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REVIEW

Echocardiography in Transcatheter Aortic Valve Replacement

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Transcatheter aortic valve replacement (TAVR) is a safe and efficient alternative for surgical valve aortic replacement in patients with symptomatic severe aortic stenosis who are inoperable or have a high risk for surgery. Randomised clinical trials have shown that TAVR is not inferior to surgical aortic valve replacement in intermediate-risk patients and ongoing trials will demonstrate the effects of TAVR in asymptomatic severe aortic stenosis patients and in patients with heart failure and moderate aortic stenosis. Continuous developments in procedural and post-procedural management along with increased operator experience and technical improvements and ongoing advances in imaging modalities (particularly in three-dimensional techniques), have reduced the procedural risks and the incidence of complications such as paravalvular aortic regurgitation. Importantly, proper selection of both patient and prosthesis, procedural guidance and follow-up of prosthesis performance remain paramount for the success of the TAVR. In all these steps, echocardiography plays a crucial role. An overview of the clinical applications and current role of echocardiographic techniques in patient selection, prosthesis sizing, periprocedural guidance and post-procedural follow-up will be provided in this review article.

Keywords Transcatheter aortic valve replacement • Echocardiography • Computed tomography • Diagnosis • Aortic stenosis

Introduction

Transcatheter aortic valve replacement (TAVR) has become a feasible alternative to surgical aortic valve replacement (SAVR) in the treatment of inoperable or high-risk symptomatic severe aortic stenosis (AS) patients. At mid-term follow-up, TAVR portends similar outcomes to SAVR and good valve durability has been demonstrated [1–3]. For this specific group of patients, TAVR has received a class I recommendation in recently updated guidelines [4,5]. In addition, TAVR has extended to intermediate-risk patients, in whom studies demonstrate promising outcomes [6–8]. Currently, ongoing large trials are assessing the safety and efficacy of TAVR in low-risk and in asymptomatic severe AS patients [9]. Continuous technical developments in TAVR systems, increased operator experience and developments in procedural (e.g. use of minimalist strategy) and post-procedural (e.g. early discharge) management, careful risk evaluation and proper patient selection remain paramount for successful TAVR.

Echocardiography is the imaging technique of first choice to evaluate patients with severe AS who may be treated with TAVR, particularly for the assessment of aortic valve morphology and AS severity. When the diagnostic accuracy of two-dimensional (2D) transthoracic echocardiography is insufficient, three-dimensional (3D) visualisation of the aortic valve or aortic valve calcium scoring using computed tomography (CT) provides incremental diagnostic value. For the proper selection of the transcatheter prosthesis size, CT is considered the preferred imaging tool. However, 3D transoesophageal echocardiography is a valid alternative to CT in the presence of contra-indications (e.g. renal dysfunction). Furthermore, echocardiography (transthoracic, transoesophageal and, less common, intracardiac echocardiography) is an important imaging technique to assist the TAVR procedure. At follow-up, evaluation of the haemodynamic

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performance of the transcatheter valve is usually performed with echocardiography.

The present review article provides an overview of the clinical applications and current role of echocardiographic techniques in TAVR for (i) patient selection, (ii) prosthesis sizing (iii) periprocedural guidance and (iv) postprocedural follow-up.

Echocardiography in Patient Selection Prior to TAVR

Two-dimensional and Doppler transthoracic echocardiography (TTE) is the imaging technique of first choice to diagnose AS severity. Furthermore, it provides information on aortic root dimensions, left ventricular (LV) dimensions and function (e.g. presence of LV hypertrophy), pulmonary arterial pressure and associated valve disease (mitral and tricuspid regurgitation), which are important factors to take into consideration in the clinical decision making of patients with severe AS [10].

Aortic Valve Morphology

The first step in the evaluation of patients with severe AS is to define the aortic valve morphology. Conventional 2D TTE permits visualisation of the number and position of cusps and qualitative assessment of calcium deposition and the movement of the cusps. However, in severely calcified aortic valves, 2D TTE may not be accurate enough to define the morphology of the valve (tricuspid vs. bicuspid). Transoesophageal echocardiography and CT provide better accuracy to identify the valve morphology (Figure 1) [10,11].

Bicuspid aortic valve (BAV) is diagnosed in systole by the presence of two commissures. However, the phenotype of BAV is highly variable depending on the presence and location of a fusion raphe between cusps. According to the classification of Sievers [12], BAV can be classified into type 0, when there are two commissures and two cusps without a raphe; type 1, when there are two commissures and three cusps with two of them fused by one raphe; and type 2, when there is one commissure with three cusps and two of them fused by two raphes. These BAV types can be further classified according to the orientation of the commissures and location of the raphe (Figure 2) [12].

Landmark randomised controlled trials on TAVR excluded BAV patients [6,7]. However, several registries have reported the feasibility of TAVR in patients with BAV. A higher incidence of significant paravalvular leakage has been reported in bicuspid AS patients treated with early-generation TAVR devices as compared to tricuspid AS patients [13,14]. However, new-generation TAVR devices showed device success rate and incidence of significant paravalvular leakage in BAV patients similar to those reported in tricuspid AS patients [15–17].

Aortic Stenosis Severity

Secondly, assessment of AS severity relies on the following echocardiographic parameters: peak aortic jet velocity, mean transvalvular pressure gradient and the aortic valve area

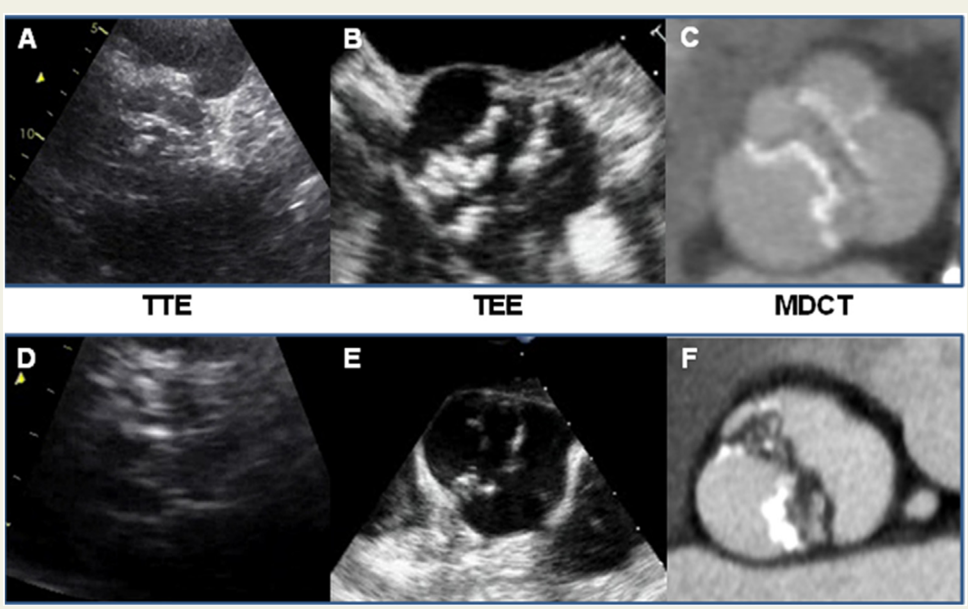

Figure 1 Comparison of transthoracic echocardiography (TTE), transoesophageal echocardiography (TEE) and multidetector row computed tomography (MDCT) for the detection of bicuspid aortic valve (BAV) stenosis. Examples of BAV with a fusion raphe (*panels A-C)* and BAV without a fusion raphe (*panel D-F)* are shown. For both examples, TTE (*panels A and D*) has insufficient accuracy to correctly detect the presence of BAV and its specific morphology. TEE (*panels B and E*) shows a better accuracy for BAV diagnosis. MDCT (*panels C and F*) allows for optimal detection of BAV and the presence and location of raphes, especially when leaflet calcification is present.

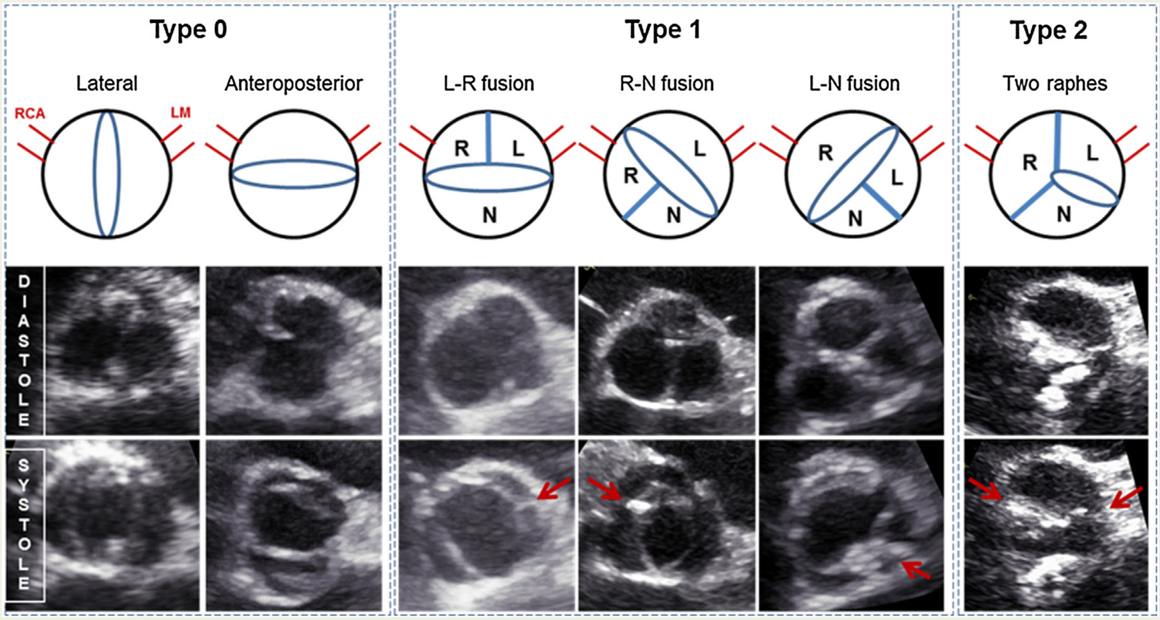

Figure 2 Schematic overview and 2-dimensional transthoracic echocardiographic views of the bicuspid aortic valve (BAV) morphologies according to the classification of Sievers [12]. The aortic valves are depicted from the short-axis views from the left ventricular view in both the diastolic and systolic phase. The raphe (commissural fusion) is represented by the blue bands and red arrows. The origins of the left main (LM) and right coronary artery (RCA) are depicted with red lines. Type 0 denotes BAV without a fusion raphe with a lateral or anteroposterior orientation of the commissures and type 1 and 2 denote BAV with one or two fusion raphes, respectively.
Abbreviations: LM, left main coronary artery; L-N; left and non-coronary cusp; L-R, left and right coronary cusp; RCA, right coronary artery; R-N, right and non-coronary cusp.

(AVA) by continuity equation. Severe AS is conventionally defined as an aortic jet velocity ≥4 m/s, a mean gradient ≥40 mmHg and/or an AVA < 1.0 cm^2 [4,18]. Although the majority of patients with severe AS meet all these criteria, around one third of the patients show discordant grading: an AVA < 1.0 cm^2 with a mean gradient <40 mmHg (so called low-gradient severe AS) [19]. Low-gradient severe AS is frequently observed when the LV ejection fraction (LVEF) is reduced, as this results in a low outflow status [19]. The presence of low flow through the aortic valve, defined as a stroke volume (SV) index <35 mL/m^2 [4,18], may result in underestimation of the mean gradient (which is the squared function of flow) [10].

In this clinical scenario, differentiation between true severe AS and pseudosevere AS is crucial to provide the most appropriate treatment to the patient. To differentiate between these two entities, low-dose (up to 20 µg/kg/min) dobutamine stress echocardiography (DSE) is utilised to increase LV contractility and subsequently increase flow rate. In true severe AS, the increased flow (defined as a >20% increase in SV) will cause an increase in mean gradient (>40 mmHg) while the AVA remains <1.0 cm^2 (Figure 3), whereas in pseudosevere AS, the mean gradient will remain <40 mmHg and the increased SV will result in an AVA > 1.0 cm^2 [10]. In patients without contractile reserve or in whom normalisation of flow rate cannot be achieved, quantification of aortic valve calcification with CT can be helpful [20]. Current recommendations indicate that severe AS is likely when the calcium score of the aortic valve is ≥1,200 arbitrary units in women and ≥2,000 arbitrary units in men [4].

Recently, transaortic flow rate (defined as SV divided by the systolic ejection period) has emerged as a potentially useful parameter for the assessment of true severe AS in patients with low-gradient severe AS [21–23]. Chahal et al. demonstrated that, in 67 low-gradient severe AS patients with either low flow or LV systolic dysfunction, normal resting transaortic flow rate (i.e. ≥ 200 mL/s) was independently associated with the presence of true severe AS on DSE and suggested that DSE may only be required for the evaluation of AS severity in patients with a resting flow rate <200 mL/s [21]. In a small study of 42 low-flow low-gradient severe AS patients, use of normalised transaortic flow rate (i.e. increase up to ≥200 ml/s) during DSE as a criterion for the assessment of true severe AS instead of the presence of flow reserve (defined as ≥20% SV increase) resulted in more conclusive tests (82% vs. 36.4%, p = 0.13) [22]. Furthermore, low transaortic flow rate was shown to be an independent predictor of mortality and provided incremental information over SV index in low-gradient severe AS patients undergoing aortic valve intervention, although these findings need to be confirmed in larger prospective studies [23].

Paradoxical low-flow low-gradient severe AS, defined by a mean gradient >40 mmHg, AVA < 1.0 cm^2 and SV index <35 ml/min with preserved LVEF (≥50%), is often characterised by pronounced LV concentric hypertrophy

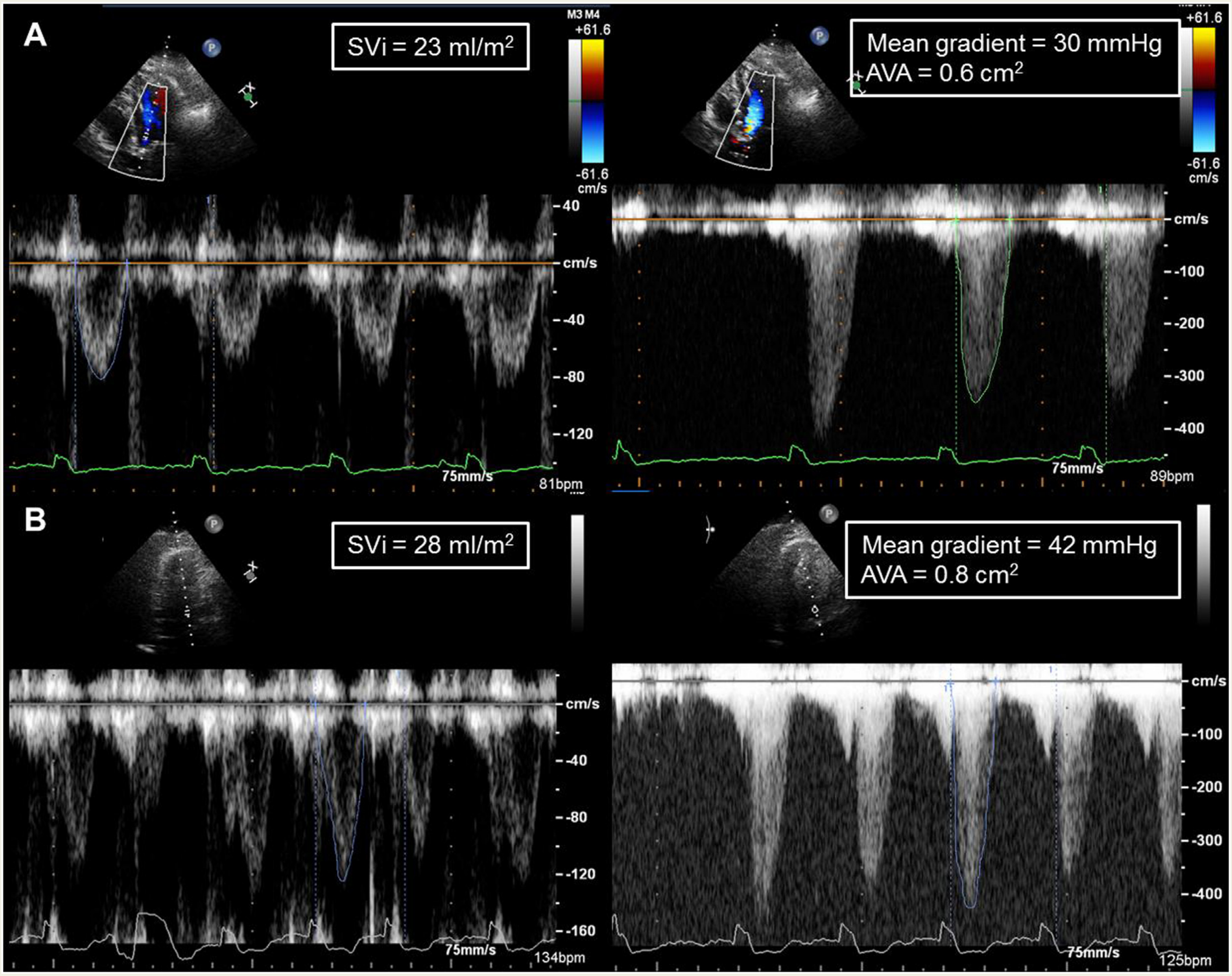

Figure 3 Evaluation of low-flow low-gradient severe aortic stenosis (AS) with reduced left ventricular ejection fraction using low-dose dobutamine stress echocardiography. At baseline, discordant grading of aortic stenosis (AS) severity was apparent: the mean gradient was 30 mmHg and the aortic valve area (AVA) was 0.6 cm^2. The stroke volume index (SVi) was 23 ml/m^2, corresponding with low-flow low-gradient AS (*panel A*). Low-dose dobutamine stress echocardiography was performed to differentiate between true severe AS and pseudosevere AS. This resulted in an increase of the mean gradient to 46 mmHg and of the SVi by 22% to 28 ml/m^2 while the AVA remained <1.0 cm^2, consistent with classical low-flow low-gradient true severe AS and the presence of flow reserve (i.e. increase of SVi > 20%) (*panel B*).

contributing to a small LV cavity with impaired LV filling, resulting in low SV [24]. To correctly diagnose paradoxical low-flow low-gradient severe AS, it is paramount to exclude measurement errors such as underestimation of the LV outflow tract (LVOT) diameter or misalignment of the sample volume resulting in underestimation of the aortic jet velocity and transvalvular gradients. In addition, it is recommended to use indexed AVA (AVAi) [10].

The optimal method to differentiate patients with true severe AS from those with probably moderate AS among paradoxical low-flow low-gradient severe AS patients remains unclear, as the feasibility and safety of DSE in these patients with restrictive physiology is uncertain [25]. Assessment of the degree of aortic valve calcification with CT or calculation of the AVA by combining 3D planimetred LVOT area (on CT or 3D transoesophageal echocardiography [TEE]) with Doppler TTE data can be helpful [26,27]. Kamperidis et al. showed that by incorporating a CT-derived LVOT-area into the continuity equation formula combined with haemodynamic echocardiographic data as assessed by Doppler TTE, resulted in larger AVA index than that calculated conventionally with 2D TTE (Figure 4) [27]. Accordingly, the use of CT to calculate the AVA resulted in reclassification of a significant proportion of paradoxical low-flow low-gradient severe AS into moderate AS [27]. In a subanalysis of the Placement of Aortic Transcatheter Valves (PARTNER) trial, treatment with TAVR was associated with reduced mortality compared to medical management at 2-year follow-up in both classical (47% vs. 80%, respectively,

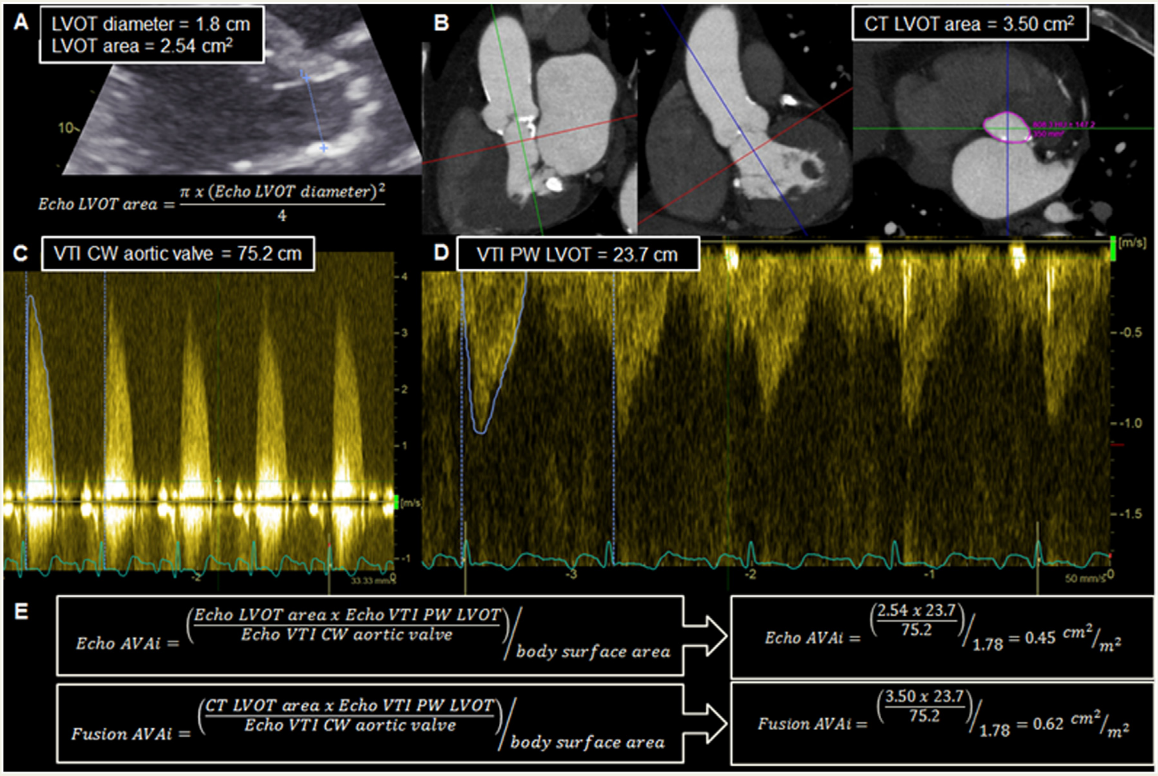

Figure 4 Evaluation of the aortic valve area index (AVAi) by 2-dimensional Doppler echocardiography (Echo) and by fusion of multi-detector row computed tomography (CT)-derived and echocardiographic measurements. Using echocardiography, the left ventricular outflow tract (LVOT) diameter was measured 5 mm below the aortic annulus in the parasternal long-axis view and the LVOT area was calculated (*panel A*). Using CT, the LVOT area was located 5 mm below the aortic annulus and planimetered in the reconstructed double oblique transverse view in systole (*panel B*). Continuous-wave (CW) Doppler on the apical 5-chamber view was performed to measure the VTI of the aortic valve (*panel C*). Pulsed-wave (PW) Doppler recordings of the LVOT were obtained by placing the sample volume 5 mm below the aortic annulus and the velocity time integral (VTI) of the flow at the LVOT was measured (*panel D*). By utilising the continuity equation, the Echo AVAi and fusion AVAi were calculated incorporating the echocardiographically estimated LVOT area and CT-derived LVOT area, respectively. In both calculations, the VTI of the LVOT and the aortic valve area were used (*panel E*). In this example, reclassification to moderate AS was possible by calculating the fusion AVAi.

$p = 0.039$) and paradoxical low-flow low-gradient severe AS (57% vs. 77%, respectively; $p = 0.047$) [28]. Therefore, accurate assessment of AS severity is crucial to provide the best treatment and improve outcomes.

The Role of 3D TEE in Prosthesis Sizing

Measurement of the dimensions of the aortic valve annulus and prosthesis size selection are crucial steps in TAVR. Over- or undersizing of the TAVR prosthesis might result in aortic root rupture, valve embolisation or paravalvular aortic leakage. The aortic annulus is an oval-shaped virtual ring which dimensions are better measured with 3D imaging techniques [29–31], with CT providing the highest spatial resolution [32]. However, in patients with renal dysfunction in whom associated comorbidities such as heart failure may increase the risk of acute kidney injury, the use of iodinated contrast should be kept at a minimum [33]. Three-dimensional TEE is a valid alternative to CT to measure the aortic annulus. Several studies have reported a moderate to high correlation for cross-sectional dimensions of the aortic annulus (area and perimeter) measured with CT and 3D TEE [34–36]. However, cross-sectional 3D TEE measurements of the aortic annulus were significantly smaller than dimensions obtained by CT, thus potentially resulting in prosthesis undersizing when implemented in the sizing algorithms recommended by manufacturers [35,36].

The advent of semi-automated quantitative software for direct planimetry of the aortic annulus has allowed a more systematic approach minimising the influence of the observer (Figure 5). Studies comparing semi-automated or automated software by different vendors have demonstrated good to excellent agreement between 3D TEE and CT for the measurements of the annular area, mean diameter and perimeter with low interobserver and intraobserver variability [37–41].

The limitations of 3D TEE include the semi-invasive approach and the acoustic shadowing due to bulky calcification of the aortic valve or annulus which can challenge the visualisation of

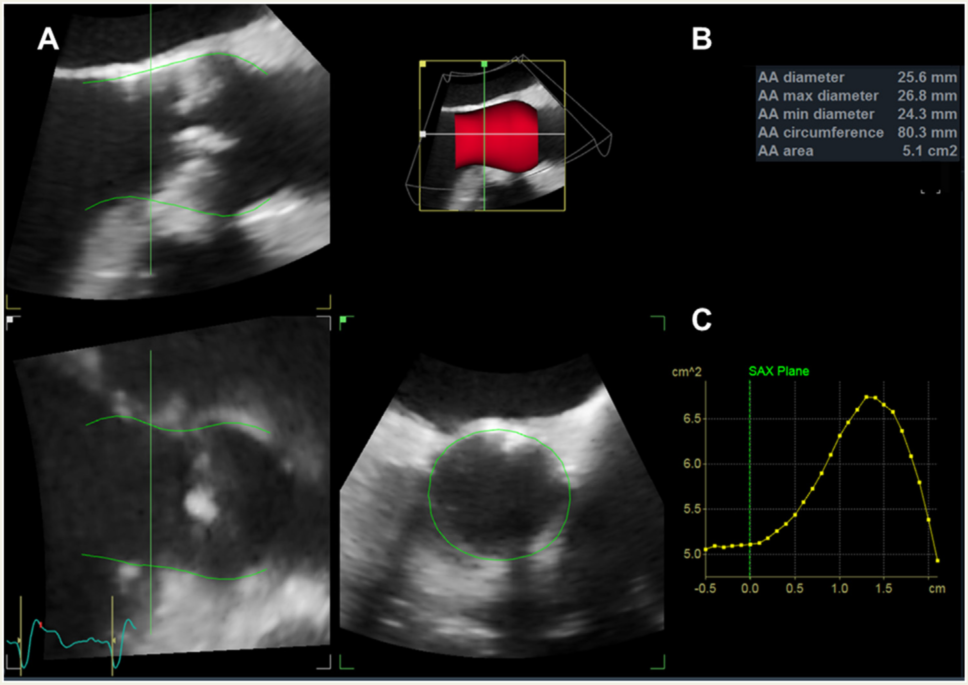

Figure 5 Evaluation of the aortic annulus by 3-dimensional transoesophageal echocardiography using automated software (4D Automated Aortic Valve Quantification (4D Auto AVQ); EchoPAC, version 201, GE-Vingmed). First, a multiplanar reconstruction of the aortic valve is constructed in mid-systole by aligning the two long-axis orthogonal planes through the aortic valve and moving the transverse plane toward the hinge points of the aortic valve leaflet insertions. Automatic delineation of the left ventricular outflow tract and aortic root is then performed by the 4D Auto AVQ program and, if needed, manual adjustments can be made (*panel A*). After approval of the contouring of the aortic annulus (AA) and aortic root, the automatic software computes the annular dimensions: average diameter (calculated based on the perimeter), maximum and minimum diameters, circumference (perimeter) and area (*panel B*). The software generates a graph representing the cross-sectional area along the aortic root and left ventricular outflow tract (*panel C*).
Abbreviations: SAX, short axis view.

the annulus [38,40]. By acquiring the 3D TEE data of the aortic root in an off-axis plane, the acoustic shadowing created by the aortic valve calcification can be minimised resulting in improved agreement between CT and 3D TEE measurements of the aortic annulus dimensions (Figure 6) [42].

With the prospect that future TAVR procedures will be performed in younger patients with low operative risk in whom radiation needs to be minimised, 3D TEE may be a good alternative to CT for aortic annulus sizing.

Echocardiographic Guidance During TAVR Procedure

Procedural guidance during TAVR is routinely performed using fluoroscopy [43]. Transoesophageal echocardiography is used as an adjunct to fluoroscopy and offers multiple advantages: it reduces the amount of nephrotoxic iodine contrast and radiation exposure and allows for early assessment of potential intra-procedural or immediate post-procedural complications [44,45]. As TEE offers real-time and continuous monitoring, it is useful for all aspects of the TAVR procedure.

Although manipulation and positioning of wires is usually monitored by fluoroscopy, TEE can help to confirm the correct positioning of the pacing wire in the right ventricular apex as well as the position of the retrograde stiff wire in the left ventricle. TEE also permits rapid assessment of potential pericardial effusion in the event of ventricular perforation. During positioning of the wire, entrapment of the guidewire within the mitral apparatus causing mitral regurgitation can be detected at an early stage [45].

If balloon aortic valvuloplasty is deemed necessary, TEE can be used to guide the balloon positioning relative to the valve and to ensure a stable position. Furthermore, it may aid in visualising how calcified aortic valve cusps will displace relative to the coronary ostia and predict whether occlusion of coronary ostia might occur. For the correct positioning of both balloon- and self-expandable prostheses prior to deployment, fluoroscopy plays a pivotal role. However, fluoroscopy can prove challenging in the setting of limited calcification of the aortic valve / annulus, in which case TEE can be particularly useful. Although the simultaneous use of TEE can cause an obstruction of the fluoroscopic view, changing the echocardiographic window or fluoroscopic angle may overcome this disadvantage [45].

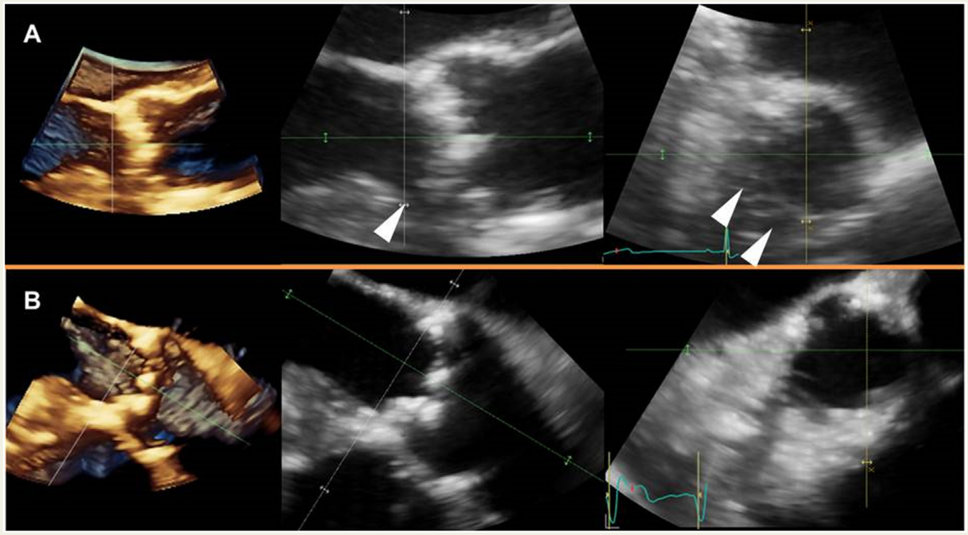

Figure 6 Assessment of the aortic valve and annulus using 3-dimensional transoesophageal echocardiography. From the 3-dimensional full volume, the 2-dimensional long-axis multiplanar reconstruction (middle) and the short-axis multiplanar reconstruction at the level of the aortic annulus (right) are displayed. In *panel A*, the ultrasound beam is angled parallel to the calcified aortic valve causing considerable acoustic shadowing over the aortic annulus, which challenges accurate assessment of the aortic annulus (white arrows). In *panel B*, the 3-dimensional echocardiographic data were acquired in an off-axis plane, causing the acoustic shadowing to be projected over the sinus of Valsalva and providing a clearer view of the aortic annulus and more accurate measurements of the aortic annulus dimensions.

Immediately after the valve is deployed, appropriate valve position and function can be confirmed by TEE. Importantly, the presence and severity of paravalvular aortic regurgitation should be assessed. Correct assessment of the severity of paravalvular aortic regurgitation is challenging as multiple paravalvular jets with an eccentric and irregular appearance can be present [43]. Aortography provides a qualitative assessment of the residual aortic regurgitation, but it does not provide information on the mechanism of regurgitation (paravalvular versus transvalvular), which is important to decide whether re-ballooning of the transcatheter valve is needed to ensure good sealing of the annulus and reduce paravalvular regurgitation, or if rescue valve-in-valve is needed to reduce transvalvular regurgitation (Figure 7).

The importance of using the recommended multi-window and multi-parametric echocardiographic approach, incorporating both qualitative (i.e. jet features) and semiquantitative (i.e. jet width at origin as percentage of LVOT diameter and circumferential extent of the jet(s)) parameters [43,46], was recently illustrated by Hahn et al. [47]. In this study, 15.9% of patients who were graded as moderate paravalvular aortic regurgitation by a method using the circumferential extent of the regurgitant jet, were reclassified as mild paravalvular aortic regurgitation when the multiparametric approach was used [47].

Growing operator experience and the development of smaller delivery systems has increased the feasibility of transfemoral TAVR with local anaesthesia or conscious sedation (also called monitored anaesthesia care) rather than general anaesthesia [48,49], resulting in the increased use of TTE to evaluate the results of TAVR. This less invasive strategy has been associated with a shorter duration of hospitalisation and improved post-procedural outcomes without safety issues [49–52]. In addition to using TTE for intraprocedural guidance, transnasal TEE and intracardiac echocardiography have been suggested as alternative imaging methods in procedures with monitored anaesthesia care [43]. Compared to conventional TEE, transnasal TEE does not have the capability for 3D assessment and the image quality is considerably less [43]. Intracardiac echocardiography provides better image quality than transnasal TEE and uninterrupted monitoring without fluoroscopic interference [53]. This is achieved by using a steerable catheter, which is introduced into the femoral vein and advanced via the inferior vena cava and right atrium towards the superior cavo-atrial junction [53]. In this position, the aortic valve and root can be continuously monitored. Real time 3D imaging, with a $22 \times 90°$ volume image, allows for the postprocedural assessment of paravalvular aortic regurgitation and potential complications [53]. Major disadvantages of this technique are the lesser image quality (particularly in 3D due to the small image volume), the possible interference of the device with the pacemaker lead with subsequent risk of lead displacement and loss of capture, lack of experience and especially the high costs of the device [53].

Echocardiography During Follow-Up After TAVR: What to Look For?

For the assessment of prosthesis function and durability after TAVR and detection of possible late complications, TTE is the mainstay imaging modality. According to current guidelines, echocardiographic follow-up of TAVR should be performed

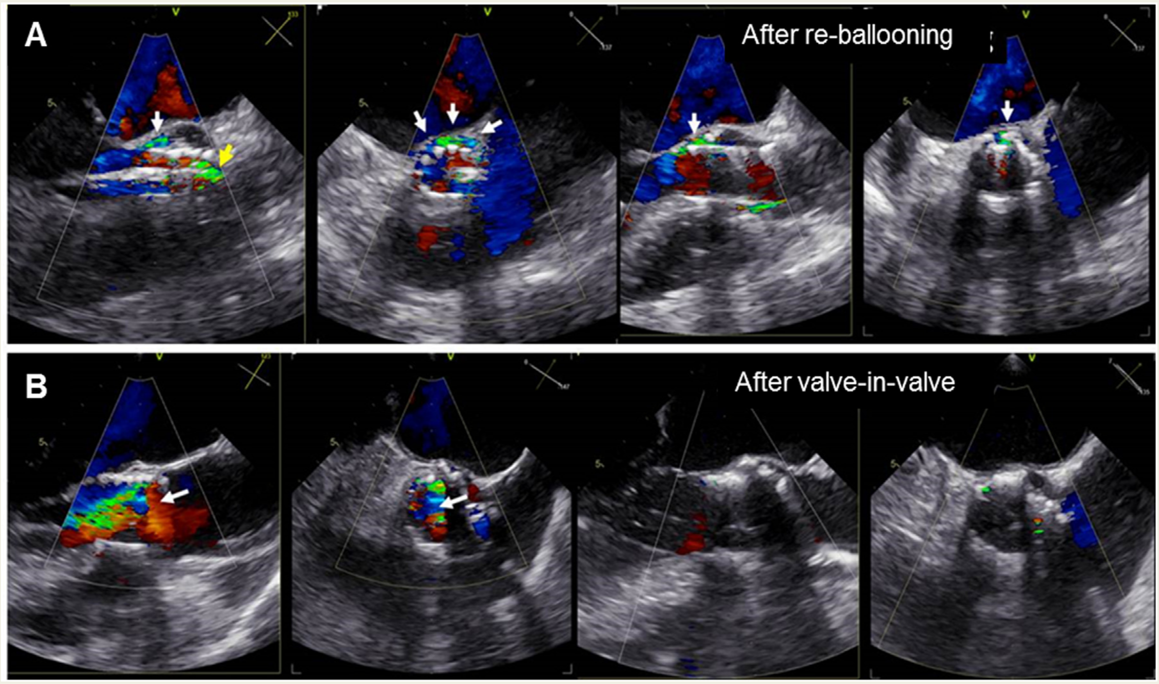

Figure 7 Evaluation of transcatheter aortic valve replacement results: differentiating paravalvular from transvalvular regurgitation. Panel A shows a patient who received a self-expanding valve prosthesis. The images on the left show the presence of paravalvular regurgitation (white arrow) and transvalvular regurgitation caused by the presence of the wire (yellow arrow). The orthogonal simultaneous view shows the short-axis of the transcatheter valve with paravalvular regurgitation along >25% of the prosthesis frame circumference (arrows). After re-ballooning of the valve, the paravalvular regurgitation significantly reduced to trace. Panel B shows a patient who received a balloon-expandable prosthesis with a frozen (i.e. not deployed) leaflet resulting in severe transvalvular regurgitation (arrow) and haemodynamic instability of the patient. The orthogonal short-axis view shows the regurgitant jet covering 50% of the internal area of the transcatheter valve (arrow). In this situation, valve-in-valve implantation is needed to haemodynamically stabilise the patient and treat the regurgitation.

prior to discharge or within 30 days after implantation, after 6 months and 1 year, and yearly thereafter [32,54]. Importantly, if new symptoms and signs of valve dysfunction appear, echocardiography should be performed and the frequency of follow-up visits should be increased when deterioration of LV function and valve haemodynamics are noted. Using TTE, the position of the TAVR stent and the morphology of the prosthesis leaflets, in particular cusp thickness and mobility, and the presence of valve stenosis or regurgitation should be assessed.

Stent Position and Leaflet Morphology

Deployment of the TAVR prosthesis lower than recommended can result in protruding native valve leaflets above the aortic edge of the frame and limited anchoring, increasing the risk of delayed migration of the prosthetic valve into the LVOT or LV [43,55]. This can cause either prosthetic regurgitation or native valve restenosis or result in mitral regurgitation due to interaction with the mitral apparatus [55]. Structural valve deterioration (SVD), i.e. acquired and permanent intrinsic deterioration of the prosthetic valve, typically manifests as prosthesis stenosis caused by thickening and calcification of the prosthesis leaflets (Figure 8). Less often, flailing or tearing of a leaflet can be observed causing new onset of transvalvular regurgitation (Figure 8).

Prosthetic Valve Stenosis

For valve stenosis, peak velocity and mean gradient (flow-dependent parameters) and the effective orifice area (EOA) (flow-independent parameter) should be evaluated. For the calculation of the EOA, it is important to measure the LVOT diameter and flow velocity immediately proximal of the prosthesis stent to prevent EOA overestimation caused by flow acceleration within the stent. The Valve Academic Research Consortium-2 (VARC-2) has proposed the use of one flow-independent (eg. EOA) and one flow-dependent (eg. mean transvalvular gradient) parameter for the assessment of prosthetic aortic valve stenosis [54]. Recent recommendations by the Valve in Valve Interventional Data (VIVID group) propose to define severe prosthetic valve stenosis by an increase in mean gradient >20 mmHg compared to the baseline post-procedural gradient accompanied by a decrease in EOA [56]. Alternatively, European recommendations suggest to define severe haemodynamic SVD as a mean gradient ≥40 mmHg and/or ≥20 mmHg change from

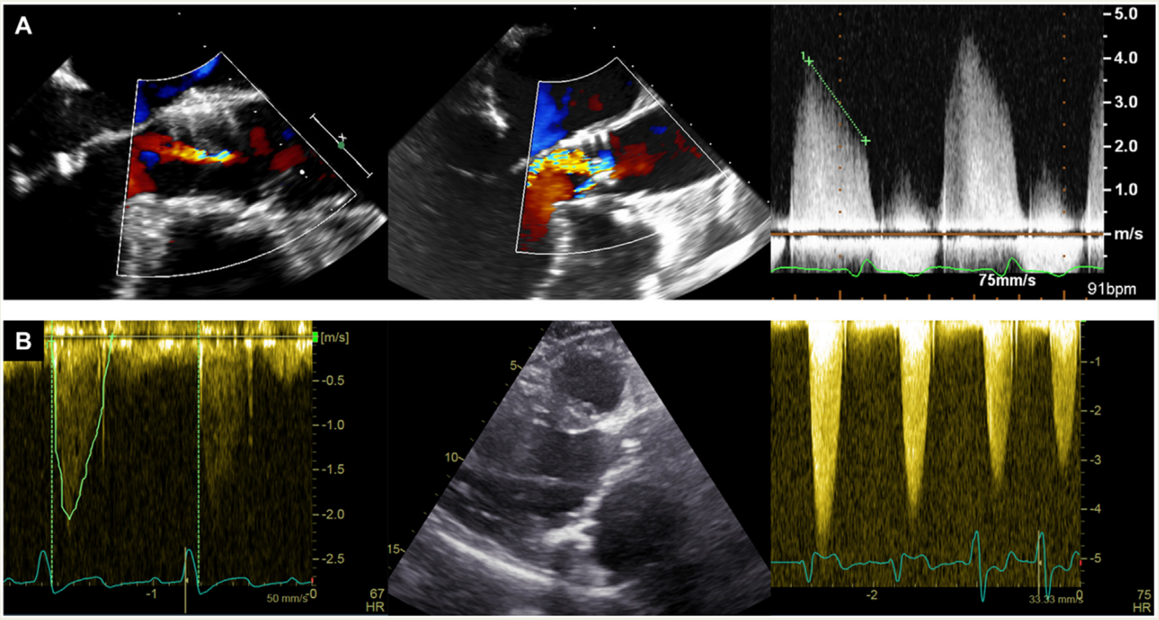

Figure 8 Structural valve deterioration after transcatheter aortic valve replacement showing severe transvalvular aortic regurgitation (panel A) or severe prosthetic valve stenosis (panel B). Panel A shows a patient receiving a balloon-expandable valve with periprocedural transoesophageal echocardiography demonstrating mild paravalvular regurgitation on colour Doppler (left panel). After 4 years follow-up, transoesophageal echocardiography showed severe transvalvular aortic regurgitation on the colour Doppler image (middle panel), confirmed by continuous wave Doppler recordings with steep downsloping of the regurgitant flow (right panel). Panel B shows a patient receiving a balloon-expandable valve with periprocedural transoesophageal echocardiography demonstrating low transprosthetic gradients (left panel). After 6 years of follow-up, transthoracic echocardiography showed thickened and calcified prosthetic valve leaflets on the long-axis view (middle panel). Increased transprosthetic gradients were observed on continuous wave Doppler (right panel), confirming the presence of severe prosthetic valve stenosis. Both patients underwent a valve-in-valve implantation.

baseline and/or severe new or worsening intraprosthetic aortic regurgitation [57].

Prosthetic Valve Regurgitation

Prosthetic valve regurgitation after TAVR is assessed using both qualitative and quantitative criteria similar to surgical prosthetic valve regurgitation (Table 1) [46,56]. Although this is primarily assessed using TTE, TEE may be considered if image quality is suboptimal. Proper evaluation of the severity of paravalvular aortic regurgitation after TAVR can be challenging, as it is often characterised by the presence of multiple eccentric and irregularly shaped jets which limit proper assessment of the circumferential extent and diameter of the regurgitant jet. Acoustic shadowing by the prosthesis stent and native valve calcifications further complicate correct quantification, particularly when measuring the vena contracta width. Furthermore, LV and aortic compliance is often lacking in elderly patients undergoing TAVR, which might influence pressure half time and potentially cause holodiastolic flow reversal in the absence of significant aortic regurgitation. These limitations and difficulties in the evaluation of paravalvular aortic regurgitation after TAVR emphasise the importance of the use of the multi-parametric approach [46]. Using this approach, both mild and moderate/severe paravalvular regurgitation were independently associated with higher late all-cause mortality in the patients of the PARTNER I trial [58], although other studies have reported no significant prognostic effect of mild paravalvular regurgitation [59]. When the severity of the paravalvular regurgitation remains uncertain after TEE assessment or insufficiently corresponds with clinical assessment, cardiac magnetic resonance imaging may help to confirm the severity of the aortic regurgitation. Ribeiro et al. quantified aortic regurgitation after TAVR in 135 patients using regurgitant fraction measured by phase-contrast velocity mapping [60]. Higher regurgitant fraction was associated with increased mortality and a regurgitant fraction $\geq$30% best predicted poorer clinical outcomes [60]. However, cardiac magnetic resonance imaging has multiple limitations, such as the inability to differentiate paravalvular from transvalvular regurgitation, and further studies are needed as variable cut-off values of regurgitant fraction have been reported.

Further Considerations

Varying rates of SVD in TAVR have been reported in mid-term and long-term follow-up studies, partly caused by differences in the definition of SVD. In both balloon-

Table 1 Parameters used for the assessment of severity of paravalvular regurgitation on echocardiography and cardiac magnetic resonance imaging.

Parameter	Severity of paravalvular regurgitation			Main limitation
	Mild	Moderate	Severe	
Echocardiography				
Qualitative or semi-quantitive parameters				
Jet length and width + number of jets and jet origins*	Non extensive, multiple jets possible	Extensive, multiple jets often present	Extensive, multiple jets often present	Jets may not be visible due to acoustic shadowing of stent and native valve or LVOT calcifications; jet length and width only weakly correlated with severity of regurgitation
Circumferential extent jet (colour Doppler)*	<10%	10-29%	≥30%	Less reliable in the presence of multiple or eccentric jets, plane position dependent, poor correlation with cardiac magnetic resonance imaging
Ratio jet width at origin/LVOT diameter (colour Doppler)*	5–30% (narrow/ intermediate)	30–60% (intermediate)	>60% (large)	May be difficult to visualise (assessed visually)
Vena contracta width (colour Doppler)	<3 mm	3–6 mm	>6 mm	Often irregularly shaped, may be difficult to visualise (assessed visually) due to acoustic shadowing and in case of multiple jets
Signal intensity of jet (CW Doppler)	Faint / variable	Dense	Dense	
Pressure half-time (CW Doppler)	>500 ms (slow)	200–500 ms (variable)	<200 ms (steep)	Heart rate and rhythm dependent, strongly influenced by compliance of LV and aorta
Diastolic flow reversal in descending aorta (PW Doppler)	Absent / intermediate	Intermediate / holodiastolic (>20 cm/s)	Holodiastolic (>25 cm/s)	Strongly influenced by compliance of LV and aorta
Quantitative parameters				
Regurgitant volume	<30 ml/beat	30–59 ml/beat	≥60 ml/beat	Large inter- and intra-observer variability, cannot be assessed in the presence of > mild mitral or pulmonary regurgitation
Other				
Left ventricular dimensions	Normal	Normal or mildly dilated	Moderately or severely dilated	More useful in the setting of chronic paravalvular regurgitation
TAVR stent position	Normal or abnormal	Normal or abnormal	Usually abnormal	
Cardiac magnetic resonance imaging				
Regurgitant fraction (phase-contrast velocity mapping)	<20%	20–30%	>30%	Variable cut-offs reported (not yet validated), often overestimation compared to TTE

Abbreviations: CW, continuous wave; LVOT, left ventricular outflow tract; PW, pulsed wave; TAVR, transcatheter aortic valve replacement; TTE, transthoracic echocardiography.

*Of particular importance for the assessment of paravalvular regurgitation severity.

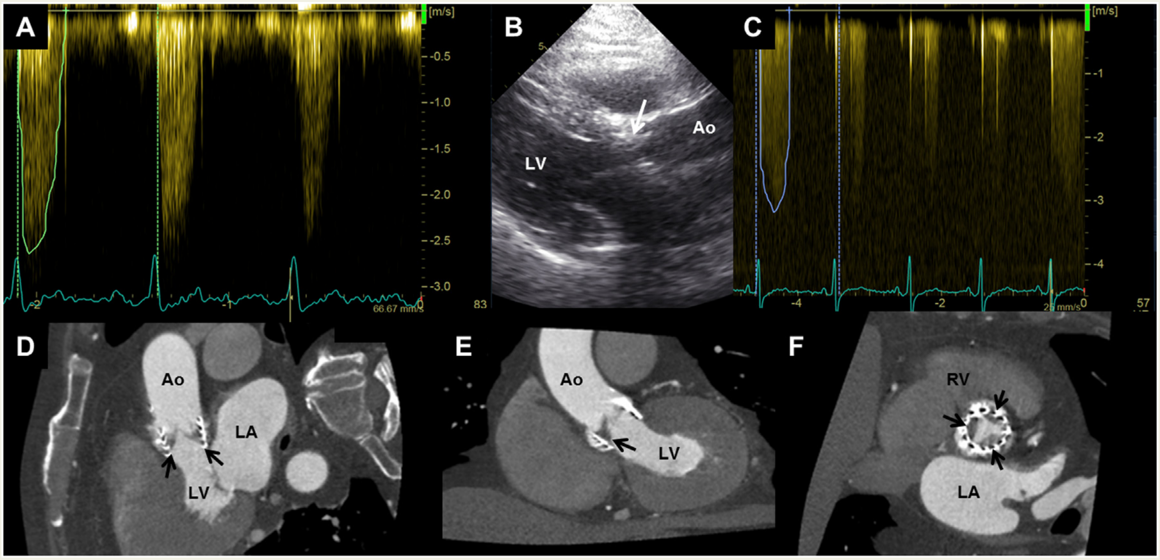

Figure 9 Prosthetic transcatheter aortic valve thrombosis in a patient presenting with heart failure symptoms 1 year after receiving a balloon-expandable valve. Directly after implantation, transoesophageal echocardiography showed low transprosthetic gradients (10 mmHg, panel A). After 1 year, follow-up transthoracic echocardiography demonstrated thickened prosthesis leaflets (white arrow, panel B) and increased transprosthetic gradients compared to baseline (25 mmHg, panel C) consistent with severe prosthetic valve stenosis. Four-dimensional computed tomography was performed showing hypo-attenuated lesions and leaflet thickening (black arrows) with reduced leaflet mobility on the sagittal oblique (panel D), coronal oblique (panel E) and double oblique (panel F) reconstruction views, confirming the presence of prosthetic valve thrombosis.
Abbreviations: Ao, aortic root; CT, computed tomography; LA, left atrium; LV, left ventricle; RV, right ventricle.

expandable and self-expandable TAVR prostheses, 3 to 5 year follow-up studies have reported low rates of SVD [57]. A recent meta-analysis including 13 studies reporting SVD rates in TAVR, based on VARC-2 definition (i.e. need for repeat procedure, increased mean gradient >20 mmHg, EOA < 0.9-1.1 cm^2 and/or Doppler velocity index <0.35 m/s), showed a pooled estimate of a SVD incidence rate of 28 per 10,000 patient years [61]. When signs of prosthetic valve stenosis are observed, prosthetic valve thrombosis should be considered. Although TEE is the reference standard for the evaluation of prosthetic valve thrombosis, the high spatial resolution of CT allows for better distinction between thrombosis and other causes of obstruction such as pannus (Figure 9) [62].

In two multicentre registries, Del Trigo et al. demonstrated that 4.5% of patients treated with TAVR presented with valve haemodynamic deterioration (VHD) defined as an absolute increase in mean transprosthetic gradient ≥10 mmHg between discharge and last follow-up [63,64]. Absence of anticoagulation therapy was an independent predictor for VHD [63], and

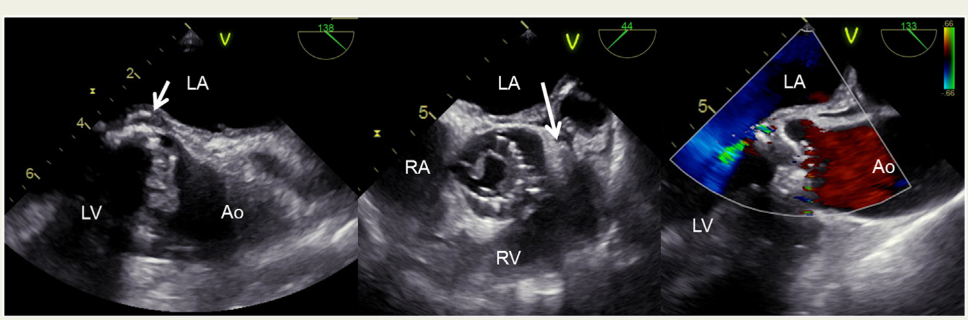

Figure 10 Prosthetic valve endocarditis 6 months after transcatheter aortic valve replacement assessed by 2-dimensional transoesophageal echocardiography. The mid-oesophageal aortic valve long-axis (left panel) and short-axis (mid panel) views show signs of a paravalvular abscess (white arrows) and of vegetations located on the prosthetic valve leaflets. Colour Doppler of the long-axis view (right panel) demonstrates mild paravalvular aortic regurgitation.
Abbreviations: Ao, aortic root; LA, left atrium; LV, left ventricle; RA, right atrium.

Table 2 Role of multimodality imaging techniques in the different stages of the transcatheter aortic valve replacement procedure.

Imaging technique	Transcatheter aortic valve replacement procedure		
	Preprocedural	Periprocedural	Follow-Up
Echocardiography			
TTE	Aortic valve morphology and degree of calcium deposition Severity AS (+/- dobutamine stress echocardiography)	Correct positioning and deployment of valve prosthesis Valve haemodynamics	Correct positioning and deployment of valve prosthesis Valve haemodynamics
	Aortic root and ascending aorta dimensions Left ventricular function and dimensions	Assessment of aortic regurgitation Detection of other complications (pericardial effusion, mitral regurgitation, myocardial ischaemia, aortic annular rupture, etc.)	Assessment of aortic regurgitation Left ventricular function and dimensions
	Pulmonary arterial pressure		Concomitant valvular disease (mitral or tricuspid regurgitation)
	Concomitant valvular disease (mitral or tricuspid regurgitation) as well assessment of aortic regurgitation		
TEE (2D or 3D)	Aortic valve morphology and degree of calcium deposition Aortic annulus and root dimensions (3D)	Correct positioning of wires and catheters Guidance of balloon positioning	Correct positioning and deployment of valve prosthesis Valve haemodynamics
		Visualisation of calcium displacement Correct positioning and deployment of valve prosthesis Valve haemodynamics	Assessment of aortic regurgitation Left ventricular function and dimensions Concomitant valvular disease (mitral or tricuspid regurgitation)
		Assessment of aortic regurgitation and distinguishing paravalvular and transvalvular regurgitation Detection of other complications (pericardial effusion, mitral regurgitation, myocardial ischaemia, aortic annular rupture, etc.)	Detection prosthetic valve thrombosis and infective endocarditis
Computed tomography	Aortic valve morphology		Correct positioning and deployment of valve prosthesis Detection (subclinical) prosthetic valve thrombosis, infective endocarditis and/or pannus
	Severity AS (by quantification aortic valve calcification)		
	Aortic annulus and root dimensions Thoracic aorta (+ degree of calcification) Peripheral artery accessibility		

Table 2. (continued).

Imaging technique	Transcatheter aortic valve replacement procedure: Preprocedural	Periprocedural	Follow-Up
	Left ventricular function Projections C-arm for fluoroscopy		
Fluoroscopy	Aortic annulus dimensions	Correct positioning of wires and catheters	
	Peripheral artery accessibility	Correct positioning and deployment of valve prosthesis Assessment of paravalvular regurgitation Detection of other complications (occlusion coronary ostia, rupture aortic annulus or ascending aorta, etc.)	
Cardiac magnetic resonance imaging	Aortic valve morphology and degree of calcium deposition Aortic root and ascending aorta dimensions Thoracic aorta dimensions		Correct positioning and deployment of valve prosthesis Assessment of aortic regurgitation Left ventricular function and dimensions
	Peripheral artery accessibility Assessment of aortic regurgitation left ventricular function concomitant valve disease (mitral and tricuspid regurgitation)		
Nuclear imaging			^{18}F-FDG PET/CT: detection of prosthetic valve infective endocarditis

Abbreviations: 3D, three-dimensional; AS, aortic stenosis; CT, computed tomography; ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography; TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

when comparing propensity-matched populations, VHD appeared to be less prevalent in patients receiving anticoagulation treatment compared to patients without anticoagulation (0.6 vs. 3.9%. $p < 0.001$) [64]. Although TEE or CT were not performed, the authors postulated that prosthetic valve thrombosis may be likely the main mechanism underlying VHD. Prior studies evaluating obstructive prosthetic valve thrombosis after TAVR, with patients often presenting with heart failure symptoms or increased transprosthetic gradients on follow-up echocardiography, have reported relatively low incidences ranging from 0.61 to 2.8% [65–67]. However, studies performing (4D) CT post-TAVR regardless of symptoms or transprosthetic gradients have detected the presence of hypo-attenuated leaflet thickening with or without reduced leaflet motion suggestive of subclinical leaflet thrombosis in a significantly higher proportion of patients, with incidences ranging from 4 to 40% [68–74].

More interesting, the time course of hypo-attenuated leaflet thickening was described by Sondergaard et al. [72] in 84 patients (61 patients treated with TAVR and 23 patients with SAVR). After a mean follow-up of 140 days, 38.1% of patients showed hypo-attenuated leaflet thickening and 20.2% displayed hypo-attentuation affecting motion (leaflet thickening with reduced leaflet motion). After a mean follow-up of 298 days, a second CT scan was performed showing that the abnormalities noted in the first CT scan progressed in 15.5% of patients, regressed in 10.7% and remained unchanged in 73.8%. Importantly, patients receiving oral antiocoagulation did not show progression of the abnormalities suggesting that this treatment prevents from further thickening and restriction of prosthesis leaflets.

Future prospective studies will likely shed more light on the incidence, optimal antithrombotic/anticoagulant treatment regimen and effect on TAVR durability of subclinical prosthetic valve

thrombosis. Endocarditis is another complication that should be suspected based on the clinical presentation and when new periprosthetic valve regurgitation is detected. Echocardiography, in particular TEE, can be used for the detection of vegetations, abscesses or pseudoaneurysms (Figure 10), and to assess potential involvement of the mitral or tricuspid valve [75]. For improved prediction of embolic risk, real-time 3D TEE can be used for more precise estimation of vegetation morphology and size [76]. Recent multicentre registries have reported a 1.1% incidence of prosthetic valve endocarditis after TAVR, with the majority of patients presenting within 1 year after the procedure [77,78]. Similarly to infective endocarditis after surgical valve replacement, the mortality rates are high (62% to 67%) [77,78], emphasising the importance of early detection and treatment. Unfortunately, the Duke criteria used for diagnosis of infective endocarditis have proven to be less sensitive if a prosthetic valve is involved and positive signs on TTE are often lacking in this setting [75]. A multimodality imaging approach adding ^{18}F-fluorodeoxyglucose positron emission (PET)/CT to the conventional modified Duke criteria has been recommended and has been shown to significantly increase diagnostic accuracy, especially in cases initially classified as ''possible infective endocarditis'' [75,79,80].

Conclusions and Future Perspectives: Will There Be Room for Echocardiography?

For symptomatic severe AS patients who are inoperable or have a high risk for surgery, TAVR has proven to be a feasible alternative to surgical valve replacement with good mid-term valve durability. Recently, TAVR has been increasingly performed in intermediate-risk patients and it is currently extending even to low-risk and asymptomatic patients. Proper patient and prosthesis selection, procedural surveillance and follow-up are paramount for TAVR success. Echocardiography is an important imaging modality in all these steps of TAVR. However, emerging multimodality imaging techniques enable a more tailored approach based on patient-specific characteristics and often provide additional information in particular settings, emphasising the importance of a multimodality imaging approach combining echocardiography with other modalities (Table 2). Numerous studies have established that 3D techniques such as CT and 3D TEE provide more accurate measurements of the aortic annulus and root, resulting in improved prosthesis selection and consequently higher procedural success rates. Additionally, growing operator experience and technical improvements in both prostheses and delivery systems have led to the increased use of conscious sedation with procedural guidance by fluoroscopy and TTE only instead of general anaesthesia guided by TEE, reducing invasiveness and procedural risks. At follow-up, echocardiography (particularly TTE) remains the main imaging modality for the assessment of prosthetic valve durability and detection of valve deterioration or late complications. However, for the detection of prosthetic valve thrombosis and endocarditis, alternative imaging modalities such as CT and PET/CT have demonstrated superior diagnostic accuracy and the implementation of these techniques in future studies will shed more light on the incidence, optimal patient management and effect on prosthetic valve durability of these complications.

Conflicts of Interest

The Department of Cardiology, Heart Lung Center, Leiden, University Medical Center (Leiden, The Netherlands) received research grants from Biotronik, Medtronic, Boston Scientific, GE Healthcare and Edwards Lifesciences. Jeroen J Bax and V. Delgado received speaker fees from Abbott Vascular. The other authors have no conflict of interest.

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