International Cardiovascular Forum Journal 6 (2016)
DOI: 10.17987/icfj.v6i0.181

Beyond the Coronary Arteries: Evolving Applications of Multi-detector Cardiac Computed Tomography in the Assessment of Non-coronary Structures

Bo Xu, Sujith Seneviratne, Arthur Nasis

MonashHeart, Monash Medical Centre, Melbourne, Australia

Corresponding author; Dr. Bo Xu, MonashHeart, Monash Medical Centre, Melbourne, Australia
e-mail: greatbear227@hotmail.com

Abstract

Beyond the assessment of coronary artery anatomy, multi-detector computed tomography (MDCT) can be used to provide detailed structural evaluation of multiple non-coronary structures. The purpose of this review is to provide a clinical update on the evolving niche applications of MDCT in the assessment of non-coronary structures, including the assessment of the left ventricle for perfusion and scar, the evaluation of the right ventricle, pericardium and coronary anomalies. Additionally, an overview of the roles of MDCT in the assessment of congenital heart disease and intra-cardiac masses will be reviewed.

Key words: Multi-detector computed tomography; Structural heart disease; Coronary anomaly; Pericardial disease; Congenital heart disease

Citation: Xu B, Seneviratne S, Nasis A. Beyond the Coronary Arteries: Evolving Applications of Multi-detector Cardiac Computed Tomography in the Assessment of Non-coronary Structures. International Cardiovascular Forum Journal 2016;6:6-12. DOI: 10.17987/icfj.v6i0.181

Introduction

The ability of MDCT to obtain a three-dimensional volumetric dataset of the entire heart and adjacent structures that can be reconstructed at any point in the cardiac cycle makes it a powerful tool for the assessment of cardiac structures. This review will focus on the evolving niche applications of MDCT in the assessment of non-coronary structures, including the evaluation of the left ventricle for perfusion and scar, the evaluation of the right ventricle, the evaluation of congenital heart disease, pericardial disease, coronary anomalies and intra-cardiac masses.

Evaluation of Non-Coronary Cardiac Structures

A large number of non-coronary cardiac structures can be studied during a routine MDCT examination. These structures include the cardiac chambers, particularly the left-sided cardiac chambers, the cardiac valves, pulmonary arteries and veins, thoracic aorta and its proximal branches, cardiac veins and pericardium. Left ventricular (LV) and left atrial walls and cavities as well as left-sided valves are uniformly opacified in a standard MDCT examination. In comparison, right-sided cardiac chambers, walls and valves may be suboptimal for interpretation due to variability in contrast infusion protocol. Structural heart abnormalities may be more common than appreciated. A large observational study of 4,543 patients who underwent MDCT for assessment of suspected coronary artery disease, demonstrated 4.4% patients had structural heart disease unrelated to atherosclerosis, with 25% of these patients having previously undiagnosed abnormalities and 30% of these patients requiring specific treatment.[1]

Left Ventricle: Evaluation of Perfusion and Scar

An emerging clinical application of MDCT is the ability to evaluate LV myocardial perfusion and detect previous myocardial infarction. In comparison to gated single photon emission computed tomography and CMR, MDCT has high accuracy in detecting myocardial infarction, although it tends to slightly overestimate the area of infarcted myocardium.[2,3]

Measurement of myocardial blood flow by computed tomography was first quantified using electron-beam computed tomography by applying the principles of indicator-dilution theory.[4,5] MDCT perfusion data are acquired during the early portion of first-pass circulation of iodinated contrast, as iodinated contrast agents are predominantly intravascular during early first-pass circulation and diffuse to the extravascular space over time. Normally, after one minute of injection, the extravascular iodine concentration exceeds the intravascular iodine concentration.[6] In regions of myocardium subtended by stenosed coronary arteries, resulting in reduced perfusion, the rate of extravascular diffusion of iodinated contrast is more pronounced.[7] Hypo-perfused myocardium (which represents reduced myocardial blood flow)

* Corresponding author. E-mail: greatbear227@hotmail.com

ISSN: 2410-2636

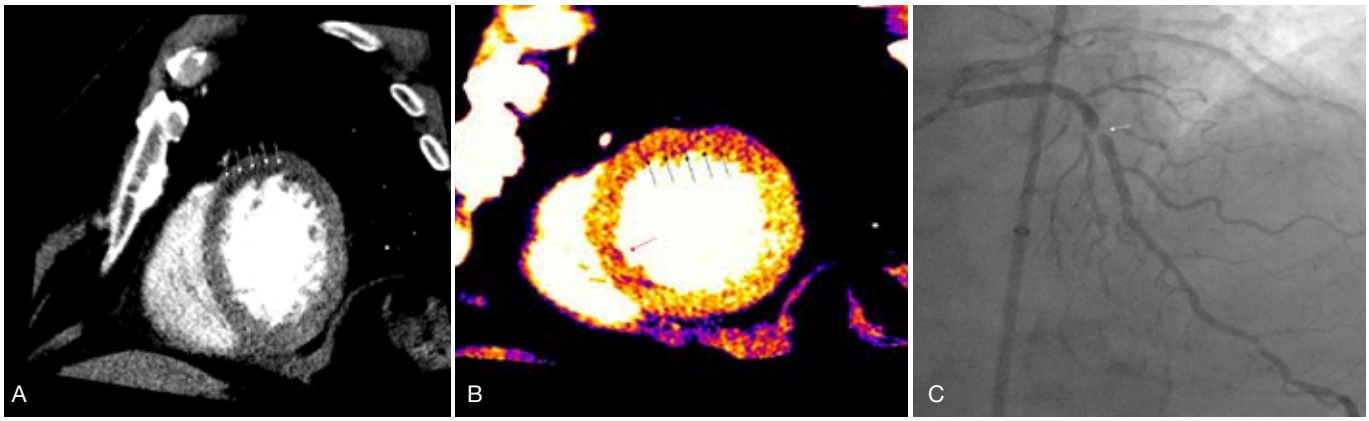

Figure 1. Demonstration of perfusion defect with MDCT in a 68-year-old man with chest pain.
(A) MDCT perfusion axial image illustrates perfusion defect in the mid anterior to mid anterolateral wall (arrows).
(B) Colour mapping also shows this perfusion defect (purple colour) in the mid anterior and anterolateral walls (black arrows) as well as additional perfusion defect in the mid inferoseptal wall (red arrow).
(C) Invasive coronary angiography left anterior oblique cranial view of the left anterior descending coronary artery, with severe stenosis in the mid vessel (arrow) accounting for the perfusion defects.

is detected by simultaneous visualisation of short-axis images for regions with hypo-enhanced myocardium compared to normally enhanced remote myocardium, aided by differences in Hounsfield unit attenuation measurements (Figure 1). If available, any areas of hypo-attenuation should be analysed in multiple phases to differentiate true perfusion defects from potential artifacts, with perfusion defects typically being present in all available phases. Semi-automated quantitative interpretation can also be performed by initially defining a defect signal density threshold relative to normal remote myocardium, which is myocardium having a signal attenuation density at least one standard deviation below the mean signal attenuation density of normal remote myocardium. Based on this defect signal attenuation density threshold, cardiac perfusion software can be utilised to detect clusters of voxels within the defined signal attenuation density range and label a hypo-attenuation defect based on the largest cluster identified. Automated software can further define myocardial perfusion defects according to their transmural extent by defining the endocardial and epicardial borders (with manual hand planimetry adjustment if required) and then calculating the mean signal attenuation density in each of three equally divided distinct myocardial layers (subendocardial, mid-myocardial and subepicardial).8 This technique may confer MDCT a significant advantage over nuclear-based techniques such as single photon emission computed tomography, which are unable to detect transmural differences in myocardial perfusion due to their limited spatial resolution. It should be noted that the current gold standard for the assessment of left ventricular scar is late gadolinium-enhanced cardiac magnetic resonance imaging (CMR).[9,10] This is performed between 10 to 15 minutes after the administration of gadolinium, when areas of scar could be maximally differentiated from regions of normal myocardium and blood pool.[9] Late gadolinium-enhanced CMR has excellent spatial resolution, with the ability to detect infarction in a small area of myocardium.[9] For a cohort of 19 patients with recent ST-segment myocardial infarction, the diagnostic accuracy of delayed enhancement MDCT in assessing the extent of myocardial infarction was compared against CMR.[11] It was found that there were strong correlations between the extent of hyper-enhanced infarcted myocardium on MDCT and CMR at 5 minutes following contrast injection (20.4 ± 2.7% versus 20.9

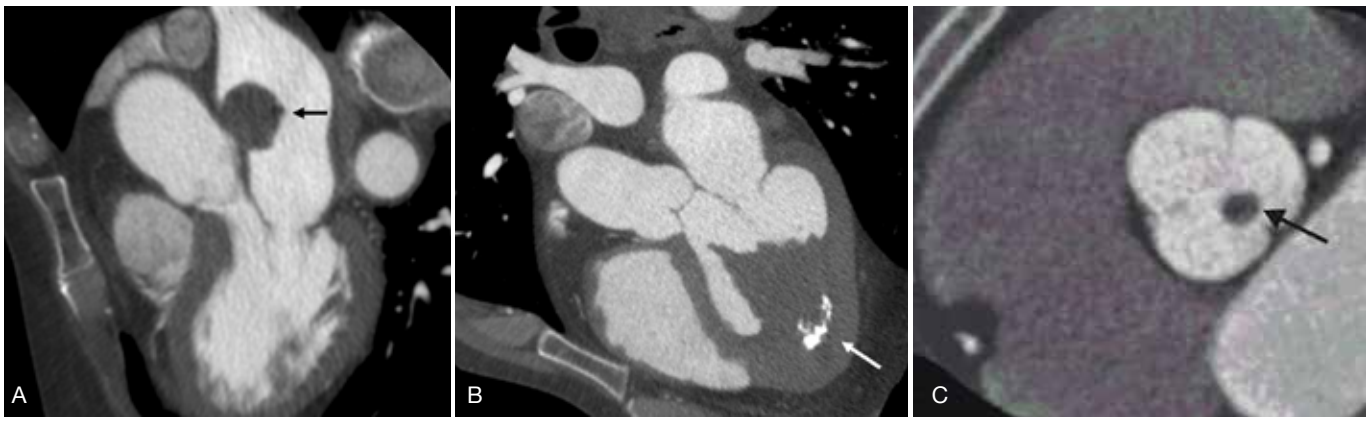

Figure 2. Contrast-enhanced MDCT images showing two common types of intra-cardiac masses.
(A) Four-chamber view showing large, non-enhancing calcified thrombus (arrow) attached to the left ventricular apex and protruding deep into the left ventricular cavity. The presence of calcifications suggests that it is chronic.
(B) Multiplanar reformatted apical three-chamber view demonstrating a well-defined low attenuation mass (arrow) attached to the anterosuperior wall of the left atrium, consistent with an atrial myxoma.
(C) Multiplanar reformatted short-axis view demonstrating a round low attenuation mass (arrow) attached to the commissure between the left and right coronary cusps of the aortic valve, consistent with a fibroelastoma.

International Cardiovascular Forum Journal 6 (2016)
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Table 1.

Study	MDCT System	Patient Number	Reference Modality	Agreement	Bland-Altman: MDCT vs. Reference ± 2 SD
Raman et al. (11)	16-slice	26	CMR (1.5 Tesla)	κ statistic: 0.88 (range: 0.78 -1.0)	N/A
Plumhans et al. (12)	64-slice	38	CMR (1.5 Tesla)	r: 0.99(EDV) r: 0.98 (ESV) r: 0.98 (SV)	-0.5 ± 5.5 -0.6 ± 3.6 0.0 ± 4.1
Sugeng et al. (13)	16-slice	28	CMR (1.5 Tesla)	r: 0.85(EDV) r: 0.87 (ESV)	0.0 ± 63 mL 0.0 ± 76 mL
Maffei et al. (14)	64-slice	79	CMR (1.5 Tesla)	r: 0.58 (EDV) r: 0.70 (ESV)	-5.2 ± 45

Table 1. Right ventricular volume assessment by multi-detector computed tomography compared to cardiac magnetic resonance imaging.

± 2.4% of the left ventricle, R = 0.85; P < 0.0001).11 However, image quality on MDCT assessment deteriorated significantly at 10 minutes following contrast injection.[11]

In addition to the standard MDCT examination, two further imaging sequences can be performed to determine the presence of inducible myocardial ischaemia and myocardial viability. MDCT stress perfusion imaging is performed after infusion of intravenous adenosine to detect inducible myocardial ischaemia, and delayed enhancement imaging is performed 10-15 minutes after the administration of intravenous contrast for further characterisation of any myocardial perfusion defect identified at rest, including assessment of myocardial viability.

Right Ventricle (Evaluation of Volume and Function)

The right ventricle (RV) has a complex trapezoidal shape, and is difficult to assess by current imaging techniques. It appears triangular on a four-chamber view and crescent-shaped on a short-axis view. RV to LV short-axis ratio is one measure used to assess RV volume. A ratio of >1 has been found to correlate well with RV dysfunction on echocardiography.[12] Other qualitative signs of increased RV volume on MDCT are based on observation of the interventricular septum, similar to echocardiography. As RV volume increases, the interventricular septum may be seen to flatten or bow towards the LV during diastole.[13] RV ejection fraction is measured by determining end-diastolic and end-systolic RV volumes on contiguous short-axis images. Assessment of RV volume and ejection fraction by MDCT has been shown to correlate well with CMR (Table 1).[14-17]

It is important to note that the evaluation of RV by MDCT can be limited by inadequate contrast opacification, resulting in problems with accurate delineation of RV contours. It has been reported that RV cannot be accurately assessed by MDCT in as many as 5 to 17% of studies.18 When accurate delineation of RV contours is necessary, biphasic or triphasic contrast protocols with a saline and contrast chaser mixture can be used.[19]

Pericardium

The pericardium is best seen in systole and appears as a bright, linear line with a mean thickness of 1.3-2.5 mm (usually <4 mm).[20] It is easily seen in both contrast- and non-contrast scans compared to the low attenuation of the surrounding fat. MDCT provides excellent delineation of pericardial anatomy of the entire chest, including the presence of any pericardial effusion, thickening or calcification. It also quantifies pericardial fat volume, a marker of cardiovascular disease[21,22] and may identify extra-cardiac lesions related to pericardial pathology.

Evolving Niche Roles of Multi-detector Cardiac Computed Tomography

While MDCT can be useful for more conventional indications such as the assessment of valvular heart disease, there are evolving niche areas for which MDCT plays a unique or complementary role. These indications range from the evaluation of cardiomyopathy and intra-cardiac masses, to the assessment of pericardial disease, coronary artery anomalies and pre-operative planning for re-operative open heart surgery.

Cardiomyopathy evaluation

Echocardiography and CMR are the primary imaging modalities in the assessment of cardiomyopathy. MDCT can play a role when echocardiographic images are not diagnostic, or the presence of pacing device and leads present a contraindication to CMR.[23] MDCT can identify changes associated with hypertrophic cardiomyopathy, including the LV wall thickness, and the presence of any aneurysm. Additionally, with retrospective electrocardiogram-triggering, cine imaging can demonstrate systolic anterior motion of the anterior mitral valve leaflet. CT coronary angiography may demonstrate the presence of prominent septal perforators that supply the hypertrophied interventricular septum. This information could assist in planning for percutaneous transluminal septal myocardial ablation. MDCT can also provide morphological assessment of the RV, including RV volumes, and the presence of fatty infiltration of the RV and aneurysmal outpouching, to guide the assessment for arrhythmogenic right ventricular cardiomyopathy.

Endocarditis evaluation

While TEE is considered the gold standard imaging method for diagnosis of endocarditis, MDCT can also be used for this purpose with high accuracy. In a recent study of patients with clinically suspected infective endocarditis, MDCT had excellent diagnostic performance in evaluating for the presence of vegetations, abscesses and pseudoaneurysms compared to TEE and operative findings. In addition, vegetation size

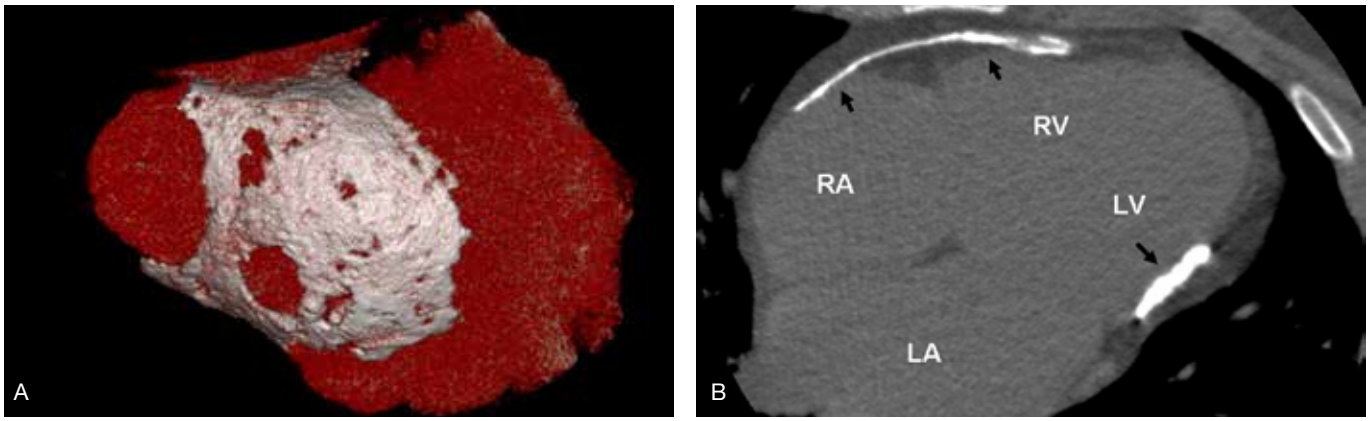

Figure 3.. Extensive pericardial calcification on MDCT in a 41-year-old dyspnoeic man with constrictive physiology on echocardiography.
(A) Three-dimensional volume-rendered image showing extensive circumferential "egg-shell" calcification, with sparing of the left ventricular apex.
(B) Non-contrast multiplanar reformatted four-chamber view demonstrating pericardial calcification (arrows) adjacent to the right atrium, right ventricle and left ventricle with sparing of the apex. LV = left ventricle, RV = right ventricle, LA = left atrium, RA = right atrium.

measurements by MDCT correlated very closely with TEE and the mobility of vegetations was accurately diagnosed in almost all patients with cine imaging.[24] MDCT also provides very accurate three-dimensional anatomic information regarding perivalvular extent of abscess and pseudoaneurysms, such as myocardial, pericardial, and coronary sinus involvement, which is helpful in peri-operative surgical planning. Therefore, MDCT may be considered as an additional imaging tool in patients with clinically suspected endocarditis after an inconclusive TEE, such as when metallic artifacts hamper the visualization of prosthetic valves.

Intra-cardiac Mass Evaluation

MDCT can accurately evaluate patients with suspected cardiac masses, particularly cardiac tumours and thrombi (Figure 2). While echocardiography is usually the primary imaging modality for assessment of suspected cardiac masses, MDCT is very useful in this setting when limited images are obtained from echocardiography, due to technical reasons.25 MDCT also has benefits over echocardiography including detecting additional lesions, more accurate tissue characterization (including Hounsfield unit attenuation measurements), assessment for the extent of invasion and the evaluation of adjacent structures for additional pathology.

Tumour evaluation

MDCT assessment of a suspected cardiac tumour involves confirming its presence, outlining its anatomical localization and tissue characterization and assessing its extent. Atrial myxoma is the most common benign primary cardiac tumour (Figures 2A-B). On contrast-enhanced MDCT, atrial myxomas are seen to arise from the endocardial surface, usually from the left atrium adjacent to the fossa ovalis. They appear as well-defined, low attenuation, heterogeneous masses with lobular contours. Malignant primary cardiac tumours are very rare, most commonly due to sarcomas. Metastatic tumours are far more common than primary cardiac tumours. MDCT features that suggest a malignant, rather than benign, cardiac tumour include a broad-based attachment, myocardial or great vessel infiltration and heterogeneous enhancement following contrast administration which persists on delayed imaging.[26]

Thrombus evaluation

Intra-cardiac thrombi are most commonly located in the LAA or in the LV apex, visualised as low attenuation contrast-filling defects. While TEE remains the gold standard for LAA thrombus, MDCT has high sensitivity and negative predictive value for LAA thrombus detection compared to TEE,[27,28] and is particularly relevant prior to pulmonary vein isolation procedures where MDCT is performed to evaluate pulmonary venous anatomy. MDCT is limited however by low specificity, with false positives commonly due to slow mixing of contrast in the LAA, particularly in the setting of atrial fibrillation where LAA emptying velocities are reduced.

Assessment of Pericardial Disease

Pericardial effusion evaluation

MDCT can provide detailed information of the presence, location and extent of pericardial effusions. It is indicated when a pericardial effusion is clinically suspected and echocardiography is inconclusive, or when loculated or hemorrhagic effusion is suspected. In addition, MDCT attenuation values may aid characterisation of the underlying cause of pericardial fluid, with Hounsfield Unit values close to water (0-25 Hounsfield Units) suggesting simple transudates, whereas Hounsfield Unit values >25 suggest an exudate due to malignancy, hemopericardium or purulent exudates.[29]

Pericardial constriction evaluation

Pericardial constriction may begin within days to weeks of a given insult and may lead to constrictive pericarditis, an end stage chronic inflammatory pericardial process with thickening, fibrosis, calcification, and adhesions of the parietal and visceral pericardium. Constrictive pericarditis may result from recurrent pericarditis or following open heart surgery. Rarer causes include connective tissue diseases, uremia, sarcoidosis, irradiation or malignancy. Its hemodynamic consequences include restricted ventricular filling with an increase in diastolic pressures and equalisation of left and right atrial and ventricular pressures. These physiological changes are diagnosed with invasive hemodynamic assessment or Doppler echocardiography.

The role of MDCT in the assessment of pericardial disease is complementary to echocardiography. MDCT can identify

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pericardial thickening (defined as pericardial thickness >4 mm), which may be diffuse or localised, as well as pericardial calcification, which may be present in varying degrees (Figure 3).[30] It can also identify abnormalities in the contour of the pericardium, narrowing and "tubular" deformation of the ventricles and flattening of the interventricular septum. Additional MDCT signs of impaired RV diastolic filling may include IVC, hepatic vein and RA dilatation, as well as hepatosplenomegaly, ascites, and pleural effusions. A thickened pericardium with clinical or echocardiographic evidence of impaired filling is most supportive of the diagnosis of constriction, however the absence of pericardial thickening does not exclude the diagnosis.30 Similarly, pericardial calcification may be present in patients without any pericardial constriction. In patients requiring pericardiectomy, the anatomic depiction and location of pericardial thickening and calcification by MDCT is a valuable pre-operative tool to aid risk stratification and surgical planning.

Pre-Operative Planning for Re-operative Open Cardiac Surgery

With the increasing frequency of re-operative open cardiac surgery being performed, MDCT is being increasingly utilized as part of a comprehensive pre-operative planning workup. This includes assessment of the distance between the RV and aorta to the chest wall (with <1 cm proximity indicating high risk), and the relationship of bypass grafts to the sternum, with a particularly high-risk feature being grafts crossing the midline < 1cm anteroposteriorly from the sternum. These findings may be associated with severe hemorrhage during resternotomy due to injury of the underlying bypass grafts, RV or aorta, and have been reported to occur in 2-6% of cases of resternotomy, with mortality of up to 37%.[31,32] If high-risk features are identified on MDCT, surgical strategies can be employed to minimize the risk of complications, including non-midline incisions, deep hypothermic circulatory arrest, initiation of peripheral cardiopulmonary bypass and extrathoracic vascular exposure before incision.[31,32] These techniques were recently demonstrated to be associated with a very low 30-day mortality of 2.5%.[31,32]

Identification of Congenital Heart Disease

While echocardiography and CMR are the most commonly used modalities in the diagnosis and follow-up of patients with congenital heart disease, MDCT has also been shown to accurately image patients with simple and complex forms of congenital heart disease.[33] As outlined above, its high spatial resolution allows evaluation of cardiac chamber volumes and function, aortic arch, great vessels, pulmonary arteries and veins as well as conduits, baffles and surrounding extracardiac structures, such as the lungs, mediastinum, and chest wall. In particular, newer wide-detector systems have several advantages over CMR, such as the ability to obtain images in less than a second within a short breath-hold without the need for general anaesthesia in children, including in patients with implanted devices. Exposure to ionising radiation and potentially nephrotoxic contrast remain important limitations of MDCT, particularly in young patients who require follow-up studies. Furthermore, contrast delivery needs to be optimally timed to adequately opacify the structures of interest.

During routine MDCT, congenital cardiac lesions may also be incidentally detected in adults that have not led to any clinical symptoms. These most commonly include intra-cardiac shunts such as atrial septal defects, ventricular septal defects or patent foramen ovale. A more in depth discussion of congenital heart disease is beyond the scope of this review.

Coronary Anomaly Evaluation

Coronary anomalies may lead to angina, myocardial infarction or sudden death.[34] In a recent large series of patients undergoing MDCT, coronary anomalies were the most commonly identified cause of nonatherosclerotic structural heart disease.[1] In a separate series of young athletes, coronary anomalies were the second most common cause of sudden death due to structural heart disease.[35] Due to the three-dimensional nature of the dataset, MDCT accurately detects and defines the anatomic course of coronary anomalies and their relationship to other cardiac and non-cardiac structures (Figure 4).
Coronary artery anomalies are often classified as either hemodynamically significant or insignificant. Hemodynamically significant anomalies are characterized by abnormalities of myocardial perfusion, and include an anomalous origin of either the left main or right coronary artery from the pulmonary artery, an interarterial anomalous course between the pulmonary artery and the aorta of either the right coronary artery arising from the left sinus of Valsalva or the left main arising from the right sinus of Valsalva, and congenital coronary artery fistulae.

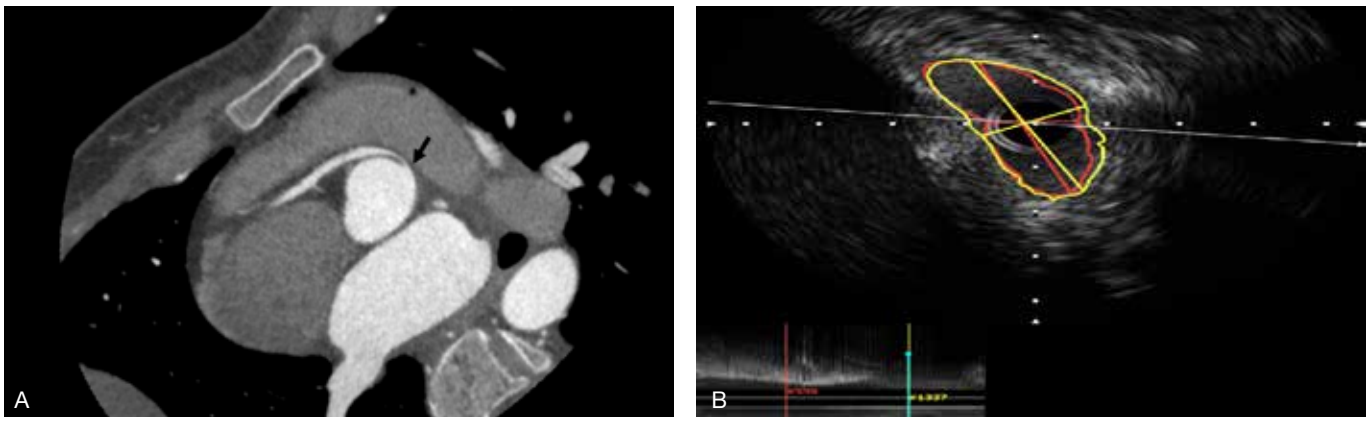

Figure 4. Coronary artery anomaly on contrast-enhanced MDCT with significant narrowing confirmed on intravascular ultrasound (IVUS) in a 40-year-old lady with exertional angina. (
A) Curved multiplanar reconstruction showing right coronary artery (RCA) arising from the left coronary cusp which runs between the aorta and right ventricular outflow tract. Note the "slit-like" appearance of the ostial RCA (arrow), suggesting significant luminal stenosis.
(B) IVUS image (40 MHz Atlantis probe) of the ostial RCA, which confirmed a significant (58%) luminal stenosis.

An anomalous origin of a coronary artery from the opposite sinus with an interarterial course is the predominant coronary artery anomaly associated with sudden cardiac death in young athletes,[36,37] with an anomalous left main arising from the right coronary sinus being most common.[38,39] This may require major prophylactic surgery to prevent sudden cardiac death in symptomatic patients or young individuals taking part in regular strenuous exercise.[40]

Conclusion

In addition to detailed assessment of coronary artery anatomy, MDCT is a powerful non-invasive imaging modality that should be utilised for the comprehensive assessment of non-coronary cardiac structures in all MDCT examinations. There are multiple evolving niche clinical applications of MDCT in the assessment of non-coronary cardiac structures. Knowledge of these non-coronary applications is important when assessing MDCT studies, as much vital structural heart information could be obtained beyond coronary anatomy.

Declarations of Interest

The authors declare no conflicts of interest

Acknowledgements

The authors state that they abide by the statement of ethical publishing of the International Cardiovascular Forum Journal[41].

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