6)       | A (7) | M (6)  | M (6) |
| Indication to repair              | A (9) | A (9) | R (1)       | A (9) | M (6)  | A (9) |
| indication to TAVI                | A (9) | A (7) | M (6)       | A (9) | A (8)  | M (6) |

CT, computed tomography; LV, left ventricle; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography echocardiogram.

disease. Aortic valve and aorta anatomy, mechanism and severity of regurgitation, and haemodynamic adaptation of the LV are well assessed with TTE and in some cases it is possible to determine the feasibility of valve-sparing aortic surgery or valve repair.

Acute severe aortic regurgitation is mostly caused by infective endocarditis and less frequently by aortic dissection or by other rare congenital or acquired conditions. Chronic aortic regurgitation can be caused by primary disease of the aortic valve cusps and/or disease of the aortic root and ascending aorta. The most common causes of chronic severe AR in the high-income countries are degenerative tricuspid and bicuspid aortic valve disease and primary diseases of the aortic root or ascending aorta. Rheumatic AR is the leading cause of AR in many low- to middle-income countries. In patients with calcific aortic valve stenosis, regurgitation is often detectable, but the degree of regurgitation usually is mild to moderate.

TTE is the first line method to assess anatomy of the valve and of aortic root/ascending aorta. In most cases, morphological aspects of the cusps (number, thickness, and calcification, echo texture) and quality of kinetic (insufficient coaptation, prolapse, distortion, or retraction) can suggest aetiology and explain the mechanism of regurgitation.

TEE is not performed routinely in patient with AR. In case of sub-optimal acoustic window and need of precise diagnosis for the management of the patient (severe aortic regurgitation without major lesions of the cusps or of the aorta at TTE), TEE is considered appropriate. Cardiac MRI is sometimes performed to assess aortic valve and aortic root anatomy in congenital patients.

TTE is the standard tool for the quantification of AR. Many 2D-TTE and Doppler echocardiographic parameters are used to have a qualitative, semi-quantitative, and quantitative quantification of regurgitation severity.<sup>36</sup> It should be emphasized the need to integrate all of this information to obtain the most accurate grading of regurgitation severity. TTE usually provides all parameters used to quantify aortic regurgitation. Additional echocardiographic methods as 3D or TEE, CT, and Cardiac MRI can be performed at the discretion of physicians in patients with suboptimal image quality or in case of equivocal or discordant results. If TTE provides an exhaustive set of data on the regurgitation, little or no additional information may be needed to manage the patient. When the reliability of TTE data is questioned, other advanced cardiac imaging methods have an important role.

There are several direct and indirect Cardiac MRI methods for quantifying AR,  $^{37,38}$  but their use depends on coexisting arrhythmias, high heart rate, or other heart valve diseses.  $^{39}$ 

Severe AR has significant haemodynamic effects on the LV remodelling suitable as useful marker of severity.<sup>40</sup> In chronic AR the volume overload progressively dilates LV and deterioration of cardiac function may occur, usually in late stage of disease.<sup>41</sup> LV dimensions and function are studied with ETT using all modalities: mono-dimensional, bi-dimensional, 3D, and speckle tracking.<sup>42</sup> ETT should be performed in advanced Echo-Lab to overcome the limits of current valvular heart guidelines. Linear measures of LV currently recommended to evaluate LV dimensions are inadequate if compared to 2D or 3D evaluation of volumes. In addition, EF may be normal in patients with ventricular

dysfunction. Subclinical irreversible myocardial damage can occur in clinically well-compensated patients and its early detection is possible using speckle tracking, i.e. 2D or 3D strain<sup>43</sup> more sensitive than traditional echocardiographic criteria to detect abnormalities before the development of irreversible damage.<sup>44</sup>

Cardiac MRI provides the most accurate measurements of LV volumes and EF. Measurement of LV remodelling with Cardiac MRI is less variable than with echocardiography and is a preferred method for longitudinal follow-up in individual patients.<sup>45</sup>

Delayed contrast-enhanced cardiac magnetic resonance is used to assess myocardial fibrosis by the documentation of late gadolinium enhancement.<sup>46</sup> Myocardial fibrosis is associated with adverse clinical outcome.

Indications for intervention are based on the integration of clinical and imaging data. In severe AR, the onset of symptoms results in a dramatic change in prognosis. Exercise testing can reveal symptoms in asymptomatic patients. Exercise echocardiography provides LV contractile reserve assessment. Even though the lack of contractile reserve was found to predict LV systolic dysfunction development post-operatively, there is limited evidence to support the extensive application of exercise echocardiography in these patients. Neither exercise nor dobutamine stress echo can be used to re-evaluate AR severity in the patient with symptoms, because the increased heart rate shortens diastole, limiting quantification of AR severity.<sup>14</sup>

The choice of the surgical procedure depends on several factors. SAVR is the standard procedure in most cases. If aortic valve repair and valve-sparing surgery of the aortic root are realistic options, anatomy of the aortic complex is studied with TEE.<sup>47</sup> Ascending aortic measurements are often discrepant between the imaging modalities and, currently, Cardiac MRI and CT are recommended to carefully assess the diameter of aorta at different levels.

Identifying the mechanism responsible for AR is mandatory in determining the reparability of the aortic valve.<sup>48</sup> Different functional classifications are used by experienced surgery centres to plan aortic repair.<sup>49</sup>

TAVI may be considered in experienced surgery centres for selected patients with aortic regurgitation ineligible for SAVR.<sup>50,51</sup>

Conflict of interest: The authors declare no conflict of interest.

# Data availability

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

# References

- Nardi F, Pino PG, Gabrielli D, Colivicchi F. ANMCO/SICI-GISE/SIECVI/ SIRM Consensus document: appropriateness of multimodality imaging in cardiovascular disease. *G Ital Cardiol* 2020;21:34-88.
- Hendel RC, Patel MR, Allen JM, Min JK, Shaw LJ, Wolk MJ, Douglas PS, Kramer CM, Stainback RF, Bailey SR, Doherty JU, Brindis RG. Appropriate use of cardiovascular technology: 2013 ACCF appropriate use criteria methodology update. JACC 2013;61:1305-1317.
- Douglas P, Iskandrian AE, Krumholz HM, Gillam L, Hendel R, Jollis J, Peterson E, Douglas P, Chen J, Gillam L, Hendel R, Jollis J,

Iskandrian AE, Krumholz HM, Masoudi F, Mohler E, McNamara RL, Patel MR, Peterson E, Spertus J. Achieving quality in cardiovascular imaging. *JACC* 2006;**48**:2141-2151.

- 4. Douglas PS, Garcia MJ, Haines DE. ACCF/ASE/AHA/ASNC/HFSA/HRS/ SCAI/SCCM/SCCT/SCCMR 2011 Appropriate use criteria for echocardiography A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians. J Am Soc Echocardiogr 2011;24:229-267.
- Carr JJ, Hendel RC, White RD, Patel MR, Wolk MJ, Bettmann MA, Douglas P, Rybicki FJ, Kramer CM, Woodard PK, Shaw LJ, Yucel EK. 2013 Appropriate utilization of cardiovascular imaging: a methodology for the development of joint criteria for the appropriate utilization of cardiovascular imaging by the American College of Cardiology Foundation and American College of Radiology. J Am Coll Cardiol 2013;61:2199-2216.
- Garbi M, Edvardsen T, Bax J, Petersen SE, McDonagh T, Filippatos G, Lancellotti P; Reviewer panel. EACVI appropriateness criteria for the use of cardiovascular imaging in heart failure derived from European National Imaging Societies voting. *Eur Heart J Cardiovasc Imaging* 2016;17:711-721.
- 7. Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P. ACC/AATS/ AHA/ASE/ASNC/HRS/SCAI/SCCT/SCCMR/STS 2017 appropriate use criteria for multimodality imaging in valvular heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and I Inter Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol 2017;70:1647-1672.
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, lung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur. Heart* J 2017; 38:2739-2791.
- 9. Nishimura RA, O'Gara PT, Bavaria JE, Brindis RG, Carroll JD, Kavinsky CJ, Lindman BR, Linderbaum JA, Little SH, Mack MJ, Mauri L, Miranda WR, Shahian DM, Sundt TM. AATS/ACC/ASE/SCAI/STS Expert consensus systems of care document: a proposal to optimize care for patients with valvular heart disease. A joint report of the American Association for Thoracic Surgery, American College of Cardiology, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2019;73:2609-2635. 2019;
- Otto CM, Nishimura RA, Bonow RO. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021; 143:e35-e71.
- 11. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sádaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention* 2022; 17:e1126-e1196.
- Bhattacharyya S, Kamperidis V, Shah BN, Roussin I, Chahal N, Li W, Khattar R, Senior R. Clinical utility and prognostic value of appropriateness criteria in stress echocardiography for the evaluation of valvular heart disease. *JACC Cardiovascular Imaging* 2013;6:987-992.
- Henri C, Piérard LA, Lancellotti P, Mongeon F-P, Pibarot P, Basmadjian AJ. Exercise testing and stress imaging in valvular heart disease. *Canadian Journal of Cardiology* 2014;30:1012-1026.
- Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, Edvardsen T, Garbi M, Ha JW, Kane GC, Kreeger J, Mertens L, Pibarot P, Picano E, Ryan T, Tsutsui JM, Varga A. The Clinical use of stress echocardiography in non-ischaemic heart disease:

recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017;**30**:101-138.

- 15. Amadio JM, Bouck Z, Sivaswamy A, Chu C, Austin PC, Dudzinski D, Nesbitt GC, Edwards J, Yared K, Wong B, Hansen M, Weinerman A, Thavendiranathan P, Johri AM, Rakowski H, Picard MH, Weiner RB, Bhatia RS. Impact of appropriate use criteria for transthoracic echocardiography in valvular heart disease on clinical outcomes. J Am Soc Echocardiogr 2020;33:1481-1489.
- 16. Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, Lancellotti P, LeFevre M, Miller F, Otto CM. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr 2017;30:372-392.
- Santangelo G, Rossi A, Toriello F, Badano LP, Messika Zeitoun D, Faggiano P. Diagnosis and management of aortic valve stenosis: the role of non-invasive imaging. J. Clin. Med 2021;10:3745.
- Troger F, Lechner I, Reindl M, Tiller C, Holzknecht M, Pamminger M, Kremser C, Schwaiger J, Reinstadler SJ, Bauer A, Metzler B, Mayr A, Klug G. A novel approach to determine aortic valve area with phase contrast cardiovascular magnetic resonance. *Journal of Cardiovascular Magnetic Resonance* 2022;24:7.
- Woldendorp K, Bannon P, Grieve S. Evaluation of aortic stenosis using cardiovascular magnetic resonance: a systematic review and metaanalysis. J Cardiovasc Magn Reson 2020;22:45.
- Benfari G, Nistri S, Marin F, Cerrito LF, Maritan L, Tafciu E, Franzese I, Onorati F, Setti M, Pighi M, Rossi A, Ribichini FL. Excess mortality associated with progression rate in asymptomatic aortic valve stenosis. J Am Soc Echocardiogr 2021;34:237-244.
- Everett RJ, Newby DE, Jabbour A, Fayad ZA, Dweck MR. The role of imaging in aortic valve disease. *Curr Cardiovasc Imaging Rep* 2016;9: 21.
- Scully PR, Treibel TA, Fontana M, Lloyd G, Mullen M, Pugliese F, Hartman N, Hawkins PN, Menezes LJ, Moon JC. Prevalence of cardiac amyloidosis in patients referred for transcatheter aortic valve replacement. J Am Coll Cardiol 2018;71:463-464.
- Bohbot Y, Renard C, Manrique A, Levy F, Maréchaux S, Gerber BL, Tribouilloy C. Usefulness of cardiac magnetic resonance imaging in aortic stenosis. *Circ Cardiovasc Imaging* 2020;13:e010356.
- 24. Kusunose K, Goodman A, Parikh R, Barr T, Agarwal S, Popovic ZB, Grimm RA, Griffin BP, Desai MY. Incremental prognostic value of left ventricular global longitudinal strain in patients with aortic stenosis and preserved ejection fraction. *Circ Cardiovasc Imaging* 2014;7: 938-945.
- 25. Magne J, Cosyns B, Popescu BA, Carstensen HG, Dahl J, Desai MY, Kearney L, Lancellotti P, Marwick TH, Sato K, Takeuchi M, Zito C, Casalta A-C, Mohty D, Piérard L, Habib G, Donal E. Distribution and prognostic significance of left ventricular global longitudinal strain in asymptomatic significant aortic stenosis: an individual participant data meta-analysis. JACC Cardiovasc Imaging 2019;12:84-92.
- Ilardi F, Marchetta S, Martinez C, Sprynger M, Ancion A, Manganaro R, Sugimoto T, Tsugu T, Postolache A, Piette C, Cicenia M, Esposito G, Galderisi M, Oury C, Dulgheru R, Lancellotti P. Impact of aortic stenosis on layer-specific longitudinal strain: relationship with symptoms and outcome. *Eur Heart J Cardiovasc Imaging* 2020;21: 408-416.
- 27. Vollema EM, Sugimoto T, Shen M, Tastet L, Ng ACT, Abou R, Marsan NA, Mertens B, Dulgheru R, Lancellotti P, Clavel M-A, Pibarot P, Genereux P, Leon MB, Delgado V, Bax JJ. Association of left ventricular global longitudinal strain with asymptomatic severe aortic stenosis: natural course and prognostic value. JAMA Cardiol 2018;3: 839-847.
- Hachicha Z, Dumesnil JG, Bogaty P, Pibarot P. Paradoxical low-flow, low-gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. *Circulation* 2007;115:2856-2286.
- Clavel MS, Burwash IG, Pibarot P. Cardiac imaging for assessing lowgradient severe aortic stenosis. J Am Coll Cardiol Img 2017;10: 185-202.
- Annabi M-S, Touboul E, Dahou A, Burwash IG, Bergler-Klein J, Enriquez-Sarano M, Orwat S, Baumgartner H, Mascherbauer J, Mundigler G, Cavalcante JL, Larose É, Pibarot P, Clavel M-A.

Dobutamine stress echocardiography for management of low-flow, low-gradient aortic stenosis. *J Am Coll Cardiol* 2018;71:475-485.

- 31. Levy-Neuman S, Meledin V, Gandelman G, Goland S, Zilberman L, Edri O, Shneider N, Abaeh N, Bdolah-Abram T, George J, Shimoni S. The association between longitudinal strain at rest and stress and outcome in asymptomatic patients with moderate and severe aortic stenosis. J Am Soc Echocardiogr 2019;32:722-729.
- 32. Maes F, Lerakis S, Barbosa Ribeiro H, Gilard M, Cavalcante JL, Makkar R, Herrmann HC, Windecker S, Enriquez-Sarano M, Cheema AN, Nombela-Franco L, Amat-Santos I, Muñoz-García AJ, Garcia del Blanco B, Zajarias A, Lisko JC, Hayek S, Babaliaros V, Le Ven F, Gleason TG, Chakravarty T, Szeto W, Clavel M-A, de Agustin A, Serra V, Schindler JT, Dahou A, Salah-Annabi M, Pelletier-Beaumont E, Côté M, Puri R, Pibarot P, Rodés-Cabau J. Outcomes from transcatheter aortic valve replacement in patients with low-flow, low-gradient aortic stenosis and left ventricular ejection fraction less than 30%. A substudy from the TOPAS-TAVI Registry. JAMA Cardiol 2019;4: 64-70.
- 33. Jilaihawi H, Chen M, Webb J, Himbert D, Ruiz CE, Rodés-Cabau J, Pache G, Colombo A, Nickenig G, Lee M, Tamburino C, Sievert H, Abramowitz Y, Tarantini G, Alqoofi F, Chakravarty T, Kashif M, Takahashi N, Kazuno Y, Maeno Y, Kawamori H, Chieffo A, Blanke P, Dvir D, Ribeiro HB, Feng Y, Zhao Z-G, Sinning J-M, Kliger C, Giustino G, Pajerski B, Imme S, Grube E, Leipsic J, Vahanian A, Michev I, Jelnin V, Latib A, Cheng W, Makkar R. A bicuspid aortic valve imaging classification for the TAVR era. J Am Coll Cardiol Img 2016;9: 1145-1158.
- Okuyama K, Jilaihawi H, Kashif M. Transfemoral access assessment for transcatheter aortic valve replacement: evidence-based application of computed tomography over invasive angiography. *Circ Cardiovasc Imaging* 2014;8:e001995.
- 35. Blanke P, Weir-McCall JR, Achenbach S, Delgado V, Hausleiter J, Jilaihawi H, Marwan M, Nørgaard BL, Piazza N, Schoenhagen P, Leipsic JA. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR). An expert consensus document of the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol Img 2019;12:1-24.
- Lidén M, Wodecki M, Thunberg P. Impact of heart rate on flow measurements in aortic regurgitation. J Heart Valve Dis 2017;26:502-508.
- 37. Spampinato RA, Jahnke C, Paetsch I, Hilbert S, Löbe S, Lindemann F, Strotdrees E, Hindricks G, Borger MA. Grading of aortic regurgitation by cardiovascular magnetic resonance and pulsed Doppler of the left subclavian artery: harmonizing grading scales between imaging modalities. *Int J Cardiovasc Imaging* 2020;**36**:1517-1526.
- Gao SA, Polte CL, Lagerstrand KM, Bech-Hanssen O. The usefulness of left ventricular volume and aortic diastolic flow reversal for grading chronic aortic regurgitation severity - Using cardiovascular magnetic resonance as reference. *Int J Cardiol* 2021;340:59-65.
- Yang L-T, Pellikka PA, Enriquez-Sarano M, Scott CG, Padang R, Mankad SV, Schaff HV, Michelena HI. Diastolic blood pressure and heart rate are independently associated with mortality in chronic aortic regurgitation. J Am Coll Cardiol 2020;75:29-39.
- 40. Ong G, Redfors B, Crowley A, Abdel-Qadir H, Harrington A, Liu Y, Lafrenière-Roula M, Leong-Poi H, Peterson MD, Connelly KA. Evaluation of left ventricular reverse remodeling in patients with severe aortic regurgitation undergoing aortic valve replacement: comparison between diameters and volumes. *Echocardiography* 2018 ; 35:142-147. Feb
- Anand V, Yang L, Luis SA, Padang R, Michelena HI, Tsay JL, Mehta RA, Scott CG, Pislaru SV, Nishimura RA, Pellikka PA. Association of left ventricular volume in predicting clinical outcomes in patients with aortic regurgitation. J Am Soc Echocardiogr 2021;34:352-359.
- 42. Zeng Q, Wang S, Zhang L, Li Y, Cheng L, Wang J, Yang Y, Wang D, Zhang Y, Xie Y, Zhang D, Li H, Xie M. Left ventricular remodeling and its progression in symptomatic patients with chronic aortic regurgitation: evaluation by speckle-tracking echocardiography. J Am Soc Echocardiogr 2021;34:360-369.
- 43. Grund FF, Kristensen CB, Bahrami HSZ, Mogelvang R, Hassager C. Layerspecific longitudinal strain detects transmural dysfunction in chronic severe aortic regurgitation before and after aortic valve surgery. Int J Cardiovasc Imaging 2021. doi: 10.1007/s10554-021-02492-w.

- 45. Kammerlander AA, Wiesinger M, Duca F, Aschauer S, Binder C, Zotter Tufaro C, Nitsche C, Badre-Eslam R, Schönbauer R, Bartko P, Beitzke D, Loewe C, Hengstenberg C, Bonderman D, Mascherbauer J. Diagnostic and prognostic utility of cardiac magnetic resonance imaging in aortic regurgitation. JACC Cardiovasc Imaging 2019;12: 1474-1483.
- 46. Senapati A, Malahfji M, Debs D, Yang EY, Nguyen DT, Graviss EA, Shah DJ. Regional replacement and diffuse interstitial fibrosis in aortic regurgitation: prognostic implications from cardiac magnetic resonance. JACC Cardiovasc Imaging 2021;14:2170-2182. Nov
- Elefteriades JA, Mukherjee SK, Mojibian H. Discrepancies in measurement of the thoracic aorta. JACC review topic of the week. J Am Coll Cardiol 2020;76:201-217.
- Klotz S, Stock S, Sievers H-H, Diwoky M, Petersen M, Stierle U, Richardt D. Survival and reoperation pattern after 20 years of experience with aortic valvesparing root replacement in patients with tricuspid and bicuspid valves. J Thorac Cardiovasc Surg 2018;155: 1403-1411.
- Elbatarny M, Tam DY, Edelman JJ, Rocha RV, Chu MWA, Peterson MD, El-Hamamsy I, Appoo JJ, Friedrich JO, Boodhwani M, Yanagawa B, Ouzounian M. Valve-sparing root replacement versus composite valve

grafting in aortic root dilation: a meta-analysis. Ann Thorac Surg 2020;110:296-306.

- 50. Sawaya FJ, Deutsch M-A, Seiffert M, Yoon S-H, Codner P, Wickramarachchi U, Latib A, Petronio AS, Rodés-Cabau J, Taramasso M, Spaziano M, Bosmans J, Biasco L, Mylotte D, Savontaus M, Gheeraert P, Chan J, Jørgensen TH, Sievert H, Mocetti M, Lefèvre T, Maisano F, Mangieri A, Hildick-Smith D, Kornowski R, Makkar R, Bleiziffer S, Søndergaard L, De Backer O. Safety and efficacy of transcatheter aortic valve replacement in the treatment of pure aortic regurgitation in native valves and failing surgical bioprostheses: results from an International Registry Study. JACC Cardiovasc Interv 2017:10:1048-1056.
- 51. Yoon S-H, Schmidt T, Bleiziffer S, Schofer N, Fiorina C, Munoz-Garcia AJ, Yzeiraj E, Amat-Santos IJ, Tchetche D, Jung C, Fujita B, Mangieri A, Deutsch M-A, Ubben T, Deuschl F, Kuwata S, De Biase C, Williams T, Dhoble A, Kim W-K, Ferrari E, Barbanti M, Vollema EM, Miceli A, Giannini C, Attizzani GF, Kong WKF, Gutierrez-Ibanes E, Jimenez Diaz VA, Wijeysundera HC, Kaneko H, Chakravarty T, Makar M, Sievert H, Hengstenberg C, Prendergast BD, Vincent F, Abdel-Wahab M, Nombela-Franco L, Silaschi M, Tarantini G, Butter C, Ensminger SM, Hildick-Smith D, Petronio AS, Yin W-H, De Marco F, Testa L, Van Mieghem NM, Whisenant BK, Kuck K-H, Colombo A, Kar S, Moris C, Delgado V, Maisano F, Nietlispach F, Mack MJ, Schofer J, Schaefer U, Bax JJ, Frerker C, Latib A, Makkar RR. Transcatheter aortic valve replacement in pure native aortic valve regurgitation. J Am Coll Cardiol 2017;70:2752-2763.