Three-dimensional imaging of the aortic valve and aortic root with computed tomography: new standards in an era of transcatheter valve repair/implantation

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Aortic stenosis: prevalence, pathophysiology, and therapeutic approaches

Valvular heart disease is a significant, global cause of morbidity and mortality. In the ageing population of industrialized nations, degenerative aortic stenosis has become the most common native valve disorder. Although surgical aortic valve replacement is associated with excellent clinical outcomes, a large number of patients with severe aortic stenosis are not considered surgical candidates. These patients have poor prognosis with continued medical therapy. In this population, catheter-based approaches for valve replacement/insertion show promising initial results. In an era of expanding catheter-based approaches to valve disease, the requirements for peri-operative imaging are evolving. Because of the lack of direct exposure during the procedure, the operator has to rely increasingly on imaging data rather than direct inspection. Novel three-dimensional (3D) imaging modalities, including computed tomography, rapidly acquire volumetric data sets and allow subsequent 3D display and reconstruction in unlimited planes. Procedural planning based on 3D imaging has already become routine for other endovascular procedures including aortic stent grafts, but is in its infancy in the context of transcatheter valve insertion.

Keywords

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Aortic stenosis: prevalence, pathophysiology, and therapeutic approaches

Valvular heart disease is a significant, global cause of morbidity and mortality. In industrialized nations, degenerative disease is the most common aetiology, and degenerative aortic stenosis has become the most frequent native valve disorder. Degenerative, calcified aortic stenosis is a dynamic disease process with similarities to atherosclerosis. The presence of modifiable risk factors and the observation that even mild valve changes are associated with an increased cardiovascular morbidity and mortality support the goal of early intervention and prevention. However, data from prospective clinical trials, examining the effect of lipid-lowering medications, do not show definitive clinical benefit. As there is no medical solution to this progressive disease, aortic valve replacement is the only effective treatment for advanced disease stages. In suitable patient, current surgical results are excellent. However, there are significant numbers of patients who are not considered candidates for aortic valve replacement surgery because of anticipated poor outcome and high operative mortality secondary to advanced age and/or co-morbidities. The poor outcome of these patients with continued medical management provides the rationale for the development of less-invasive interventional procedures, including balloon aortic valvuloplasty (BAV) and transcatheter valve insertion. However, BAV provides only temporary relief of symptoms, because restenosis develops within 6–12 months following the procedure. More recently, several transcatheter aortic valve implantation (TAVI) techniques have been developed using either a retrograde transfemoral or a transapical approach. Different generations of balloon-expandable or self-expandable valve prostheses have been implanted in
several thousand high-risk patients (Figure 1). The results are encouraging, with an implantation success rate of about 90% and significant haemodynamic and clinical improvements. Short-term follow-up studies suggest low post-procedural cardiovascular event rates. Mortality rates at 30-day follow-up range from 5 to 18% and 12-month survival rate is about 70–80%.21 – 26

Complications of transcatheter valve procedures are associated with local vascular injury at the access site, and device positioning, including paravalvular leakage, cardiac tamponade, arrhythmias, coronary artery occlusion, and prosthetic valve embolization.23 – 26 These procedure-related complications can be reduced or avoided with a careful selection of potential candidates, procedural risk assessment, and detailed evaluation of the aortic valve/root anatomy and vascular access strategy before the procedure. According to guidelines by the European Association of Cardio-Thoracic Surgery and the European Society of Cardiology, patient selection for TAVI should include confirmation of aortic stenosis severity, clinical evaluation and operative-risk analysis, and assessment of feasibility, and exclusion of contraindications.27 Typical assessment includes a dedicated history, physical examination, and laboratory studies including assessment of renal function. Current standard pre-procedural and intra-operative imaging is based on cardiac catheterization and 2D echocardiography. The role of other imaging modalities, including 3D computed tomography (CT) imaging is emerging.

Role of three-dimensional imaging for procedural planning

Pre-operative imaging in the context of conventional open-heart valve surgery is focused on the description of leaflet anatomy, severity of valve dysfunction, and haemodynamic consequences. This information is obtained with echocardiography in a standardized approach and allows determining the need for surgery on the basis of extensive evidence-based data.28 During the surgery itself, direct inspection of the valvular apparatus guides details of the surgical approach. For transcatheter approaches to valve disease, the requirements for peri-operative imaging are different. Because of the lack of direct exposure during the procedure, the operator has to rely increasingly on pre- and intra-procedural imaging data rather than direct intra-operative inspection. This approach is supported by advanced cardiovascular imaging modalities with fast acquisition of volumetric data sets, and subsequent 3D display and reconstruction in unlimited planes (Figures 2 and 3).

Theoretically, 3D imaging provides an advantage over direct intra-operative inspection, because the root is seen under physiological condition rather than in the collapsed state after the initiation of cardiopulmonary bypass. However, the use of CT in the context of novel, less-invasive approaches to valvular disease is a recent development. Although emerging data demonstrate potential benefits in the pre-operative understanding of root anatomy and planning of surgical and interventional procedural detail, there is no prospective evidence of clinical benefit.29,30

The use of CT has become possible because of recent improvements of spatial and temporal resolution and increased number of detector systems.31,32 Using dual-tube technology, temporal resolution of 83 ms can be achieved with a spatial resolution of 0.5 mm. Imaging of the aortic root is performed with minimal slice thickness of about 0.5–0.75 mm using protocols similar to those used for coronary imaging. Therefore, the resulting data sets are almost isotropic, allowing oblique reconstruction without degradation of spatial resolution. Electrocardiogram-synchronized image acquisition throughout the cardiac cycle (standard retrospective gating with the use of dose modulation) allows reconstruction at any point throughout the R-R interval. Although the temporal resolution of CT is lower than that of echocardiography and magnetic resonance imaging (MRI), cine-display of multiple phases throughout the cardiac cycle permits limited dynamic display of cardiac and valvular motion.33 The significant radiation exposure and

Figure 1 This figure shows the CoreValve® (left panel, image courtesy of Medtronics) and Edwards Sapien™ transcatheter heart valve (right panel, image courtesy of Edwards Lifesciences). The Edwards Sapien™ transcatheter heart valve is a lower profile balloon-expandable valve, whereas the CoreValve® is a higher profile self-expandable system. Both systems are implanted with good success.
administration of iodine-based contrast material must be considered in planning the CT protocol for individual patients. For example, limiting craniocaudal coverage to only the aortic root and routine use of dose modulation (decreased tube current outside a pre-specified, typically diastolic acquisition window) is associated with significant reduction in radiation exposure. Novel protocols using prospective triggering could be considered in younger patients, but are limited to single phases in the cardiac cycle. Computed tomography acquisitions without contrast administration in patients with renal insufficiency allow assessment of calcification of the valve and root and overall root size, but is limited for the description of the annulus. Magnetic resonance imaging allows anatomic and functional assessment of the aortic valve and aortic root. However, similar to standard echocardiography, most MRI sequences are 2D (i.e. the plane of imaging has to be chosen at the time of the examination and cannot be changed by subsequent manipulation of the data set). Another limitation of MRI in the context of TAVI is the signal void caused by calcium and metal, which preclude precise assessment of densely calcified valves and the stent/valve after TAVI.

The anatomy of the aortic root is complex and involves the aortic annulus, the commissures, the sinuses of Valsalva, and the sinotubular junction (STJ) as the framework, in which the valve leaflets are suspended (Figure 4). In addition, the origin of the coronary arteries is located in the aortic root. Post-mortem studies have described the anatomy of the aortic root and the relationship between complex geometric pattern and aortic valvular function.

Aortic annulus and commissures
The aortic annulus describes the interface between the left ventricular outflow tract (LVOT) and the aortic root and is defined by the hinge-point/commissures of the aortic valve leaflets. Although the clinical terminology suggests a ring-shaped structure, the commissures extend upwards into the aortic root describing the shape of a crown, similar to the struts of a bioprosthetic valve (Figure 5). In clinical imaging, the level of the annulus is defined at the lowest
Detailed 3D analysis demonstrates that this clinically defined annulus is not circular, but frequently elliptical. Tops et al.\textsuperscript{37} retrospectively examined coronary CTA examination of 150 patients with no or mild aortic stenosis and 19 patients with moderate-to-severe aortic stenosis. The aortic annulus diameter was measured in reconstructed coronal and sagittal views. Mean difference between the two projections was $2.9 \pm 1.8$ mm, indicating an oval shape of the aortic annulus. This is similar to other studies using 3D echocardiography, MRI, and CT.\textsuperscript{38–41} The geometry of

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**Figure 4** This figure shows computed tomography images of the calcified leaflet margins of a stenotic aortic valve (upper right panel), the sinotubular junction (STJ) with dense, circumferential calcification (right middle panel), and the level of the aortic annulus (left lower panel). The ostia of the coronary ostia (RCA, right coronary artery; LM, left main) are seen in the lower panels.

**Figure 5** The aortic annulus describes the interface between the left ventricular outflow tract and the aortic root and is defined by the hinge-point/commisures of the aortic valve leaflets. Although the clinical terminology suggests a ring-shaped structure, the commisures extend upwards into the aortic root, describing the shape of a crown, similar to the struts of a bioprosthetic valve.
the LVOT and annulus has implications for the assessment of the aortic valve area (AVA). Using transthoracic 2D echocardiography, the LVOT area is derived from a single diameter measurement on the basis of the assumption of a circular geometry. The LVOT area is then used for the calculation of the AVA with the continuity equation. However, if the AVA is calculated taking into account the elliptical rather than circular geometry of the LVOT, there is better agreement with the anatomical AVA assessed with 3D planimetry.39–41

Aortic valve leaflets
Direct planimetry of AVA with CT has been shown to provide reproducible results in comparison with transoesophageal echocardiography, and MRI.42,43 Using CT data sets, a plane at the tip of the leaflets can be reconstructed retrospectively at different times during the cardiac cycle.33,44 Thus, the maximal opening of the aortic valve during the cardiac cycle (typically mid-late systole) can be identified for the quantification of AVA. In comparative studies of patients with AS, planimetry of the AVA with CT was compared with calculated AVA using the continuity equation on the basis of TTE measurements.45 Sensitivity and specificity of CT for the identification of patients with degenerative AS were high, and quantification of AVA by MSCT showed a good correlation to TTE. Similarly, planimetry of the regurgitant orifice area in patient with aortic regurgitation has been examined and showed a significant correlation with semi-quantitative classification with TTE.46

An advantage of the direct observation of the aortic valve opening area is the ability to correlate the pattern of valve opening with leaflet anatomy. Previous studies have described the extent of leaflet calcification.44,47 More detailed analysis allows assessing location of calcification, leaflet thickening, fusion, geometry, and symmetry of the opening area. This appears important for symmetric deployment of percutaneous valve prosthesis.

Coronary ostia
Importantly, CT also allows describing the relationship of the leaflet calcification to the coronary artery ostia (Figure 6). However, several recent papers examining the distance between the annulus and the ostia of the coronary arteries and the length of the coronary leaflets provide conflicting results. Knight et al.48 examined coronary ostial location in 75 cadavers using open measurement techniques and 150 patients with normal valve function undergoing dual-source CT. Comparison of cadaver and in vivo

**Figure 6** This figure shows images of the aortic root before and after TAVI. The upper panels show the calcified valve leaflets and the origin of the right coronary artery (star) and the left main coronary artery (triangle) before (centre) and after TAVI. The lower panels show cross-sectional images at the annulus (left), level of the valve (middle), and level of the right coronary artery (right). The arrow shows the upper end of the prosthetic valve leaflet in relation to the right coronary artery ostium.
CT data showed statistically significant differences for right but not left coronary ostia. In a paper by Tops et al., the length of the left coronary leaflet exceeded the distance between the annulus and the ostium of the left coronary artery in 49% of patients. However, the authors found no significant differences in the distance between the annulus, coronary artery ostia, and STJ between the patient with and without severe aortic stenosis. In contrast, Akhtar et al. comparing patients with severe AS undergoing evaluation for pAVI vs. elderly gender-matched controls found significant differences between the two groups. Specifically, subjects with AS had reduced distance from the aortic valve annulus to the inferior margins of the left coronary artery ostium, right coronary artery ostium, and STJ. These findings would suggest longitudinal remodelling/shrinkage of the aortic root in calcified aortic stenosis. However, in a paper by Stolzmann et al. comparing patients with severe AS and controls, coronary ostial locations were similar in both groups. Contrary to Akhtar et al., the authors found differences in root dimensions, suggesting transverse remodelling/expansion of the aortic root. Such changes of the root would have implications for the design and deployment of PAVR devices, but validation in future studies is necessary.

**Sinotubular junction**

The STJ describes the interface between the aortic root and tubular ascending aorta. Ex vivo studies, using direct endoscopic and ultrasound imaging techniques, have examined the effect of changes in the size of the aortic annulus and STJ on aortic root geometry and aortic valve function and demonstrated an important role in maintaining valve competence. For transcatheter valve insertion, the role of STJ and calcification at the STJ appears critical for correct positioning during the deployment of the valve, but data are limited.

**Dynamic display and relationship to adjacent structures**

Importantly, the geometry and relationships of the aortic root structures change throughout the cardiac cycle. Experimental studies using 3D sonomicrometry show the precise chronology of dynamic changes of the root during the cardiac cycle. Therefore clinical measurements have to be described in relationship to the position in the R-R interval. Four-dimensional cine analysis has been applied to the examination of the aortic annulus and the 3D motion of the semi-lunar attachment of leaflets in the aortic root.

In addition to understanding the internal geometry of the aortic root, 3D analysis allows understanding its relationship to the body axis for the planning of surgical or interventional access planes. For example, in the context of minimally invasive replacement of the aortic valve, pre-operative CT has been applied in order to predict annulus location/projection over the chest wall and to minimize the length of the incision. It has also been described that 3D data sets allow predicting 2D angiographic projections orthogonal to the AVA, simplifying the insertion of percutaneous valves (Figure 7).

![Figure 7](https://academic.oup.com/eurheartj/article-abstract/30/17/2079/506182/06 February 2019)
Conclusion

Precise pre- and intra-operative imaging are critical for surgical/interventional procedures with reduced direct intra-operative exposure. Complementing standard echocardiography and catheterization, novel 3D imaging modalities, including CT, rapidly acquire volumetric data sets and allow subsequent 3D display and reconstruction in unlimited planes.

The above described emerging data suggest an important role of 3D imaging for novel surgical and transcatheter approaches to valve repair and, in particular, percutaneous aortic valve implantation. However, although the benefit of image guidance has been demonstrated for aortic endovascular stent procedures, for which pre-procedural planning and imaging follow-up with CT is critical, there is currently no prospective data, comparing the utility of different imaging modalities and demonstrating clinical impact of image guidance in the context of transcatheter valve procedures. Eventually, evidence-based data demonstrating favourable risk/benefit impact on clinical outcome in controlled clinical trials are necessary.

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