Multimodality imaging for myocardial injury in acute myocardial infarction and the assessment of valvular heart disease

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Transcatheter aortic valve replacement: advantages and limitations of different cardiac imaging techniques

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ABSTRACT

Transcatheter aortic valve replacement is an established therapy for patients with symptomatic severe aortic stenosis and contraindications or high risk for surgery. Advances in prosthesis and delivery systems designs and continuous advances in multimodality imaging, particularly the 3-dimensional techniques, have led to improved outcomes with significant reductions in the incidence of frequent complications such as paravalvular aortic regurgitation. In addition, data on prosthesis durability are accumulating. Multimodality imaging plays a central role in the selection of patients who are candidates for transcatheter aortic valve replacement, procedure planning and guidance, and follow-up of prosthesis function. The strengths and limitations of each imaging technique for transcatheter aortic valve replacement will be discussed in this review article.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has become a safe and feasible alternative treatment for patients with severe aortic stenosis (AS) who have contraindications or are at high risk for surgical aortic valve (AV) replacement. In terms of survival and improvement in clinical symptoms, large randomized clinical trials have proven TAVR to be superior to medical therapy (and balloon valvuloplasty) in patients deemed inoperable[1,2] and non-inferior to surgical AV replacement in patients with high operative risk.[3,4] These results encouraged the rapid implementation of TAVR in current practice with more than 200.000 patients treated worldwide.[5] Patient selection, accurate sizing of the prosthesis and procedural planning require the use of several imaging modalities to optimize results and minimize the complications such as paravalvular regurgitation (PVAR), pacemaker implantation, vascular injury or annulus rupture. Procedural guidance is mainly performed under fluoroscopy assistance and, still, in many laboratories, with the help of transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE). The steep learning curve of the procedure and the low number of periprocedural complications in high-volume centers have allowed less invasive TAVR by implanting the device under conscious sedation. Therefore, the need for TEE during the procedure has recently been questioned. In addition, prosthesis durability is an important factor to eventually expand this procedure to patients with low-intermediate operative risk. Five years follow-up data from the Placement of AoRTic TraNscathetER valves (PARTNER) trial showed no structural degeneration of the balloon expandable prosthesis with stable transvalvular gradients and aortic valve areas (AVA).[6,7] However, the use of high spatial resolution imaging techniques such as multidetector row computed tomography (MDCT) have raised concern due to the presence of thickening and restriction of the prosthetic leaflets suggesting subclinical thrombosis that could not be appreciated with echocardiography.[8] The present review article summarizes the role of multimodality imaging for preprocedural planning (patient selection, device sizing and procedural access), procedural guidance and follow-up, highlighting the pros and cons of each imaging modality.

PREPROCEDURAL PLANNING

Accurate assessment of AS severity, aortic valve and root anatomy and geometry and evaluation of feasibility of peripheral vascular access are three key steps during planning of TAVR.

Aortic stenosis severity

Doppler TTE is the imaging technique of choice to assess AS severity.[9,10] It provides key insights into AV anatomy, degree of calcification, hemodynamic consequences of AS (left ventricular [LV] size, wall thickness and function, pulmonary arterial pressure), concomitant valve disease and aortic pathology. Aortic jet velocity >4 m/s, mean transvalvular pressure gradient >40 mmHg and calculated aortic valve area (AVA) <1.0 cm^2 define severe AS.[9,10] There are situations however where these parameters are not congruent, challenging the diagnosis of severe AS and the management of the patients.

When severe AS coexists with reduced LV systolic function, the flow derived indices may underestimate the degree of AS. Such condition is termed classical low-flow low-gradient AS and is characterized by reduced LV ejection fraction (LVEF), an AVA <1.0 cm^2, aortic velocity <4 m/s, mean gradient <40 mmHg and stroke volume index <35 mL/m^2.[10,11] In this subgroup of patients differentiation between true severe AS and pseudosevere AS has important therapeutic implications.[12,13] Using low dose dobutamine stress echocardiography (DSE), the contractile reserve of the left ventricle is increased leading to an increase in LV stroke volume (flow).[11] In a true severe AS the increase in flow is associated with an increase in transvalvular gradients while the AVA remains <1.0 cm^2 (Figure 1). In contrast, in pseudosevere AS the increase in LV contractility and flow results in an increase in AVA >1.0 cm^2 while the transvalvular gradients remain low. However, 30-40% of patients with classical low-flow low-gradient severe AS do not show contractile reserve during low dose DSE.[13] In this specific group of patients, the use of computed tomography and the assessment of aortic valve calcification burden may help to estimate the severity of AS (Figure 1).[14,15] A cut-off value of aortic valve calcification of ≥1,274 AU in women and ≥2,065 AU in men were more frequently associated with severe AS.[14]

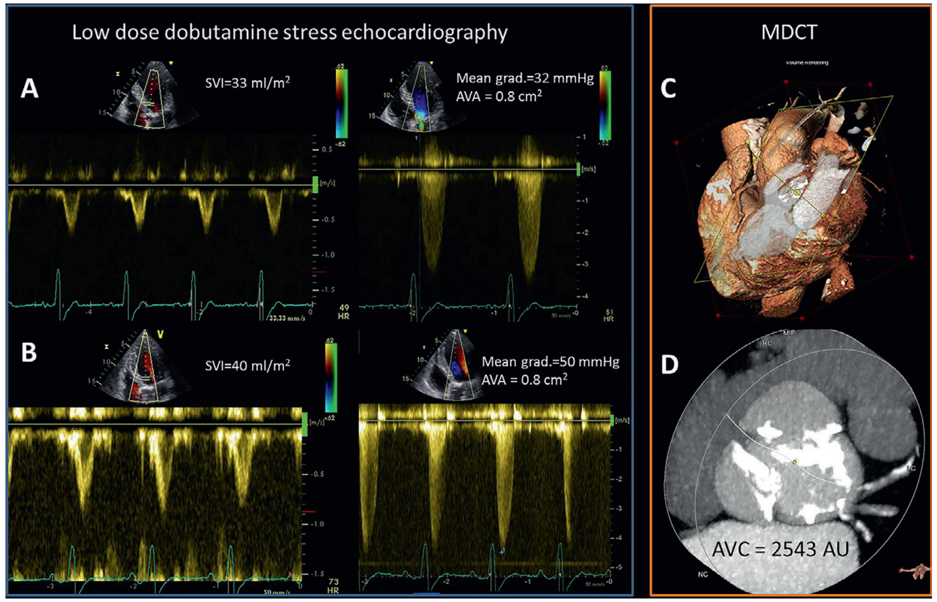

Figure 1: **Low-dose dobutamine stress echocardiography (DSE) and aortic valve calcification (AVC) assessment with multidetector row computed tomography (MDCT) in a patient with low-flow low-gradient severe aortic stenosis (AS) with reduced left ventricular systolic function. (A)** Baseline echocardiographic assessment revealed discrepant indices of AS severity. The mean gradient was 32 mm Hg and aortic valve area (AVA) was 0.8 cm^2. Stroke volume index (SVI) of 33 ml/m^2. **(B)** Low-dose DSE resulted in an increase of the mean gradient to 50 mm Hg, the AVA remained unchanged and the SVI increased by 21%. This indicates that the patient had classical low-flow low-gradient severe AS and a presence of flow reserve (SVI increased >20%). **(C)** Volume rendered cardiac MDCT with a plane across the aortic annulus. **(D)** AVC load, using the Agatston method, was measured 2543 arbitrary units (AU), indicating severe aortic stenosis (cut-offs for severe AS ≥2,065 AU in men and ≥1,274 AU in women[14]).

Patients with paradoxical low-flow low-gradient severe AS present with preserved LVEF, AVA <1.0 cm^2, mean gradient <40 mmHg and LV stroke volume index <35 mL/m^2.[9,10] In this subgroup of patients, the low-flow condition is determined by the small LV cavity due to severe LV hypertrophy. The management of these patients remains challenging. Clavel *et al.*[16] compared the outcome of 187 patients with paradoxical low-flow low-gradient severe AS with 187 patients with severe AS and high gradient (matched according to AVA) and with 187 patients with moderate AS (matched according to mean transvalvular gradient) and showed that patients with paradoxical low-flow low-gradient severe AS have reduced overall survival (1-year 89±2%; 5-year 64±4%) compared with patients with high gradient severe AS (1-year 96±1%; 5-year 82±3%) or moderate AS (1-year 96±1%; 5-year 81±3%). Moreover, AV replacement was significantly associated with improved survival in patients with paradoxical low-flow low-gradient severe AS, but not in the moderate AS group.[16] Of note, the study population was relatively heterogeneous with a significant proportion of patients being asymptomatic and with heterogeneous management (80% of patients with severe AS and high gradient underwent AV replacement compared with 56% in the group of paradoxical low-flow low-gradient and 40% in moderate AS). In contrast, Jander *et al.*[17] demonstrated that patients with asymptomatic severe AS, low gradient and preserved LVEF (low stroke volume index <35 mL/m2 was present in 51%) had comparable outcome to that of patients with moderate AS (major cardiovascular events 14.8±1.0% versus 14.1±1.5%, respectively; P=0.59).

According to current guidelines the finding of paradoxical low-flow low-gradient AS has to be approached stepwise.[9] Any source of error in measured parameters of the continuity equation used for AVA calculation has to be addressed first. Left ventricular outflow tract (LVOT) cross-sectional area (CSA) is one of the key parameters. With 2-dimensional (2D) echocardiography, LVOT CSA is traditionally derived by measuring mid-systolic sagittal LVOT diameter in the parasternal long-axis view assuming a circular geometry. However, a sigmoid septal basal hypertrophy characteristic of elderly patients may challenge the accuracy of this method since the LVOT may become elliptical (Figure 2).[18,19] By measuring the planimetric area of the LVOT with a 3-dimensional (3D) imaging technique such as MDCT and introducing the value into the continuity equation it has been demonstrated that 33% of the low-gradient severe AS patients with preserved LVEF could be reclassified into moderate AS.[20] In case of small body surface area (BSA) the correction for BSA is necessary, with an AVA index <0.6 cm^2/m^2 indicating severe AS. A severely increased global hemodynamic afterload (i.e. valvulo-arterial impedance) should be also excluded. Furthermore, particular attention has to be paid to accurately determine the LV stroke volume, preferably by confronting measurements from other independent methods (2D or 3D volumetric methods by means of echocardiography, cardiac magnetic resonance imaging [CMR] or MDCT). Low dose DSE can provide additional information about the actual severity of the AS and can predict the risk of adverse events, but safety of DSE in patients with pronounced LV concentric remodeling and small LV cavities has yet to be established.[21] In addition, evaluation of the degree of AV calcification by computed tomography may be of help in this group of patients.[14,15]

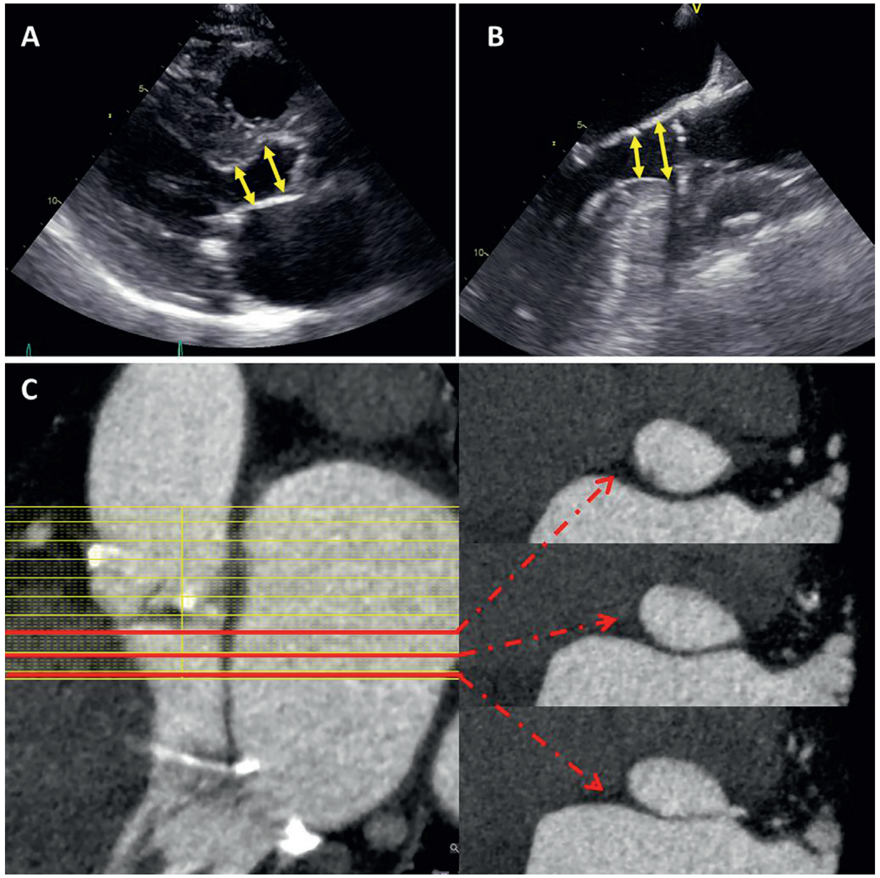

Figure 2: Assessment of left ventricular outflow tract (LVOT) with transthoracic (A) and transesophageal (B) echocardiography and multidetector row computed tomography (C). On 2-dimensional transthoracic and transesophageal echocardiography the measurement of the LVOT may vary significantly (arrows), particularly in patients with sigmoid septum, having important implications on aortic valve area calculation. On MDCT, the cross-sectional area of the LVOT at each level shows the increase of the elliptical shape for the aortic annulus toward the left ventricle. Red lines depict LVOT areas at 3 different levels showing the change in area and ellipticity of the LVOT.

Aortic annulus size

In contrast to surgical AV replacement, where surgeons can directly determine the optimal prosthesis size and visualize the adaptation of the prosthesis to the aortic root, in TAVR appropriate prosthesis selection rely mostly on preprocedural imaging. Too small prosthesis increases the risk of significant paravalvular regurgitation (PVAR) and prosthesis migration, while oversized prostheses may lead to incomplete deployment, potentially resulting in both, valvular and paravalvular regurgitation, or even catastrophic aortic annulus rupture.[22,23]

3D imaging techniques (3D echocardiography, MDCT, CMR) are currently the preferred tools to assess the aortic annulus size. Sagittal aortic annulus diameter, normally measured with 2D echocardiography tends to underestimate the true aortic annulus size.[24] In contrast, studies using 3D TEE or MDCT have shown that selection of prosthesis size based on these imaging modalities is associated with lower incidence of significant PVAR.[25 26,27] These 3D imaging techniques permit the measurement of the aortic annulus area and perimeter using direct planimetry and diameters derived from the area and the perimeter. The majority of manufacturers have also included these measurements into the prosthesis size charts allowing the standardization of the prosthesis selection.

The MDCT provides high spatial resolution images of the aortic annulus and aortic root. This imaging technique has become key in TAVR due to its low invasiveness and comprehensive evaluation of candidates for TAVR, including assessment of aortic annulus, burden of aortic valve and root calcification and peripheral arteries anatomy (Figure 3). In addition, MDCT permits planning of the C-arm projections needed for AV balloon dilation and prosthesis deployment, reducing the need of repeated angiographies during the procedure.[28,29] However, in patients with associated impaired renal function, the use of MDCT should be tailored in order to reduce the risk of periprocedural acute kidney injury. 3D TEE has also shown to be of value to size the aortic annulus, aortic root dimensions, aortic valve calcification burden and height of coronary ostia relative to the aortic annulus (Figure 4).[30] This imaging modality is however relatively uncomfortable for patients and the acoustic shadowing caused by the aortic cusp calcifications may impact on the spatial resolution of the images and on the accuracy of the measurements. CMR permits 3D analysis of the aortic annulus and root anatomy similarly to MDCT. However, this imaging technique is less available and not feasible in patients with non-MRI compatible implanted devices. These 3D imaging modalities have been compared in several studies showing similar accuracy to size the aortic annulus.[24,31,32] Of note, the data acquisition should be preferably performed with electrocardiogram (ECG) gating to obtain the systolic and diastolic dimensions of the aortic annulus. A recent study by Murphy and co-workers including 507 patients with severe AS who underwent ECG-gated MDCT showed significant changes in aortic annulus area and perimeter between systole and diastole (8.23% and 3.36%, respectively).[33] The implications of these findings are relevant since the use of the diastolic measure would have resulted in change of the prosthesis size (undersizing) in 50% of the patients. Therefore, assessment of systolic and diastolic measurements is recommended.[34]

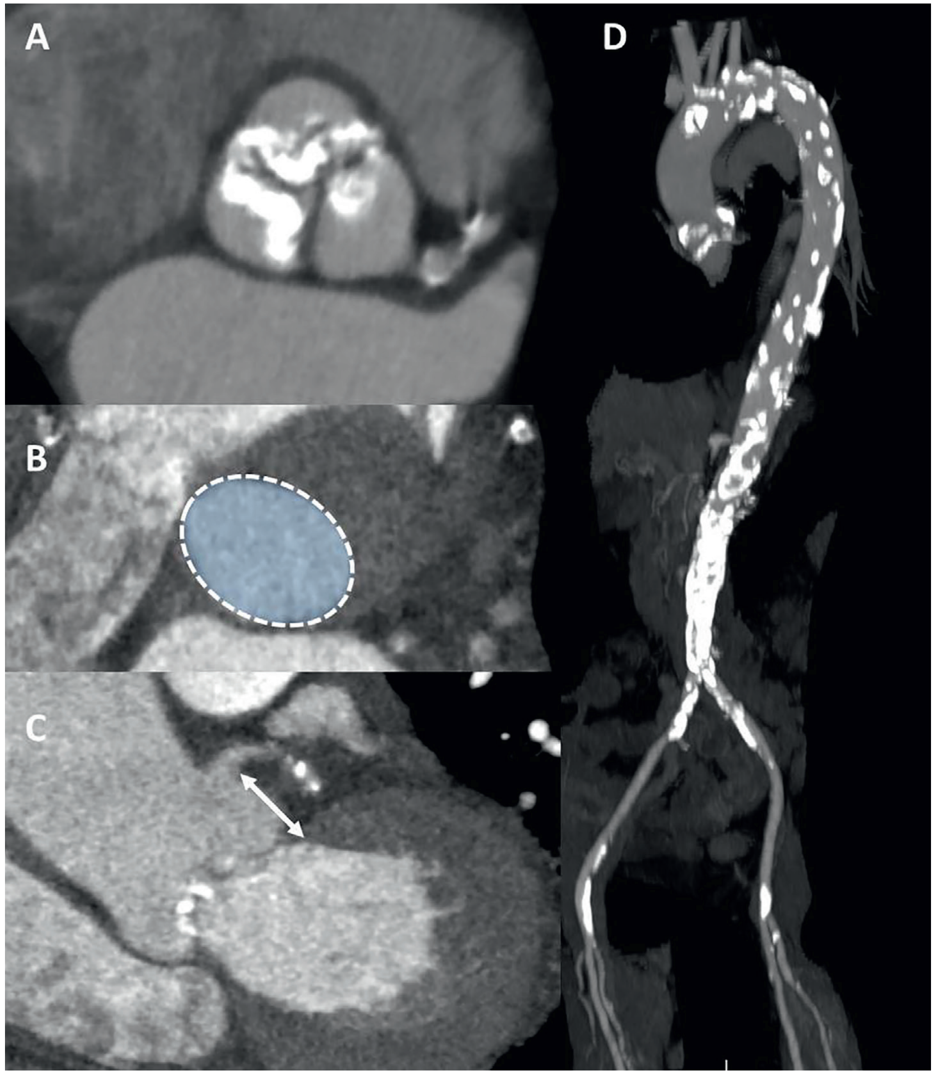

Figure 3: The role of multidetector row computed tomography (MDCT) in preprocedural assessment. (A) Double oblique transverse view of severely calcified tricuspid aortic valve. **(B)** Planimetry of the aortic annulus. **(C)** Measurement of the distance between the left main coronary artery and the aortic annulus (white arrow). **(D)** CT aortography reveals severely calcified aorta, particularly in the aortic arch and in the descendent part. Calcifications are present in both iliofemoral arteries as well.

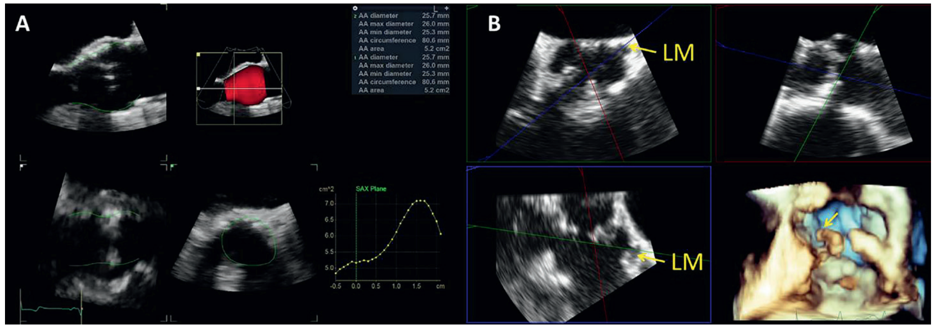

Figure 4: 3-dimensional transesophageal echocardiography (3D-TEE) in TAVR planning. (A) Automated analysis of the aortic root (AVQ software, GE, Horten, Norway) allows quick alignment of the orthogonal planes across the aortic annulus (AA) and accurate sizing. **(B)** Multiplanar 3D reconstruction of the aortic root to measure the distance between the main (LM) coronary artery from the aortic annulus (yellow arrows). At the same time the presence of bulky calcified cusps that may obstruct the coronary ostia can be appreciated, particularly in the 3D reconstruction.

During the procedure, aortic annulus can be also measured with supraaortic angiography during balloon aortic valvuloplasty (Figure 5). Several studies have shown the accuracy of this methodology to size the prosthesis.[35,36] During the balloon valvuloplasty, the presence of residual PVAR on angiography indicates undersized balloon.[36] Other authors have proposed the measurement of the balloon with sterile calipers during inflation at 2 atms and during full volume balloon inflation at the level of the valve any additional increase in the intraballoon pressure >2 atms will indicate that the diameter of the balloon is equal or larger than the aortic annulus.[35]

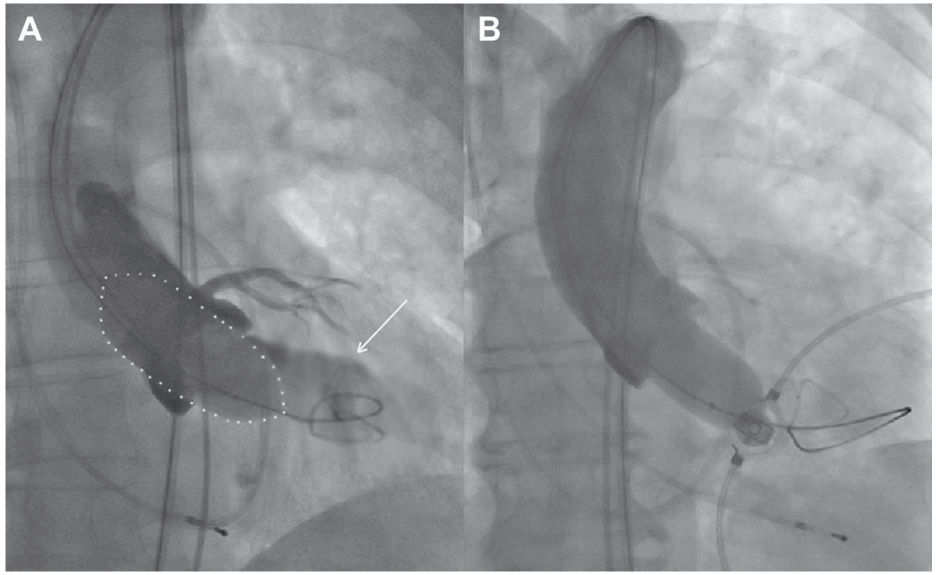

Figure 5: Supra-aortic angiography during balloon aortic valvuloplasty (BAV) for prosthesis size selection. (A) A 23-mm balloon (white dotted line) was chosen for a preparatory BAV according to the 2-dimensional transesophageal echocardiography (2D TEE) data on the aortic annulus size. Concurrent supra-aortic angiography, showing contrast regurgitation into the left ventricle (white arrow), indicated annulus size underestimation by 2D TEE and resulted in the selection of a bigger prosthesis. **(B)** Absence of contrast regurgitation into the left ventricle during BAV with a 23-mm balloon confirmed correct annular sizing based on pre-interventional 2D TEE. Reproduced with permission from Patsalis *et al*.[36]

Procedural access

One of the key aspects of preprocedural planning in TAVR is to choose the optimal access route. Potential TAVR access sites are transfemoral (TF), transapical (TA), transaortic (TAo), transsubclavian, transaxillary and transcarotid. The predominant approach worldwide is TF, since it is the least invasive and the most familiar to interventional cardiologists. According to the data from TAVR registries TF approach is chosen in Europe in 71-75%[37,38], while in USA in 56%.[39] Suitability of TF approach is predominately evaluated with angiographic assessment of the iliofemoral anatomy during coronary angiography. However, MDCT has shown better characterization of iliofemoral arteries and aortic size, tortuosity, degree of calcifications and plaque burden (Figure 6). Moreover, a detailed vascular anatomy can be clearly visualized with 3D volume rendered and multiplanar reconstructions. For currently available TAVR delivery catheters, a 6-6.5 mm threshold for minimal luminal vessel diameter of the femoral artery is considered to be acceptable.[40]

Traditionally the TA approach is preferred for patients whose peripheral vasculature is not suitable for TF. However, TA is the most invasive technique and it might be contraindicated in patients with certain comorbidities or high frailty indexes (severe pulmonary disease, chest wall deformity, very poor LV function, intracavitary thrombus). Alternatively, TAo has gained popularity due the simplicity of the procedure and superior results compared with the TA access in terms of survival.[41,42] MDCT analysis of the ascending aorta is essential in selecting patients for the TAo TAVR. The anterolateral portion of the ascending aorta 5-7 cm above the aortic annulus, where the cannulation of the aorta takes place (the so called TAo landing zone), should be free of calcium (Figure 6). Bapat *et al.*[43] have shown that the TAo approach is feasible in patients with severe aortic calcifications (porcelain aorta) since the TAo landing zone is frequently spared. Moreover, MDCT permits the evaluation of the spatial relationships between sternum and major vessels in the thorax. This is particularly important in patients with previous coronary artery bypass surgery, where a close proximity of the aforementioned structures or high proximal venous graft anastomoses affect the preferred TAo access route (e.g. opting for mini right thoracotomy instead of mini J sternotomy).[42]

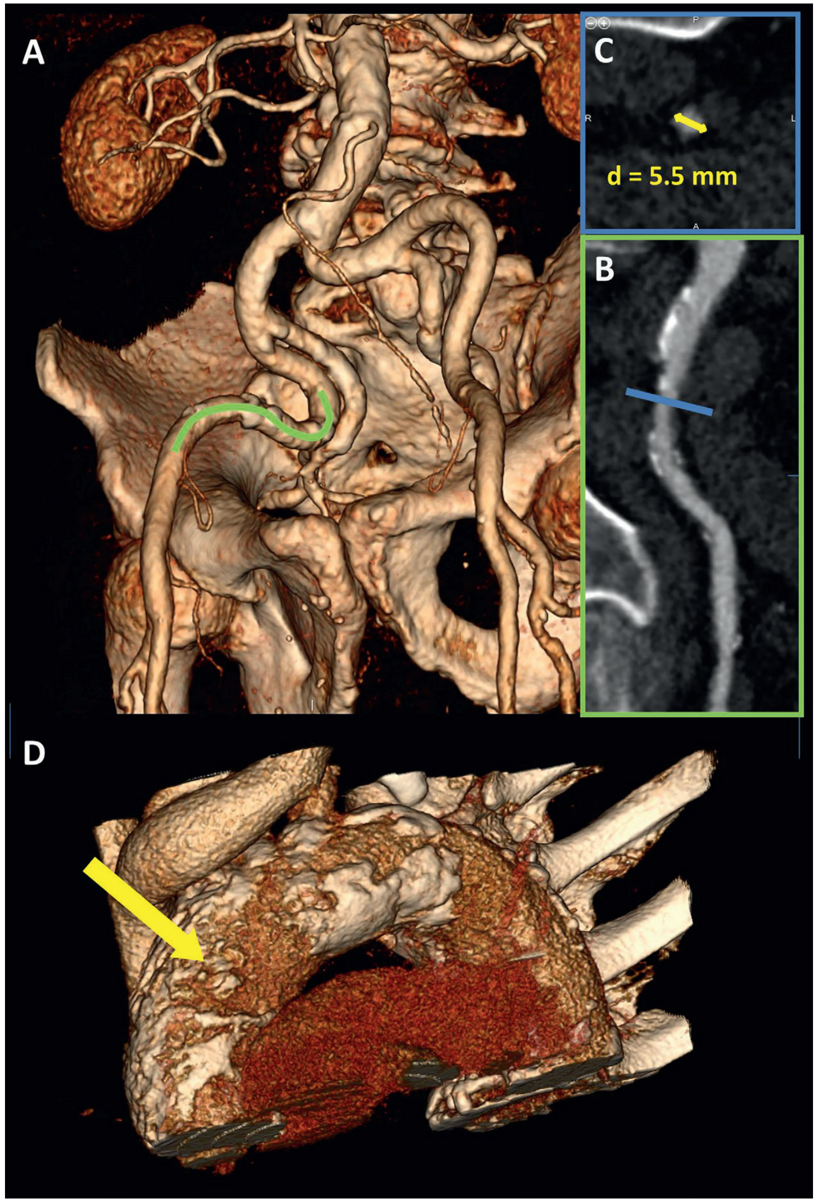

Figure 6: Assessment of TAVR access with multidetector row computed tomography (MDCT). (A) Severely tortuous iliofemoral arteries visualized with 3D volume rendering. **(B)** Segment of the right external iliac artery (green line) was more closely studied in a multiplanar reconstruction plane outlining high atherosclerotic burden with multiple plaques. **(C)** The cross-sectional lumen of the narrowest part of the vessel (blue line) was assessed. The smallest diameter was 5.5 mm (yellow arrow), precluding a safe transfemoral approach for the transcatheter aortic valve replacement (TAVR). **(D)** Severely calcified thoracic aorta – porcelain aorta particularly in the anterolateral portion of the ascendant aorta, corresponding to the landing zone for transaortic approach (yellow arrow).

IMAGING DURING TRANSCATHETER HEART VALVE IMPLANTATION

Procedural guidance during TAVR has been traditionally performed under fluoroscopy and angiography with the support of TEE (Figure 7).[44] This approach is still advocated by the European Association of Cardiovascular Imaging/American Society of Echocardiography (EACVI/ASE) recommendations.[45] However, current generation of TAVR devices with smaller delivery systems have increased the feasibility of TF approach, reduced procedural timings and invasiveness (similar to balloon valvuloplasty) questioning the need of general anesthesia. Indeed some large European TAVR centers have demonstrated excellent feasibility and safety of a simplified TF approach, performed using monitored anesthesia care (defined as cardiovascular and respiratory monitoring of the patient by a qualified anesthesiologist who may or may not be administering concomitant sedation[46]) or local anesthesia only.[47-49]

However, TEE, especially the real time 3D TEE, offers an incremental value over fluoroscopic and angiographic guidance in TAVR: it supports crossing severely calcified native aortic valve, significantly reduces radiation exposure and the use of nephrotoxic iodine contrast[50] and it allows detection of life-threatening complications at an early stage. Aortic annulus rupture, perforation of the myocardium with subsequent pericardial hemorrhage, coronary ostia occlusion resulting in myocardial ischemia, aortic perforation or dissection, prosthesis malpositioning or dislodgement and valvular or paravalvular leaks are the complications that TEE can immediately detect and influence the decision making (Figure 7).

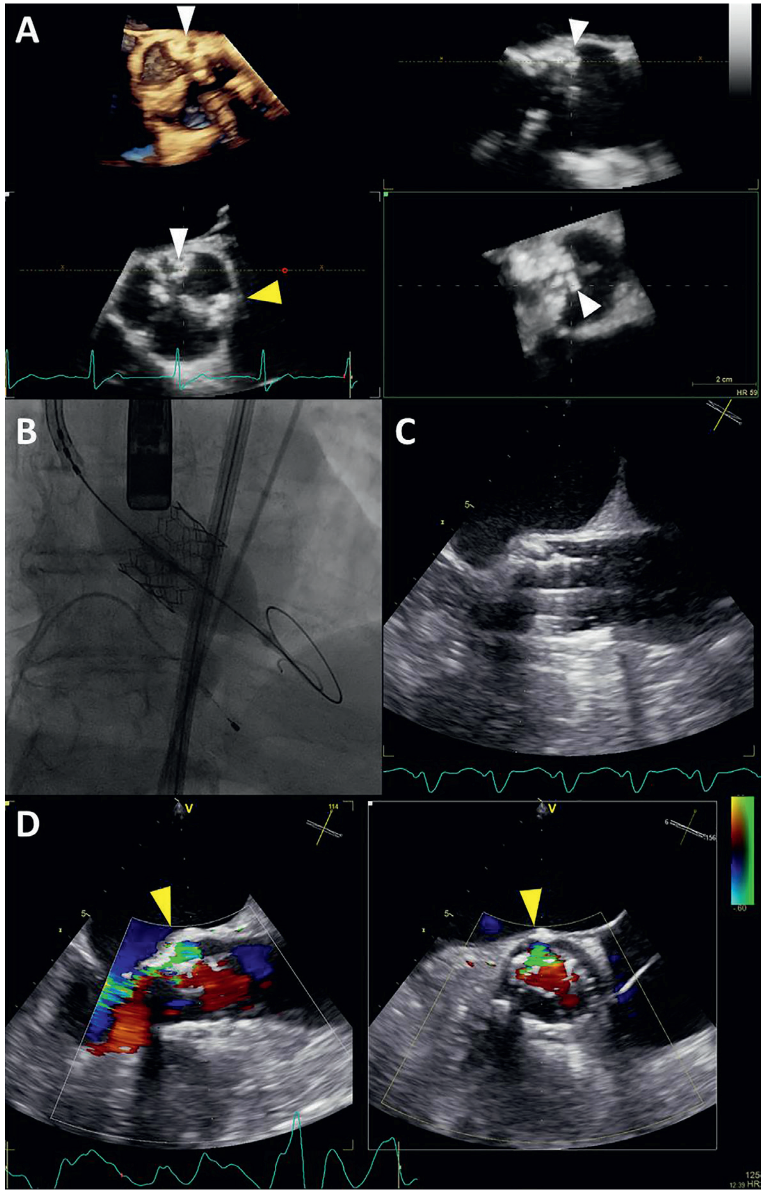

Figure 7: Multimodality imaging during transcatheter aortic valve replacement (TAVR). (A) Periprocedural 3-dimensional transesophageal echocardiography (3D-TEE) revealed severely calcified tricuspid aortic valve (AV). Particularly prominent calcifications were at the level of left- and non-coronary cusps commissure (white arrowheads) and at the level of left- and right-coronary cusps commissure (yellow arrowhead). **(B)** Balloon expandable transcatheter valve deployment, guided by fluoroscopy. **(C)** Concurrent real-time 2D-TEE image of the valve deployment. **(D)** Paravalvular aortic regurgitation (PVAR) visualized with colour Doppler biplane echocardiography (yellow arrowheads). PVAR originates at the level of highest annular calcification burden. The circumference of the PVAR is 20% of the prosthesis frame (short axis view on the right side), suggesting moderate PVAR according to Valve Academic Research Consortium-2 (VARC-2) criteria.[44]

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Although currently available prostheses have been associated with lower incidence of significant aortic regurgitation (AR) after TAVR[51,52], this complication remains still of concern since it has been associated with poor prognosis[7,53]. Evaluating the presence and severity of AR should include assessment of both central and paravalvular components, with a combined measurement of "total" AR, reflecting the total volume load imposed on the LV. The methods used in native valve regurgitation (qualitative assessment of the color flow Doppler, vena contracta, pressure half-time on the continuous-wave Doppler recordings) are limited in the setting of paravalvular jets, which are frequently multiple, eccentric and irregular in shape. Moreover, certain portions of the prosthesis ring and LVOT may be difficult to image due to acoustic shadowing. The EACVI/ASE guidelines for evaluation of the prosthetic valves propose the proportion of the circumference of the sewing ring, occupied by the jets, as an alternative semi-quantitative measure of paravalvular aortic regurgitation (PVAR) severity: <10% of the sewing ring suggests mild, 10–20% moderate and >20% suggests severe PVAR.[54] The Valve Academic Research Consortium-2 (VARC-2) has slightly modified these cut-of values in the TAVR setting; mild, moderate, and severe PAVR are defined by <10%, 10 – 29% and ≥30% of the circumference of the prosthesis frame, respectively (Figure 7).[44] Regurgitant volume calculation can be helpful in the TAVR setting as well. The method relies on the comparison of stroke volumes across the AV and another non-regurgitant valve (either mitral or pulmonary). The former can be obtained by subtracting the LV end-systolic volume from the end-diastolic volume or (more commonly) by employing the continuity equation and calculating the stroke volume across the AV. The difference between the stroke volume across AV and the non-regurgitant valve represents the estimate of total AV regurgitant volume. Secondary indices, such as diastolic flow reversal in descending aorta, may provide additional help in assessing the severity of PVAR after TAVR.

Another alternative periprocedural imaging method is the transnasal TEE.[23,45] Smaller transnasal probes allow prolonged monitoring without general anesthesia. However, image quality is lower compared with conventional TEE and transnasal probes do not have 3D capabilities. Some centers have adapted intracardiac echo (ICE) for TAVR guidance.[55] The ICE probe is advanced through the femoral vein into the right atrium, where it brings a close-up view of the aortic root. In addition to obviating the need for general anesthesia, ICE allows uninterrupted monitoring in TAVR (no fluoroscopic interference) and more feasible Doppler-based assessment of pulmonary artery pressures.[55] ICE technology is quickly developing allowing also live 3D imaging (though with a limited 22-90° volume). However, the

need for high expertise, lower image quality in comparison to TEE (especially 3D), possible interference with the pacemaker lead and particularly its high cost limit the widespread use of ICE in TAVR.

LONG-TERM FOLLOW-UP

After TAVR, TTE remains the imaging technique of first choice to evaluate the procedural results, the durability of the prosthesis and changes in LV dimensions and function. Post-discharge clinical, ECG and TTE evaluations at 30 days after TAVR are mandatory.[23,44] Further follow-up recommendations suggest TTE evaluation at 6 months and 1 year following implantation and yearly thereafter.[44] The frequency of follow-up evaluations should be increased if there is any change in clinical status or worsening of echocardiographic findings. However, as the experience with TAVR grows, the frequency of TTE assessment may likely decline towards that of surgical AV replacement with proposed annual check-ups 5 years after valve implantation.[54]

In terms of durability of the implanted prosthesis, valve position, morphology of the prosthetic leaflets and indices of valve stenosis and regurgitation should be evaluated with echocardiography. When calculating the effective orifice area (EOA) or another index of valve opening that employs the ratio of pre- to post-valvular velocities (e.g. Doppler velocity index [DVI]) it is essential to record the pre-valvular velocity (and LVOT CSA) immediately proximal to the stent of the implanted prosthesis. Due to the flow acceleration within the stent, measuring velocities even proximal to the valve cusps results in an overestimation of EOA or AVA.[23,44,45] Clavel *et al.*[56] reported slightly superior hemodynamic performance of transcatheter prostheses compared with the surgical bioprostheses. Fifty patients, who underwent TAVR were matched 1:1 for sex, aortic annulus diameter, LVEF, body surface area, and body mass index with 2 groups of 50 patients that underwent surgical AV replacement with stented or stentless valve prosthesis. Mean transvalvular gradients at 6-12 months after the procedure were significantly lower in the TAVR group (10 ± 4 mm Hg) compared to the surgical AV replacement group with a stented frame prosthesis (13 ± 5 mm Hg) and non-significantly different to the surgical AV replacement group with a stentless valve (9 ± 4 mm Hg).[56] Better hemodynamic results of the transcatheter valves were attributed to the thinner stent frameworks. In addition, the 5-year follow-up results of the PARTNER trial show stable hemodynamic performance of the transcatheter and surgical prostheses without signs of valve degeneration (Figure 8).[7] However, Latib *et al.*[57]

showed in a retrospective analysis of 4266 patients who underwent TAVR in 12 different centers worldwide an incidence of 0.61% of transcatheter valve thrombosis after a median follow-up of 6 years. Of the 26 patients with suspected valve thrombosis, 92% presented with raised mean transvalvular gradients >20 mm Hg and 65% had exertional dyspnoea. Anticoagulation resulted in a significant decrease of transvalvular gradients in all medically treated cases.[57] However, recent studies using 4-dimensional MDCT have suggested that transcatheter valve thrombosis may be more frequent. Leetma *et al.*[58] reported an incidence of 4% in a cohort of 140 patients who underwent MDCT 1-3 months after TAVR. Transcatheter valve thrombosis was defined by the presence of leaflet thickening (low-attenuation masses attached to valve cusps or a diffuse thickening of ≥1 valve cusps) and restriction. Anticoagulation treatment was successful, leading to a complete resolution of thrombi on a control MDCT.[58] Theses MDCT findings may not be accompanied by changes in symptoms or changes in valve hemodynamics as assessed with TTE suggesting that MDCT may detect valve thrombosis at an earlier stage. Makkar *et al.*[8] reported reduced bioprosthesis leaflet motion, detected on 4-dimensional volume-rendered CT scans in 40% (22 of 55 patients) in the Portico Re-sheathable Transcatheter Aortic Valve System US IDE Trial (PORTICO IDE) and in 13% (17 of 132 patients) in two registries of aortic transcatheter and surgical bioprostheses in USA and Denmark. Restoration of leaflet motion was noted in all 11 patients who started warfarin anticoagulation after the CT findings and only in 1 of 10 patients who did not.[8] Of note, again no echocardiographic indices of valve dysfunction were noted. These findings indicated the need for prospective, well-designed, and adequately powered studies that will provide relevant answers about the clinical significance of these findings (both, in terms of neurological outcome and prosthesis durability), the optimal antithrombotic treatment after TAVR as well as the imaging approach in the long-term follow-up.

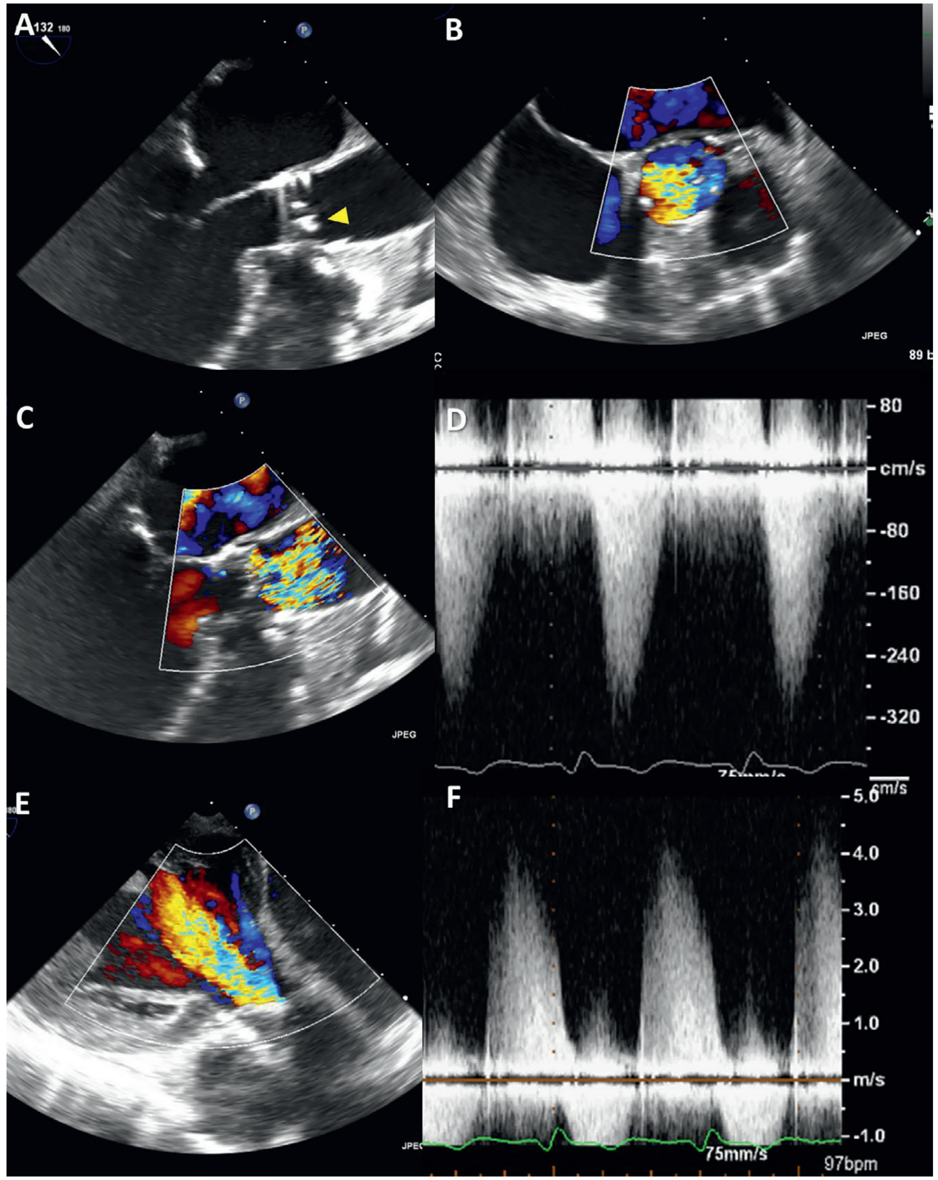

Figure 8: Prosthesis degeneration 4 years after transcatheter valve replacement (TAVR). (A) Transesophageal echocardiography (TEE) shows focally thickened and calcified prosthesis leaflets (yellow arrowhead). **(B)** Color Doppler image in the mid-esophageal short-axis view of the aortic valve reveals turbulent antegrade flow in a limited cross-sectional area. **(C)** Color Doppler of the long-axis view confirms high turbulence downstream the prosthesis, implying severe prosthetic valve stenosis. **(D)** High gradients obtained with continuous wave Doppler confirm significant prosthesis stenosis. **(E)** Color Doppler transgastric view shows severe aortic regurgitation. **(F)** High density and steep downsloping of the continuous wave Doppler recordings of the regurgitant flow confirm severe AR.

Changes in PAVR grade over time should be also evaluated at follow-up. In addition to TTE and TEE, CMR may be employed to assess the severity of PVAR. CMR phase-velocity mapping of the blood flow in ascendant aorta allows independent estimation of the AV regurgitant volume and regurgitant fraction.[59] Sherif *et al*.[60] have shown that quantitative measurements of AR by CMR is superior to semi-quantitative echocardiographic assessment with color flow Doppler imaging and that the latter may underestimate the degree of PVAR after TAVR.

Another adverse outcome after TAVR is infective endocarditis. Results from a large multicenter study report 0.50% incidence of infective endocarditis at 1 year after TAVR.[61] However, the outcome is devastating, with 47% and 66% mortality during the index hospitalization and at 1 year follow up, respectively.[61] TTE and, particularly with prosthetic valves, TEE are the first choice imaging techniques in the diagnostic workup of suspected infective endocarditis, helping to reveal the presence of vegetations, abscesses, pseudoaneurysms, their hemodynamic consequences (usually severe valvular or paravalvular AR), possible involvement of other valves (e.g. extension to anterior mitral leaflet) and to evaluate LV function. Importantly, infective endocarditis should always be suspected in patients with new periprosthetic regurgitation until proven otherwise.[62] Real time 3D TEE is of incremental value for the analysis of vegetation morphology and size and may lead to a better prediction of the embolic risk.[63] MDCT can be used to detect abscesses/pseudoaneurysms with a diagnostic accuracy similar to TEE, and is possibly superior in assessing the extent of perivalvular infective endocarditis extension.[64] In addition, nuclear molecular techniques, particularly radiolabeled white blood cell SPECT/CT and ^{18}F-FDG PET/CT imaging, are evolving as important supplementary methods for patients with suspected infective endocarditis. The main added value of these techniques is the reduction in the rate of misdiagnosed infective endocarditis, classified in the “Possible infective endocarditis” category using the Duke criteria, as well as the detection of peripheral embolic events.[65]

Table 1: Multimodality imaging techniques in TAVR.

Imaging technique	Pre-procedural	Peri-procedural	Follow-up
Echocardiography (TTE/TEE)	• AS severity • AV anatomy and degree of calcification • Aortic annulus size and root anatomy (3D) • Concomitant valvular disease • LV function	• Guiding catheters • Position and deployment of the prosthesis • Valve hemodynamics • Other procedure related complications (pericardial effusion, myocardial ischemia, aortic dissection…)	• Prosthesis deployment and hemodynamics • LV function • Concomitant valvular disease • Valve thrombosis, infective endocarditis (TEE)
Multidetector row Computed Tomography	• Aortic annulus size and root anatomy • AV anatomy and degree of calcification • Thoracic aorta, including calcification burden • Peripheral arteries • LV function • C-arm projections		• Deployment of prosthesis • Valve thrombosis (subclinical) • Infective endocarditis
Cardiac Magnetic Resonance	• Aortic annulus size and root anatomy • AV anatomy • LV function • Thoracic aorta • Peripheral arteries		• Prosthesis deployment and hemodynamics (regurgitation volume) • LV function
Fluoroscopy	• Aortic annulus dimension • Peripheral arteries	• Guiding catheters • Position and deployment of the prosthesis • Valve hemodynamics • Other procedure related complications (aortic annulus rupture, coronary ostia occlusion, aortic dissection…)	
Nuclear Imaging			• SPECT/CT and ^{18}F-FDG PET/CT in assessment of infective endocarditis

3D = 3-dimensional; ^{18}F-FDG PET = ^{18}F-fluorodeoxyglucose positron emission tomography; AS = aortic stenosis; AV = aortic valve; CT = computed tomography; LV = left ventricle; SPECT = single-photon emission computed tomography; TEE = transesophageal echocardiography: TTE = transthoracic echocardiography.

CONCLUSIONS

TAVR is an established therapy for patients with symptomatic severe AS and contraindications or high risk for surgery. To optimize the results of this therapy, accurate selection of patients, planning of the procedure and appropriate surveillance at follow-up are essential. Multimodality imaging plays a central role in these steps. The possibilities are numerous and the strengths and limitations of each imaging technique, the local expertise and availability are important to select the imaging technique to answer the questions arising at each procedural step (Table 1). The learning curve and cumulative evidence show superior accuracy of 3D imaging techniques to size the aortic annulus and select the prosthesis and the refinement in prosthesis design has led to important changes, reducing the invasiveness of the procedure which is more frequently performed under conscious sedation, fully fluoroscopy guided and using TTE to evaluate the prosthesis function. However, the use of MDCT and CMR at follow-up has provided interesting findings that may have an impact on the management of the patients. Additional studies providing data on durability of the TAVR prostheses will shed light into the incidence of valve thrombosis and infective endocarditis.

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