
Aortic stenosis and role of multi-detector row computed tomography in diagnosis: whom, when and why?

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Aortic valve calcification is often seen incidentally on chest computed tomographic scans obtained for a variety of noncardiac indications. As a consequence of improved technology, introduction of multi-detector row computed tomography in the year 2000 led to a significant improvement in the temporal and spatial resolution of computed tomographic, which permitted substantial expansion of potential indications for cardiac computed tomographics technology. Because computed tomographic is a sensitive method for the detection of calcification, it is potentially useful for the assessment of aortic valve morphology and quantification of the degree of calcification. The assessment of aortic valve stenosis using multi-detector row computed tomography is feasible with good diagnostic accuracy. In addition, the most recent generations of multi-detector row computed tomography, with the ability to acquire 64 and 256 slices simultaneously, allow relatively robust morphological and functional imaging of the heart including noninvasive coronary angiography.

Keywords: Multi-detector row computed tomography – Aortic valve calcification – Coronary angiography

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Kalcifikácie aortálnej chlopne sú často viditeľné pri počítačovej tomografii hrudníka z nekardiologických indikácií. Zdokonalenie technológie po zavedení multidetektorovej počítačovej tomografie v roku 2000 so významným zlepšením rozlíšení viedlo k významnému rozšíreniu kardiologických indikácií. Vzhľadom na vysokú senzitivitu počítačovej tomografie v detekcii kalcifikácií je táto metóda dôležitá pri posúdení morfológie aortálnej chlopne a kvantifikácie rozsahu jej kalcifikácií. Diagnostika aortálnej stenózy pomocou multidetektorovej počítačovej tomografie má adekvátnu hodnotu. Navyše posledné generácie prístrojov so 64, respektíve 256 obrazmi simultánne umožnia relatívne rozsiahle morfológické a funkčné zobrazenie srdca, vrátane neinvazívnej koronárnej angiografie.

Kľúčové slová: multidetektorová počítačová tomografia – kalcifikácie aortálnej chlopne – koronárna angiografia

Introduction

Aortic stenosis (AS) has become the most commonly occurring type of valvular heart disease in Europe and North America. It primarily presents as degenerative AS in adults of advanced age (> 65 years) accounting for 80% of cases. The second most frequent aetiology, which dominates in the younger age group, is rheumatic AS, although it has become rare (15%). Other aetiologies such as endocarditis, inflammatory, congenital, and ischemic are rare (5%). The incidence of degenerative AS should still increase because of the ever-increasing life expectancy. There are no massive geographical variations in the incidence of valvular heart diseases in different parts of Europe. However, AS appears more often in western than in eastern

European countries, according to Euro heart survey on the prevalence of valvular heart diseases (1–4).

Calcific AS is a chronic progressive disease. During a long latent period, patients remain asymptomatic. However, it should be emphasized that duration of the asymptomatic phase varies widely among individuals. Sudden cardiac death is a frequent cause of death in symptomatic pts but appears to be rare in the asymptomatic ($\leq 1\%$ per year). Reported mean symptom-free survival at 2 years ranges from 20 to more than 50% (5–9).

Predictors of the progression of AS and, therefore, of poor outcome in asymptomatic patients have been identified. They are:

- Clinical: older age, presence of atherosclerotic risk factors (3, 4).
- Echocardiography: valve calcification, peak aortic jet velocity, left ventricular ejection fraction (LVEF), haemodynamic progression, and increase in gradient with exercise. The combination of a markedly calcified valve with a rapid increase in velocity of ≥ 0.3 m/s within 1 year has been shown to identify a high-risk

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- group of patients (80% death or requirement of surgery within two years).
- Exercise testing: symptom development on exercise testing in physically active patients, particularly those younger than 70 years, predicts a very high likelihood of symptom development within 12 months. Recent data demonstrates a lower positive predictive value for abnormal blood pressure response, and even more for ST-segment depression, than symptoms for poor outcome (6, 7, 9, 10).

The cardinal manifestations of aquired AS, which commence most commonly in the fifth or sixth decade of life are exertional shortness of breath, angina, dizziness, or syncope (11). As soon as symptoms occur, the prognosis is worse and mortality has been reported to be quite significant even within months of symptom onset (12), which is often not promptly reported by patients.

Moderate or severe aortic valve calcification has been shown to be a strong and independent predictor for an adverse clinical outcome, including an increased risk of death and a need for aortic valve replacement (6). Therefore, timing for surgical treatment is the main concern in medical management of AS and requires accurate measurement of the aortic valvular area (AVA) (13). Thus, interest is growing in the detection and accurate quantification of AVA.

Approaches to diagnostic imaging in aortic valve stenosis

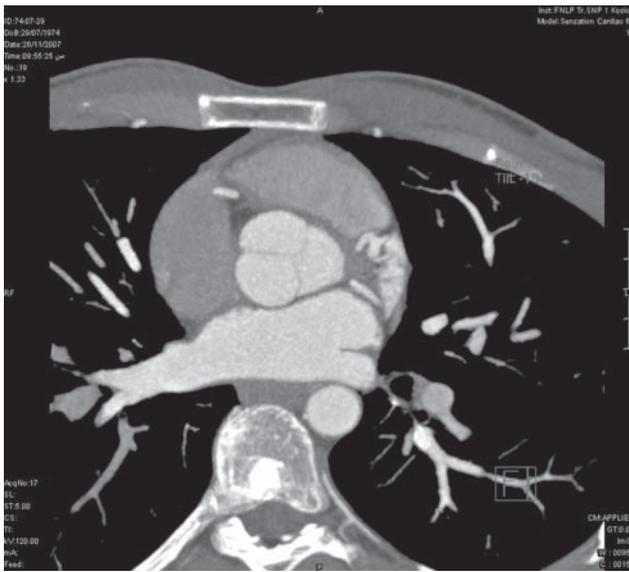
Management of patients with AS is based on disease severity, which is usually classified by determination of the AVA. AVA >1.5 cm² indicates mild AS, an AVA between 1.5 – 1 cm² indicates moderate, and an AVA below 1 cm² is considered as severe AS according to American College of Cardiology/American Heart Association guidelines (13), in addition to an increased peak transvalvular velocity > 4 m/s. Various non-invasive technologies are available to assess aortic valve morphologic features and function. Currently, Transthoracic Echocardiography (TTE) is widely used for primary diagnostic evaluation of AS; TTE is real-time imaging basically relying on dynamic flow parameters by using velocity-time integral for the calculation of the AVA. AVA is routinely assessed by TTE using the Doppler continuity equation approach. However, several limitations associated with the use of the continuity equation include difficulty in accurately measuring the left ventricular outflow tract (LVOT) diameter and estimating

the maximal velocity of the LVOT and the aorta before flow acceleration. Furthermore, low cardiac output, concomitant aortic valve regurgitation, severe valve calcifications, and other unusual anatomic configurations impairing the echocardiographic window may also limit TTE results. However, TTE may be technically inadequate for some pts, and semi-invasive transesophageal echocardiography (TEE) or cardiac catheterization is required to establish a firm diagnosis. TEE is semi-invasive (14, 15), and caution is needed because of shadowing and reverberation artifacts from the calcified leaflets. The non-planar aortic valve anatomy may also lead to errors. TEE determination of AVA is planimetric in its approach, but has been shown to provide a reproducible measurement of the AVA. Invasive Coronary Angiography (CA) has been the standard method of evaluation, but is declining in use because of the rare but serious concerns regarding the risk of catheter-related damage such as stroke (16), aortic or coronary dissection, myocardial infarction, procedure related and technical limitations.

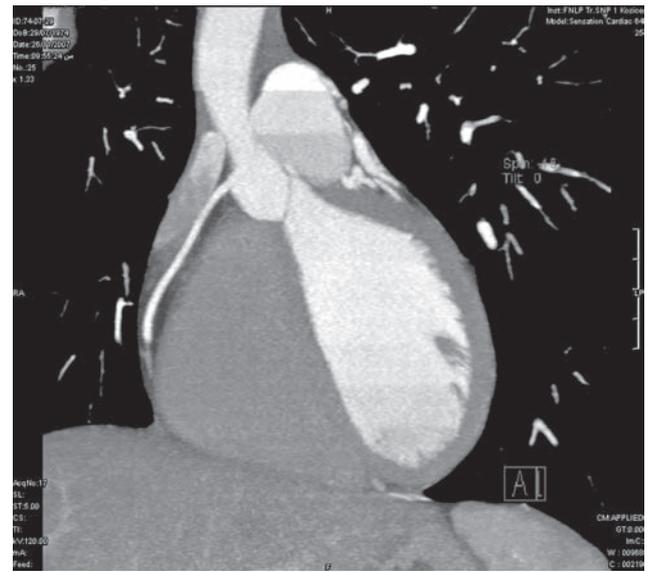
Meanwhile, recent technical improvements in multi-detector electrocardiography (ECG) – gated computerized tomography (MDCT) allows for visualization of the aortic valve throughout the cardiac cycle (**Figure 1a**). Over the recent years, a number of papers have addressed the use of MDCT in patients with AS. The ability of the technique to detect and quantify calcifications was the first reason for its application to calcific AS. Indeed, quantification of valvular calcification first by electron-beam computed tomography (EBCT) (17), and later on by MDCT (18, 19) has been well validated by studying patients prior to surgery and comparing the results with examinations of the pathological specimen. In addition, cardiac MDCT gives information about the left ventricle, ascending aorta, coronary artery anatomy (**Figure 1b**) and myocardial perfusion. Thus, cardiac MDCT could be an alternative and integrated imaging technique in the management of valvular disease.

Evolution of MDCT

Since its introduction in the early 1970s, computed tomography has become a gold standard to non-invasively image the aorta, pulmonary arteries, great vessels, and renal and peripheral arteries. However, cardiac anatomy evaluation with this modality was not possible, until 1982 with the creation of the EBCT, since when the diagnosis and workup of cardiac structures has become possible. However, limited reimbursement, high cost of



A



B

Figure 1 64-MDCT showing normal semilunar aortic valve of 34-year-old man without calcification (A). Right coronary artery of the same patient without any visible calcification (B).

acquisition, and very limited industry support kept this technology from expanding. Despite these hurdles, functional cardiac analysis (wall motion, cardiac output, wall thickening, and ejection fraction), perfusion imaging, non-invasive angiography, and coronary calcium assessment were validated (20).

With the advent of helical CT in the mid-1990s and MDCT in 1999, the widespread availability of scanners created a marked increase in utilization of, and interest in, cardiac CT. The preliminary studies, with helical CT, had very limited cardiac applications and significant motion artifacts. In addition, the early exposure MDCT, specifically the 4-slice scanner, was also disappointing due to the rapid coronary motion and limited scan speeds available with these early scanners, accurate and reliable imaging of the heart and coronary arteries was significantly limited (21). Now, with the development of multislice scanners capable of 16, 64, 128, 256, and beyond simultaneous slices, spatial resolution is approaching that of conventional cineangiography and the holy grail, non-invasive coronary arteriography, appears attainable.

Whom and when?

Currently, a routine clinical implementation of MDCT for diagnostic evaluation of AS cannot be recommended. However, MDCT may play a role in patients in

whom a direct measurement of AVA is important but cannot be obtained by TTE. MDCT can also be applied in clinical practice to detect asymptomatic AS in pts who undergo coronary MDCT angiography, for example in pts with suspected coronary artery disease. Furthermore, it has been shown to be highly accurate for detection of significant (CAD) $\geq 50\%$ (22, 23). With the introduction of 16 and 64 MDCT systems, improved temporal and spatial resolutions as well as substantially shorter scan times led to improved image quality throughout the entire coronary tree (24). A recent meta-analysis demonstrated a significant improvement in the accuracy for the detection of coronary artery for 64-slice CT when compared with previous scanner generations: the mean sensitivity increased from 84% for 4-slice and 83% for 16-slice to 93% for 64-slice CT. The 256-slice MDCT, whose large coverage along the patients longitudinal axis may allow imaging of the entire heart in a single cardiac cycle and will make coronary CT angiography less susceptible to arrhythmias or heart rate variability, has been introduced (25). **Table 1** below shows several implications on possibilities of when and to whom to indicate MDCT investigation.

Several other indications are being applied and introduced into cardiac imaging (**Table 1**). These include coronary artery bypass grafts when cardiac CT can detect occluded grafts and stenosis in the body of bypass conduits with very high diagnostic accuracy. The robust visualization and

Table 1 Clinical strategy for considerations of multi-detector CT in patients with aortic stenosis

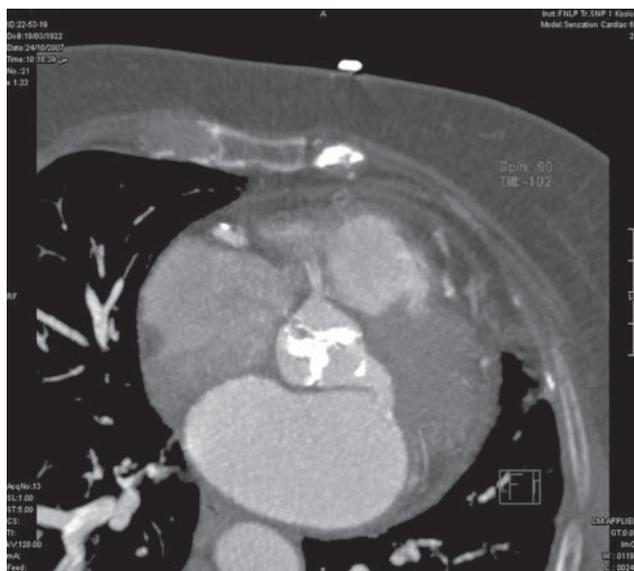
WHOM:	WHEN:
AVA measurement can not be obtained by TTE	Acute chest pain – Emergency department
Asymptomatic AS with suspected CAD	Coronary artery bypass grafting
Coronary plaque imaging – Calcium scoring	Coronary artery anomalies
Assessment of left/right ventricular function and volumes	Assessment of myocardial perfusion/viability
Congenital heart diseases	Radiofrequency ablation in AF

classification of anomalous coronary arteries make CT angiography a first-choice imaging modality for the investigation of known or suspected coronary artery anomalies. Moreover, MDCT permit coronary plaque imaging with accurate detection and quantification of coronary artery calcium. There is pre-clinical evidence that contrast enhanced MDCT can provide assessment of myocardial perfusion. Last but not least, multi detector row computed tomography has proven success in non-coronary imaging with assessment of right ventricular function and volumes, coronary venous system, congenital heart disease, left atrial and pulmonary vein anatomy for radiofrequency ablation procedures in patients with atrial fibrillation (26).

Why MDCT – technical and clinical aspects

Cardiac MDCT is a promising new technique for comprehensive assessment of aortic valvular anatomy and

for diagnosis of AS. Although TTE examination is the current first-line imaging, limitations of this modality may also include a restricted field of view in patients with emphysema and inter-observer variability. Thus, MDCT can be of value when echocardiographic examination is technically difficult and/or does not match the clinical data. The CT diagnosis of AS is based on the demonstration of left ventricular hypertrophy, mild to moderate dilatation of the ascending aorta (“poststenotic dilatation”), calcification of the aortic valve (**Figure 2a, 2b**), and limited motion and reduced area of the aortic valve in diastole at 4dimensional (4D) MDCT. Because of the excellent spatial resolution of multi-detector row CT angiography, anatomic details of the valve leaflets, chordae tendinae, and papillary muscles can be visualized. It has been most feasible for cardiac valve evaluation to upload the entire 4D data set (0% – 100% reconstruction at 10% intervals) and use maximum intensity-projection (MIP) or volume-rendering (VR) software to cre-



A



B

Figure 2 64-MDCT for an 86-year-old woman showing severe calcifications across semilunar aortic valve before bioprosthesis (A). 3-dimensional cut view at the level of aortic valve for the same patient (B).



A



B

Figure 3 MDCT significant calcification and stenosis in both branches of left main stem of 72-year-old man (A). 70-year-old woman with significant calcification in LAD (B).

ate reformatted images in any plane desirable (27). Contrast-enhanced MDCT is feasible in most cases and allows for reliable diagnosis: quant-detector row CT is superior to unenhanced multi-detector row CT for the characterization of abnormal valve anatomy, routinely providing excellent visualization of the aortic valve and thereby allowing good evaluation of congenital or acquired structural anomalies of these valves. The number of valve leaflets, leaflet thickness, opening and closing of the leaflets and presence of valve calcification can be observed (28).

Recent study (29) to evaluate planimetry of the aortic valve area with 64-slice CT in comparison with transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in patients with aortic stenosis. Thirty-six patients with aortic valve disease referred for coronary 64-slice CT angiography were examined. Planimetry of the aortic valve area with 64-slice CT was compared with TTE using the Doppler continuity equation for calculation of the aortic valve area and with planimetric measurement of the aortic valve area using TEE. Planimetry of the aortic valve area with CT ($1.11 \pm 0.42 \text{ cm}^2$) showed a good correlation with TTE ($1.05 \pm 0.42 \text{ cm}^2$) ($r = 0.88, p < 0.001$) in 32 patients and a good correlation with TEE ($1.41 \pm 1.61 \text{ cm}^2$) ($r = 0.99, p < 0.0001$) in 10 patients. The mean and maximum transvalvular pressure gradients were correlated with the aortic valve area as measured with CT ($r = -0.68, p = 0.0001$; and $r = -$

$0.67, p = 0.0001$, respectively). Beta-blockers were not given (mean heart rate, 62.5 ± 10.7 beats per minute). They concluded that MDCT allows accurate planimetry of the aortic valve area in patients with aortic stenosis. In addition, patients referred for 64-slice CT coronary angiography, concomitant aortic stenosis can be identified and evaluated.

Moreover, a very recent study (30) aimed at evaluating the accuracy of MDCT, as a single non-invasive preoperative test, for simultaneous evaluation of the AVA, LVEF and coronary status (**Figure 3a, 3b**) in patients with AS. 40 consecutive patients with AS scheduled for aortic valve replacement who underwent TTE, MDCT and coronary angiography within a time span of 1 week. MDCT measurements could be performed in all patients. A good correlation was observed between mean data scatter (SD) AVA measured by MDCT and by TTE ($0.87 (0.22)$ vs $0.81 (0.20) \text{ cm}^2$, $p = 0.01$; $r = 0.77, p < 0.001$). Mean difference between methods was $0.06 (0.15) \text{ cm}^2$. LVEF measured by MDCT correlated well with, and did not differ from, echocardiographic measurements [$59\% (13\%)$ vs $61\% (10\%)$], $p = 0.34$; $r = 0.76, p < 0.001$; mean difference $1\% (8\%)$. Coronary angiography showed 33 lesions in 13 patients. MDCT correctly identified 26 of these 33 lesions and overestimated three $< 50\%$ stenosis. On a segment-by-segment analysis, MDCT sensitivity, specificity, positive and negative predictive values were 79%, 99%, 90%

and 98%, respectively. For each patient, MDCT had a sensitivity of 85% (11/13 patients), a specificity of 93% (25/27 patients) and positive and negative predictive values of 85% (11/13 patients) and 93% (25/27 patients), respectively. As a result MDCT can provide a simultaneous and accurate evaluation of the AVA, LVEF and coronary artery anatomy in patients with AS. In the near future, with continuous technological improvements, MDCT could achieve an exhaustive and comprehensive preoperative or interventional assessment of patients with AS. In addition, for the assessment of AS severity in difficult cases, MDCT could be considered as an alternative to transoesophageal echocardiography or cardiac catheterisation.

Current MDCT limitations

There remain a considerable number of disadvantages: time resolution remains a problem; blooming artifacts due to calcifications may limit the accuracy; arrhythmias, in particular atrial fibrillation, still preclude the application of the technique; high heart rates at least limit it and the use of betablockers to lower heart rate may be particularly undesirable in patients with AS; radiation exposure is similar to invasive coronary angiography and at least limits repeat use during follow-up; contrast media, if they are used, have the potential for renal and allergic complications; the examination time (including post-processing) for only one piece of information regarding AS assessment is long, 20 – 30 min. However, improvements in MDCT systems and introduction of 64, 128, and 256 multi-slices CT should reduce limitations caused by the current techniques.

Future perspectives of MDCT

The true promise of MDCT is to visualize the coronary artery, including the lumen and wall. Thereby improving diagnosis and treatment of coronary artery disease (31). Finally, MDCT may gain a role for the pre-operative exclusion of CAD but, so far, only in patients with low likelihood of atherosclerosis (29). In the near future, with improvements in the quality of coronary artery imaging, MDCT may replace all preoperative tests. In addition, for the assessment of AS severity in difficult cases, MDCT could be considered as an alternative to TEE or cardiac catheterisation. Because CT is a sensitive method for the detection of calcification, it is

potentially useful for the assessment of aortic valve morphology and quantification of the degree of calcification (32, 33). For cardiac CT in general, ease of use and diagnostic capabilities, as well as improvements in both spatial and temporal resolution will continue to push this diagnostic tool to the forefront of cardiology. For MDCT, increased number of detectors will allow for better collimation and spatial reconstruction. Having more of the heart visualized simultaneously will also allow for reduction in contrast requirements and breath-holding, further improving the methodology. At the moment there is little published randomized controlled trial data to evaluate the role of MDCT in various clinical scenarios. However, this is being addressed in various ongoing trials.

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