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The Role of Imaging in Transcatheter Aortic Valve Implantation (TAVI)

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ABSTRACT

Aortic Stenosis (AS) is by far the most prevalent form of VHD in the elderly. The contemporary etiologies of AS are due to degenerative mechanisms rather than rheumatic diseases, especially in the western world. Transcatheter aortic valve implantation (TAVI) has evolved dramatically as an alternative treatment to surgical aortic valve replacement (SAVR) in patients with severe AS. The fast development of TAVI can be linked to the rising competence of interventionists and the improvements in technology and imaging techniques.

In order for the TAVI procedure to be successful, multiple imaging modalities (TTE/TEE, MDCT, etc.) must be utilized. These imaging modalities are utilized for a variety of purposes, including but not limited to guiding pre and post-procedural evaluation and planning, intra-procedural imaging, and follow up. Both patient and implant selections greatly depend on a thorough pre procedural evaluation of the aortic valve structure, ascending aorta, and vascular access. The use of 2D TEE has been superseded by 3D TEE which offers better measurement planes and tissue resolution.

There is accumulating scientific data supporting the immense importance of MDCT among other imaging modalities in evaluating the anatomy, access appropriateness, and determining optimal coaxial angles for measurement. In post-procedure imaging, MDCT is also useful for evaluating valve position and functionality. This review summarizes the main elements of the TAVI procedure and the use of various imaging modalities. In addition to discussing the role of these modalities in minimizing procedural complications and optimizing TAVI outcomes.

INTRODUCTION

A primary concern of public health is valvular heart disease (VHD), and aortic valve stenosis (AS) is known to be the most common type of VHD especially in the western world. Contemporary population studies and clinical registries have shown that the clinical distribution of the aetiology of AS has moved away from rheumatic diseases and toward degenerative processes. AS is most commonly seen in the elderly with accompanying comorbidities and cardiac risk factors [1]. The Helsinki Ageing Study reported a 40% to 75% increase of detected cases with aortic valve calcification which was mainly at ages between 65- 85 years [2]. The AS can be defined as a decrease in the opening of the aortic valve (AV) during systole, due to a combination of fibrosis and calcium build-up around the AV annulus which causes the AV to be stiff and less flexible with reduced ability to open fully. In turn, this leads to a significant increase in the left ventricular (LV) afterload. Moreover, degenerative AS is not only associated with the known "wear and tear" phenomena but also inflammatory processes can play a significant role in the development and progression of AS [3]. Until a few years ago, surgical aortic valve replacement (SAVR) was the standalone treatment for symptomatic adult patients with severe AS. Although the risk of SAVR is generally consid-

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ered low in cases of isolated AS, the risk rises when there is a pre-existing coronary artery disease or reduced LV function as well as other comorbidities (e.g. vascular, renal or respiratory diseases) [4].

Transcatheter aortic valve implantation (TAVI) has firstly introduced as an alternative treatment to SAVR in high-risk patients in 2011. A few years later and following the PARTNER 2A and SAPIEN 3 trials, the indication of TAVI has expanded to include an intermediate-risk patient population. Intermediate risk is mainly determined by the treating Heart Team with the help of some risk stratification tools such as STS-PROM or EuroSCORE [5]. In the NOTION trial, which is been recently completed, it was found that in low-risk patients with severe AS, there were no significant differences between TAVI and SAVR in terms of all-cause mortality, stroke, or myocardial infarction, in addition to bioprosthetic valve failure after 8 years follow-up [6]. Consequently, TAVI for low-surgical risk patients has now been included in the American Heart Association (AHA) guideline for VHD. Despite this, the data about the durability of TAVI valves is limited, as well as the long-term outcome of TAVI in comparison to SAVR [7]. This rapid evolution of TAVI is attributed to advances in technology and multimodality imaging in parallel to increases in competency of interventionists who perform this type of procedure [8]. However, TAVI still has certain risks, including vascular injuries, valvular leakage, stroke, and heart block that necessitates a pacemaker [9]. This paper will discuss the role of these imaging modalities in the TAVI procedure. Therefore, the following section emphasizes on each modality with its function in TAVI.

Before discussing each imaging modalities' contribution in TAVI, the characteristics of the aortic apparatus should be highlighted. The annulus used in TAVI measurements is a virtual basal ring rather than an anatomic annulus. Additionally, this virtual structure consists of an elliptical (oval) ring shaped by three hinge points at the nadir of each aortic cusp (**Figure 1**). In addition to the anatomical features of the aortic annulus, it is worth knowing that the cardiac cycle affects the measurements of the annulus. The dimension and geometry of the aortic annulus may vary between systole and diastole, it is thought that during mid systole the annulus reaches its most widest and circular shape [10].

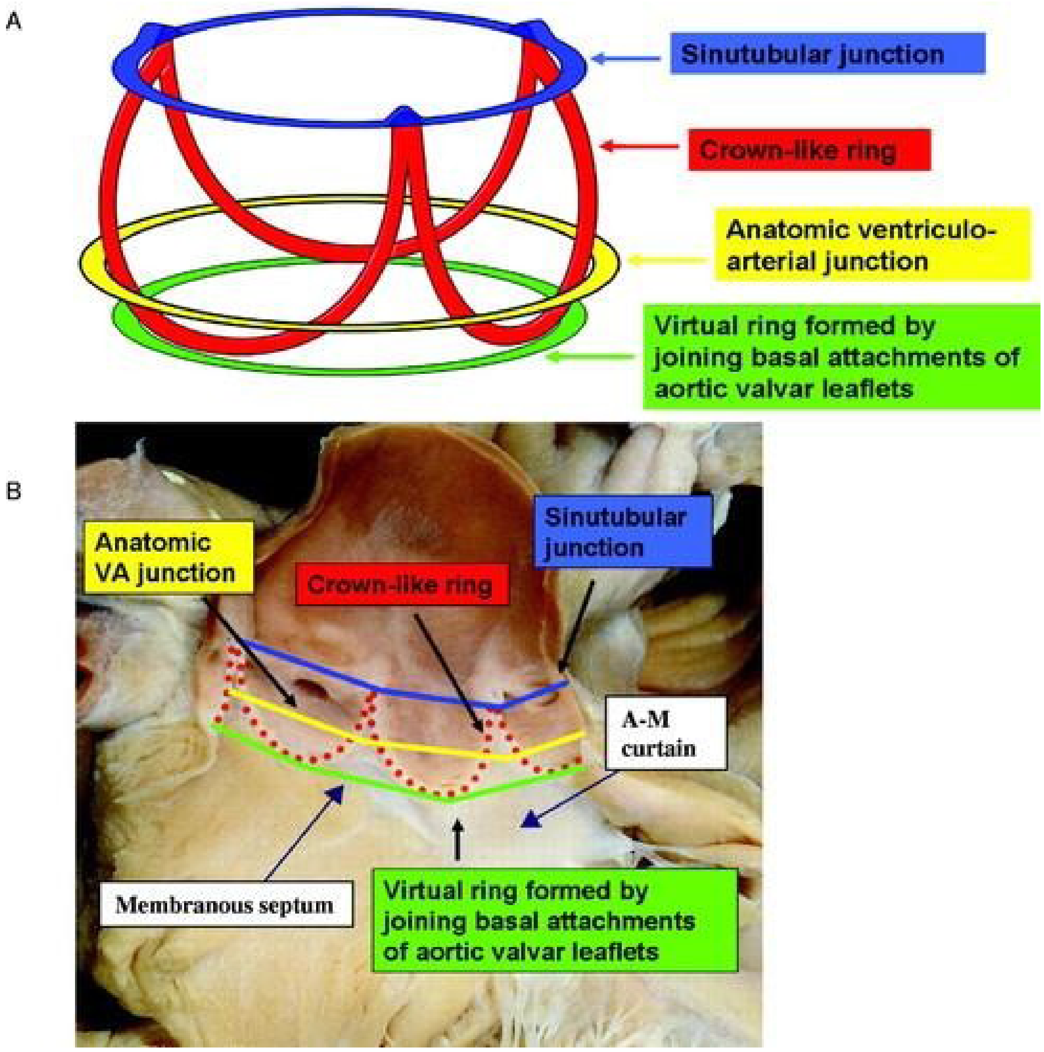

Figure 1: The green oval ring represents the virtual annulus or TAVI sizing. Nicoló Piazza. Circulation: Cardiovascular Interventions. Anatomy of the Aortic Valvar Complex and Its Implications for Transcatheter Implantation of the Aortic Valve, Volume: 1, Issue: 1, Pages: 74-81, DOI: (10.1161/CIRCINTERVENTIONS.108.780858) [11].

Transthoracic Echocardiography (TTE)

Echocardiography (TTE or TEE) is employed in TAVI candidates to obtain the following measurement parameters: the severity of aortic stenosis, anatomy of the aortic valvular complex (**Figure 2**), quantification of mitral regurgitation (MR), and LV function [11]. Transthoracic echocardiography (TTE) is the initial tool to assess patient eligibility to TAVI. The indication for AV replacement for either TAVI or SAVI relies predominantly on the severity of AS and the presence of reduced LV function (LVEF <50%) in symptomatic patients. As per the current guidelines, the AV is classified as severe when the opening of AV area is ≤1.0 cm² (or if indexed ≤0.6 cm²/m²), a transvalvular jet velocity of >4 m/s, and a mean gradient ≥40 mmHg, all of which can simply be acquired using the Doppler technique. Most AS cases present with a high transvalvular gradient; nevertheless, there are few patients who can exhibit a low-flow low gradient AS. Low flow is known as a stroke volume index (SVI) ≤35 ml/m² and low gradient as a mean gradient less than 40 mmHg. This low gradient AS is most commonly seen in patients who have a systolic dysfunction with LVEF <40% though can also occur in those patients with a normal LVEF who have small LV cavities secondary to LV hypertrophy. In such patients, dobutamine stress echocardiography (DSE) may be used to confirm true severe AS (≤1.0 cm²) and roll out pseudo-severe AS which is an increase in AV area (>1.0 cm²) with blood flow during stress (**Figure 3**) [12].

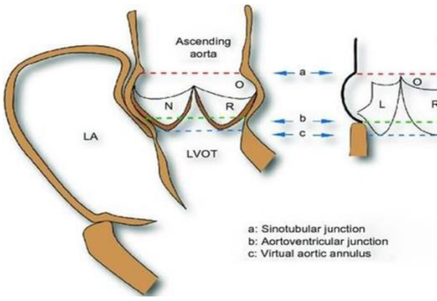

Figure 2: Diagram showing the main components of the AV complex (this may refer to as aortic root plus LVOT). (a) is the sino-tubular junction, (b) middle annulus is at the atrioventricular junction, and a third a virtual ring at the nadir of the AV leaflets (c) is the annuals used for the valve size in TAVI. Two small circles in the right and left sinus of Valsalva representing the right & left coronary ostium. Imaging techniques in transcatheter aortic valve replacement. Res Reports Clin Cardiol. 2013 [14]

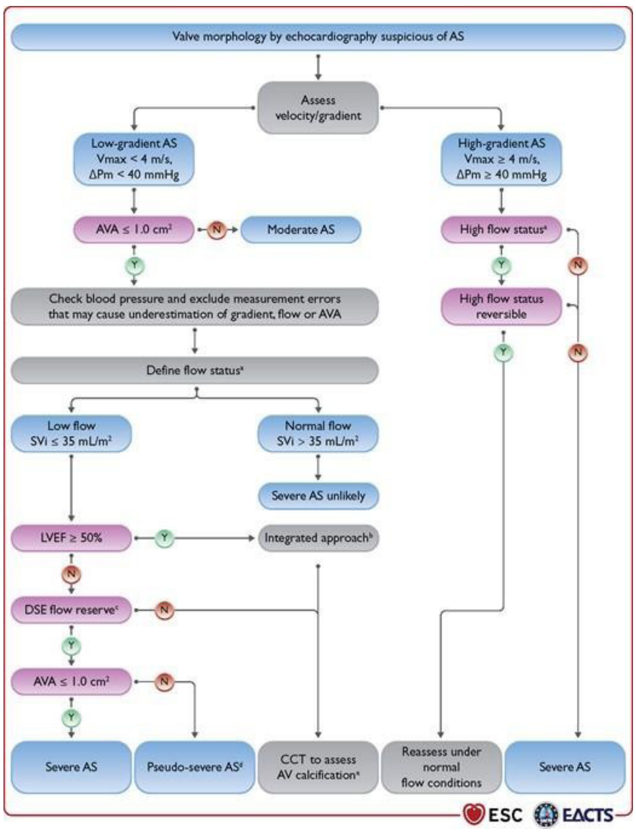

Figure 3: 2021 ESC/EACTS Guidelines for the management of valvular heart disease [13]

The AV complex is composed of the left ventricular outflow tract (LVOT), the aortic annulus, the AV leaflets, and the sinuses of Valsalva up to the sinotubular junction [13]. 3D imaging echo has contributed to a better comprehension of the anatomy of this complex. Just as important, the use of TTE to identify the morphology of the AV, as the presence of bicuspid aortic valves (BAV) may challenge TAVI due to the risk of malposition; nevertheless, the current-generation devices have supersede this defect [14]. Additionally, the extent of calcifications and its location in AV is a significant predictor of complications during the procedure. For instance, calcium embolization can cause stroke or coronary artery occlusion if the calcium is around the coronary ostia [15]. Additionally other calcification present in the AV complex can result in annular rupture, paravalvular leak (PVL), aortic root perforation or wall dissection [16].

Another important assessment which made by echo is the quantification of MR, if present. MR is known to be associated with AS in TAVI candidates in up to 74% of cases [17]. A metanalysis found that moderate to severe MR post-TAVI is linked with increased mortality [18]. Thus, MR quantification by echo prior to the procedure is neccessary for the proper management of these patients. The echo assessment of the LV function has similar importance, as improved systolic and diastolic LV function predicts a successful TAVI outcome [19]. Furthermore, those individuals with reduced LVEF less than 40% have a high post-TAVI mortality [20]. Similarly, the assessment of the LV structure can show any accompanying LVOT obstruction due to increased afterload or hypertrophic cardiomyopathy (HCM). This may help the interventionist to anticipate any challenges arising during the implantation. The detailed approach to assessing the aortic valve and mitral valve is discussed in the guidelines of the European Association of Cardiovascular Imaging and the American Society of Echocardiography [21].

The quality of TTE images tends to be low compared to TEE. Additionally, TTE may have a lower sensitivity in detecting paravalvular leak (PVL) [22]. However, a meta-analysis showed nonsignificant results when comparing TTE-guided versus TEE-guided TAVI in terms of safety and incidence of PVL, while TTE-TAVI has lower the cost with less resources usage [23]. Whether to use TTE or TEE is still debatable; however, the choice is dependent on cardiac center's capabilities and experience in using such tools.

Transesophageal Echocardiography (TEE)

TEE can be a superior option in selected patients with AS when the TTE is inconclusive [24]. TEE measurements are best acquired during mid-systole and that is when the annulus is at its largest and most circular shape. This is the preferred time point to size the annulus, as TAVR implants predominantly assume a circular shape after the deployment of the prosthesis. It is desirable to use high resolution techniques such as 3D-TEE or MDCT in imaging the AV complex and morphology, because they offer more precise quantification of the aortic root and LVOT with the desired plane compared to TTE. Moreover, since the posterior structures (including LVOT) are less visualized by TTE, it is preferable to perform TEE for precise window and assessment of the AV complex. Careful preprocedural imaging of this complex by TEE has important implications for the correct positioning of the TAVI valve within the aortic root with regard to the adjacent structures particularly coronary arteries, mitral valve, and the conduction system. In turn, TEE facilitates better prediction of the potential complications that may exist during the implantation such as: paravalvular leak, annular rupture, occlusion of the coronary arteries, etc. [25].

Due to the fact that the atrioventricular node is close to the subaortic region, TAVI implantation can lead to bundle branch block or complete AV block especially if it is placed too low. Thus, the estimated incidence of permanent pacemaker implantation after TAVI ranges between 2.3% and 28.2% depends on the type of the valve and patient's characteristics [26]. Alternatively, TAVI deployment that is too high may cause coronary occlusion and ischemia, or aortic injury, also the implant may detach or migrate. Therefore, TEE should be used to examine the feasibility of a TAVI procedure with respect to the following factors: the aortic annulus, assessment of aorta and coronary artery anatomy, evaluation of LV function. Indeed, an aortic root diameter of more than 45 mm at the sinotubular junction is considered as a limitation for self-expandable prosthesis implantation.

TEE may have a value for the intraprocedural imaging as well, to provide an immediate feedback of the valve function and detection of the aforementioned procedural complications. Interventionists tend to have a difficulty when passing a guidewire through the stenotic AV to the LV which is the first step before advancing the TAVI delivery system retrogradely *via* the femoral artery to the aorta; the use of TEE as a guide can facilitate the wire insertion and position (e.g, to exclude perforation or pericardial effusion) particularly with the use of 3D and biplane features. While if the TAVI access is *via* an apical approach, TEE is needed to avoid any cannulation of the mitral orifice. Furthermore, TEE may help to exclude any aneurysm or thrombus in the apex before transapical TAVI [27].

The use of 2D TEE has been replaced by 3D to a great extent, and that is due to the limitations of the 2D echo in imaging the AV which is an oval structure (**Figure 4**). 3D TEE technology provides biplane imaging of both the short-axis and long-axis view at the same time; this helps to ensure imaging is at the designated plane. TEE with 3D can also offer superior tissue characterization to rule out infective endocarditis (IE), thrombus, and tumor at pre procedural assessment or during follow up [28]. Inadequate annulus size that is less than 18 mm or more than 29 mm would be a limitation for TAVI; however, a 34 mm Evolut R TAVI has been released but limited data about its safety with chance to interfere with the conduction system and MV function. A tool to assess the discrepancy between the AV annulus and implant size named "cover index%" {100 x (prosthesis diameter-transesophageal echocardiography annulus diameter)/ prosthesis diameter} can be used to predict the risk of aortic regurgitation (AI) after TAVI deployment. A low cover index is associated with more PVL rates [29].

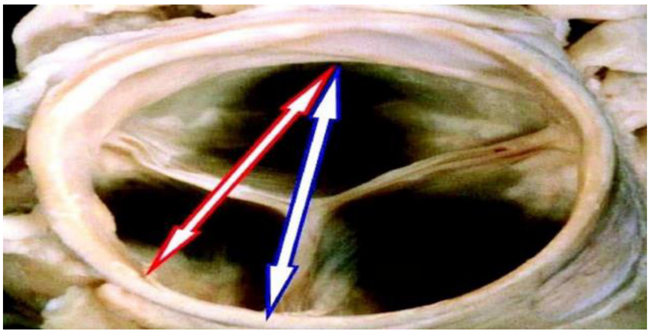

Figure 4: Circulation: Cardiovascular Interventions. 2008: Anatomy of the Aortic Valvar Complex and Its Implications for Transcatheter Implantation of the Aortic Valve (11): an oval shape of the AV. Red arrow shows 2D image while blue arrow is found in 3D.

Cardiac and Vascular CT

MDCT is now the most frequently used technique worldwide to conduct pre-procedural imaging of the aortic annulus, and it has obtained the recommendations of the American College of Cardiology expert consensus statement on TAVI. Moreover, the consensus document highlights that the routine use of TEE before TAVI may be an unnecessarily invasive technique, especially in a high-risk population (e.g., frail patients) [30]. When DSE measurements are inconclusive in patients with suspected low-flow low-gradient severe AS, calcium scoring *via* CT has the advantage of identifying true severe AS and predicting the associated risk. (Figure 3).

Unlike TEE, MDCT obtains the annular size at any point in the cardiac cycle depending on when the optimal image has been acquired. A trial that compared TEE to CT measurements found that CT measurements during diastole tend to be similar to the mid systolic 3D TEE measurements [31]. The optimum MDCT imaging of the aortic annuals is achieved at an orthogonal plan to the center line of the LVOT with the appearance of the three cusp hinge points, which allows for the detailed measurement of the diameter (maximum and minimum), perimeter (circumference), and area [32]. (**Figure 5**).

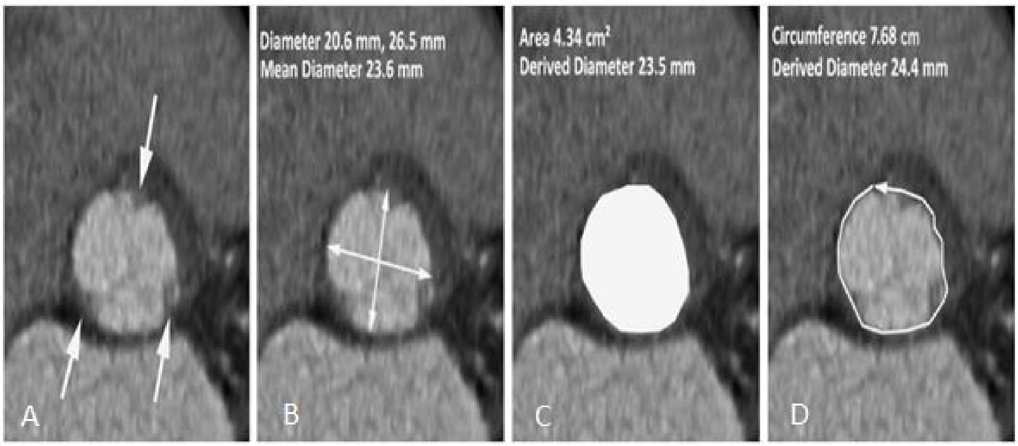

Figure 5: Examples of aortic annular dimensions in MDCT A: shows the three cusp hinge points in the aortic annuals plane, B: Average diameter, C: area, D: perimeter or circumference. SCCT expert consensus document on computed tomography imaging before transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): J. Cardiovasc. Comput. Tomogr., 6 (6) (2012), pp. 366-380 [32]

Besides the MDCT capabilities to assess the AV complex and the suitability for TAVI, it can be used to evaluate the feasibility of different vascular accesses (e.g., femoral, transcaval, subclavian, carotid, or transapical). MDCT can assess three main characteristic of the vascular access which are the diameter of the vessel, tortuosity, and calcification burden [33]. The identification of appropriate fluoroscopic projection is another future for preprocedural CT, that may lower the number of aortograms particularly for those with renal impairment [34]. Despite this, MDCT has not been adopted yet in the intra procedural assessment. MDCT can precisely assess aortopathies (e.g., aortic dissection) that may contradict with the femoral approach [35]. To avoid coronary artery obstruction, the height of coronary ostia (space between the annulus and the ostium of coronary arteries) can easily be measured by MDCT. (**Figure 6**). It is suggested to have a minimum distance of 14 mm between the coronary ostia and cusp insertion. CT may have no standard role for as routine imaging for TAVI follow-up, unless patient has an evidence of PVL or device degeneration on echocardiography.

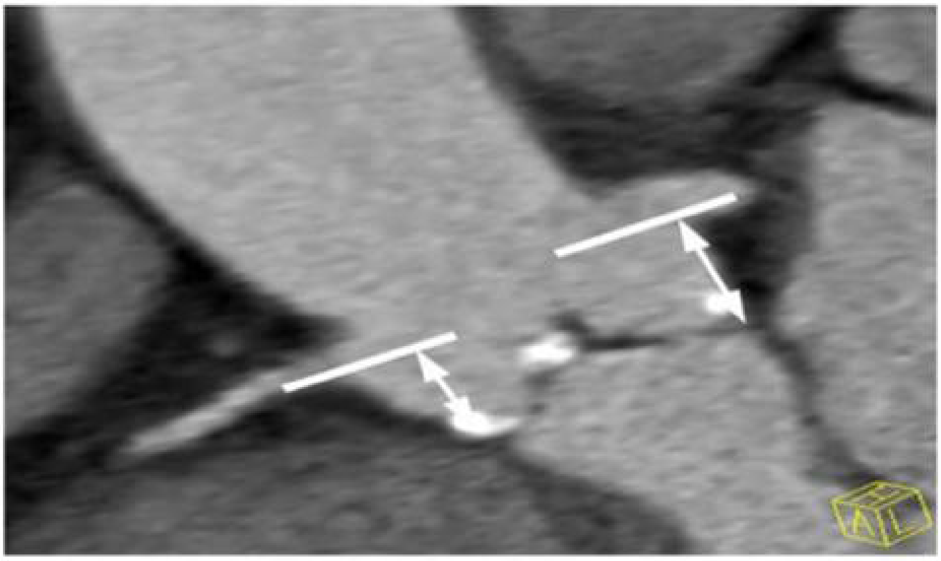

Figure 6: A MDCT image to measure the height of coronary ostia prior to TAVI, Coronary heights > 10 mm are generally considered safe when considering coronary obstruction. SCCT expert consensus document on computed tomography imaging before transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): J. Cardiovasc. Comput. Tomogr., 6 (6) (2012), pp. 366-380 [32].

Other Imaging Techniques (Angio/MRI/PET)

Fluoroscopy still acts as the main intra-procedure imaging modality to guide TAVI. Recently, there is growing literature of integrated “fusion” imaging (e.g., 3D TEE with fluoroscopy) to produce a 3D imaging prototype. Left heart catheterization can be performed prior to TAVI to provide invasive hemodynamic measurements as well as to rule out any coexisting coronary artery disease (CAD). Further angiography of the ilio-femoral arteries may be required to assess the vascular access [36]. Additionally, balloon sizing may be performed before valve deployment, also to assist the device deployment and expansion [37]. Fluoroscopy has a significant role during device deployment in adjunct to TTE or TEE imaging to confirm the correct positioning. During deployment, cusp overlap and commissural alignment is thought to reduce the risk of AV block (**Figure 7**). Beside TEE, aortography may be performed post TAVI deployment to assess any residual AR or PVL which has a significant predictive value in survival rate. Cardiac MRI may be performed for measurement of the aortic valve opening area with instant calculation of the LVEF as an alternative to MDCT when iodinated contrast cannot be given to patient. Additionally, MRI can be used to measure low flow and low gradient aortic stenosis in patients who are contraindicated to stress echocardiography [38]. Beside TTE in follow up, PET scan can identify degeneration of the TAVI valve which may early predict the risk of valve dysfunction. However, the high cost of this modality should be weighed against its benefits [39].

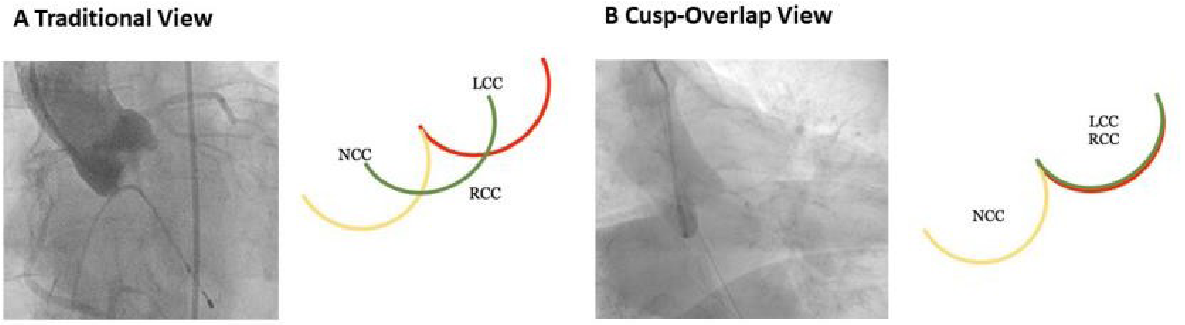

Figure 7: (A) shows no overlapping of the right and left cusps, while (B) shows the Angio projection after the cusp overlap, by separating the NCC which allows precise implantation depth and reduces interaction with the conduction system, this usually achieved in the RAO-Caudal view. Advancements in Transcatheter Aortic Valve Implantation: A Focused Update [36].

DISCUSSION

Since its first introduction, TAVI has changed rapidly. Now, it is used for patients with severe, symptomatic AS in all risk groups. TAVR has clear benefits because it focuses on minimally invasive techniques to decrease complications and duration of hospitalization. TAVI is currently employed for 12.5% of overall aortic valve replacements [40]. Nevertheless, TAVI still carries several safety concerns such as vascular injuries, paravalvular leaks (PVL), stroke and atrioventricular (AV) heart block requiring pacemaker implantation. The success of the TAVI relies on multiple imaging modalities which are not only intended to select an appropriate prosthesis size but also to guide preprocedural assessment and planning, intraprocedural imaging, and post-procedural follow up. Imaging techniques in TAVI include transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) either two- or three- dimensional, multidetector computed tomography (MDCT), as well as other modalities. There is an ongoing debate as to which of these imaging modalities give the most accurate results in the measurement of the aortic annulus, and whether the benefits of intraprocedural 3D-TEE imaging for real-time guidance would outweigh the possible risks of general anesthesia (GA) which may be needed if intraprocedural TEE is used. However, nowadays there fewer TAVI procedures are performed using intraoperative TEE guidance as precise preprocedural imaging provides sufficient data, thereby avoiding the potential risks of TEE and GA.

A study done at the Duke University Medical Center has compared TEE and CT measurements of the aortic annuals size to direct intraoperative sizing, found that generally CT tends to overestimate the annulus size while TEE underestimates the annulus size [41]. However, it is worth noting that this discrepancy in sizing between the two modalities has not been found to be a source of significant inaccuracy in selecting the proper device [42]. That tells us we should consider both TEE and CT readings when measuring the aortic annulus size. In addition, in patients with renal disease contrast use during CT scan may be difficult or contraindicated. On the other hand, those with abnormalities in the esophagus would not be suitable for TEE. Thus, it is a rational to have both options (MDCT and 3D-TEE) accessible in a cardiac center. Nonetheless, it should be acknowledged that when undertaking valve planimetry using either TTE and TEE, severe AV calcification may result in acoustic shadows and artefacts, which interfere significantly with the delineation of the valve resulting in imprecise measurements. In this case using another imaging modality like CT may give more reliable results [43].

Nevertheless, TEE is now less frequently used intra procedure in many high volume cardiac centers, as they rely more on TTE to identify peri procedure issues and measure post procedure PVL. This can be due to many factors, particularly a desire to avoid GA complications with TEE and reduce the length of the procedure, but also the experience of the operators has evolved dramatically making them more willing to dispense with intra-procedure TEE. Having said that, using intraprocedural TEE may still a necessity in advanced TAVI cases like valve in valve (VIV) implantation [44].

Stroke

As been mentioned above procedural complications still accompany this procedure. Important cause of morbidity and death in TAVR is stroke. The incidence of stroke following TAVR is highly variable. Stroke affects between 2.7% to 5.5% of patients after the 1st month, but it is frequently underreported in clinical studies [45]. In the PARTNER III trial, severe stroke occurred in just 1.2% of TAVI recipients after 12 months, compared to 3.1% in the surgical AVR group [46]. After 2 years follow-up, TAVI wasn't statistically better than SAVR [47], this may be due to the high rate of peri-procedural (within 1 month). In many studies, only the most severe clinical strokes are reported, and less nuanced assessments of stroke, such as neurologic defects or imaging, are ignored. According to studies that used standard MRI screening at 30 days following TAVR, stroke occurs in 9% to 28% of patients [48]. Hence, MRI screening appears necessary step towards preventing such a fatal complication. However, there remains scarcity of evidence about predictors of stroke in TAVI patients.

CONCLUSION

Multimodality imaging in TAVI aims firstly to detect the severity of AS and assess procedural feasibility with careful measurement of aortic valve and its complex. Secondly, to exclude any contraindications or possible complication that may arise during the procedure, and this can be achieved by precise imaging and preplanning. The third function is to select the appropriate vascular approach based on the patient's anatomy. Intraprocedural imaging is crucial for optimal TAVI deployment and to anticipate/immediately detect any complications. Finally post -procedural imaging is required to follow up the patient's clinical outcomes and the function of the prosthetic valve. TTE, TEE, MDCT, and angiography are complementary imaging modalities, and the choice of which combination to use will be influenced by the operator's experience and expertise. The combination of 3D TEE and MDCT may give the most accurate estimate of the anatomy and dimensions of the aortic complex to facilitate optimal selection of both patient and prosthesis for TAVI

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