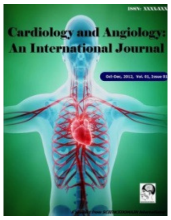

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Cardiac Computed Tomographic Angiography: Clinical Applications

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Authors' contributions

This work was carried out in collaboration between all both authors. The authors proposed the article format, reviewed the literature and wrote the first draft of the manuscript. The team joined again to make the second review and link the information together and select the appropriate figures and tables in the related sections. All both authors read and approved the final manuscript.

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ABSTRACT

Cardiovascular disease is the leading cause of morbidity and mortality worldwide. Cardiac imaging plays an important role in diagnosis and risk stratification of various cardiac diseases. Cardiac computed tomography added a major diagnostic value and led to reducing the need for invasive cardiac measures in many cardiac conditions. Cardiac computed tomography has emerged as an accurate anatomic method for detection of coronary artery disease. The negative predictive value to exclude significant coronary artery stenosis approaches 100%. Advances in multidetector computed tomography technology improved coronary arteries imaging during a single breath hold in a wide range of coronary pathologies. Appropriate patient preparation, image acquisition, and post processing techniques to detect coronary artery stenosis and plaque are prerequisites to achieving diagnostic image quality. Cardiac computed tomography applications also include assessment of cardiac structure and function, post myocardial infarction complications, electro anatomical mapping, and delineation of the pericardium.

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1. INTRODUCTION

Cardiac computed tomography (CCT) has been increasingly used in the diagnosis of coronary artery disease (CAD) due to significant technological developments that led to improved spatial and temporal resolution [1]. High diagnostic accuracy has been achieved with multidetector computed tomography (MDCT) scanners (64 slice and higher). Furthermore, coronary CT angiography (CCTA) is considered as a reliable alternative to invasive coronary angiography [2-21]. Image quality must be ensured through multiple steps, including patient preparation, the actual protocol, and the synchronization of raw image data with electrocardiography (ECG) (Table 1). Additionally, some attention must be given to the potential risks associated with the ionizing radiation received during CT examinations. Various methods for reducing radiation dose have been implemented [22-25].

Table 1. Recommendations for patients undergoing computed tomography coronary angiography

• In sinus rhythm
• Heart rate <65 beats per minute
• Able to take B-blockers or alternative medication
• Able to hold breath for 10 seconds.
• Normal renal function
• No history of contrast allergy
• Able to hold arms above head during scan
• Sublingual nitroglycerin for coronary vasodilatation

2. CORONARY CT ANGIOGRAPHY

In the current American College of Cardiology Foundation appropriateness criteria guidelines for cardiac CT and (magnetic resonance) MR, CCTA is deemed to be appropriate in the evaluation of intermediate risk patients presented with chest pain whose ECG cannot be interpreted or who are unable to exercise. Although noncontract-enhanced CT can detect calcific coronary atherosclerosis in its early stages, it cannot accurately predict coronary stenosis. On the other hand, contrast-enhanced CTA can detect subclinical atherosclerosis and coronary stenosis and this has proven to be of diagnostic and prognostic value, incremental to traditional risk stratification methods.

2.1 Diagnostic Value of Coronary CT Angiography in Coronary Artery Disease

Coronary artery calcification (CAC) detected by non-contrast enhanced CT is pathognomonic for atherosclerosis [26-28] (Fig. 1). The original calcium score developed by Agatston et al. [29]. Standardized categories for the calcium score have been developed with scores of 1–10 considered minimal, 11–100 mild, 101–400 moderate, and >400 severe. While the presence of CAC is nearly 100% specific for atherosclerosis, it is not specific for obstructive disease since both obstructive and nonobstructive lesions have calcification [30-32] (Fig. 2). However the likelihood of significant coronary stenosis increases with the total CAC score [33,34]. CAC alone is not justified in the symptomatic population since noncalcified plaques and even obstructive disease may present in many young adults [35]. CCTA should perform in symptomatic patients even with 0 CAC (Fig. 3).

Clinical applications of CCTA depend mainly on its accuracy for detection of significant coronary artery stenosis. Numerous studies have evaluated the accuracy of CCTA for stenosis detection in comparison to invasive coronary angiography [2-21] (Fig. 3). The sensitivity for the detection of coronary artery stenosis has ranged from 86 to 100% and specificity has been reported between 91 and 98%. Several trials have demonstrated that high heart rates and extensive coronary calcification negatively influence accuracy [19-21,36-38]. Meijboom et al. correlate the diagnostic accuracy of CCTA to the clinical presentation and pretest likelihood of coronary artery disease [39]. It was demonstrated that the diagnostic value of CCTA was highest in patients with a relatively low pretest likelihood of disease and lowest in patients with a high likelihood of disease based on the clinical presentation.

The "ACCURACY" trial studied 230 patients with suspected CAD [37]. Prevalence of disease was 25%, and per patient sensitivity and specificity for detecting individuals with at least one stenosis ≥ 50% were 95 and 83%. In addition to that the negative predictive value was 99%.

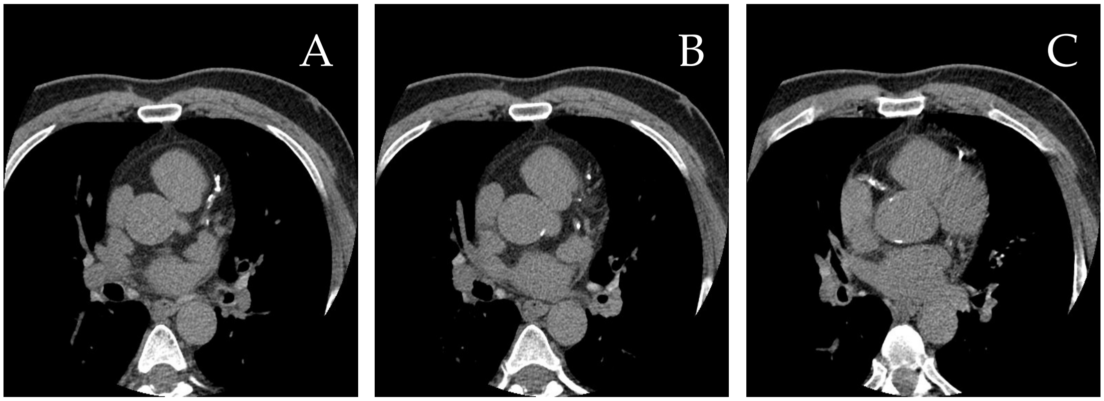

Fig. 1. A non contract-enhanced cardiac CT revealed significant calcifications in all coronary arteries and the ascending aorta

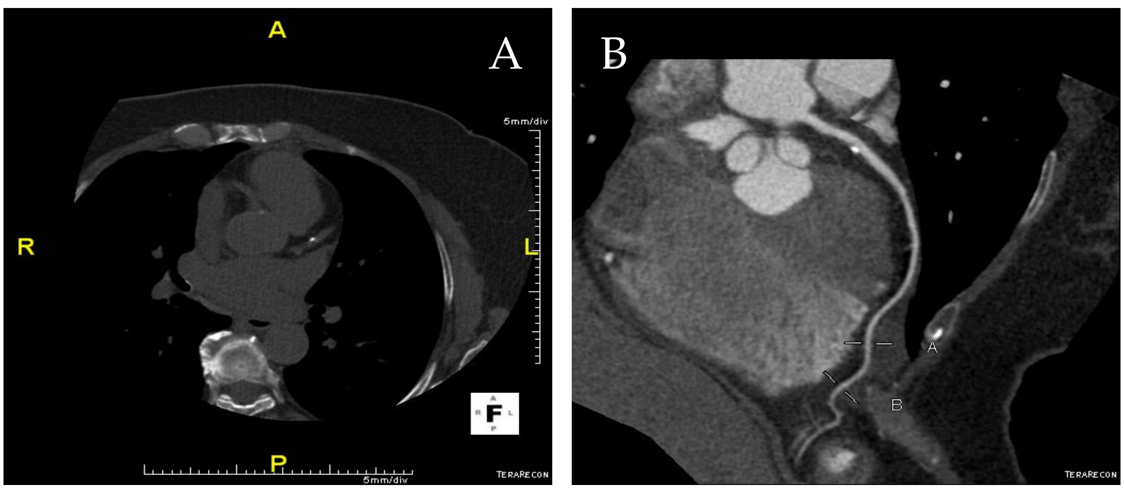

Fig. 2. Coronary CT angiography of the left descending coronary artery showing non-obstructive calcified plaque

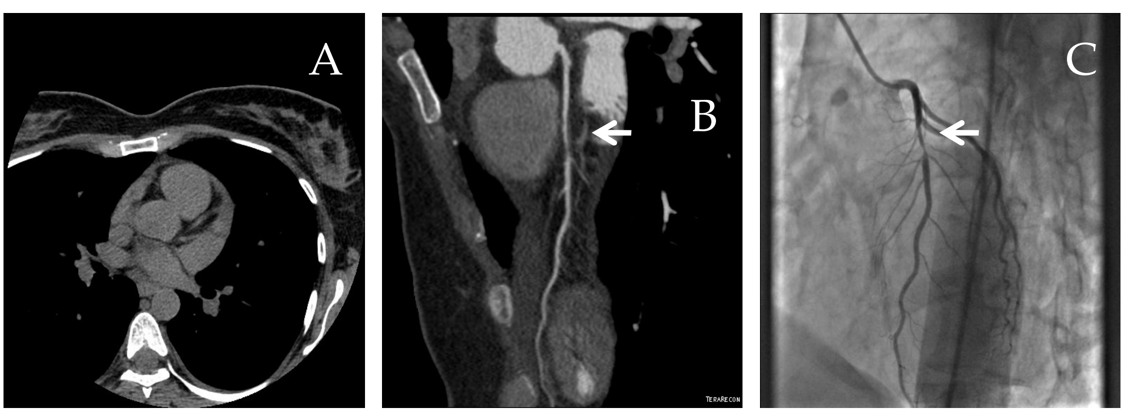

Fig. 3. A 45-year-old woman with hypertension presents with chest pain. (A) No coronary artery calcification was seen on the non contrast CT. (B) A severe left descending coronary artery stenosis was seen with CT coronary angiography (arrow). (C) Stenosis confirmed with invasive coronary angiography (arrow)

Several observational trials have demonstrated that symptomatic patients, when high quality CCTA scan was negative, had a very favorable clinical outcome even without further additional testing [40-42]. Another clinical situation in which noninvasive imaging is indicated to rule out coronary stenosis is the setting of acute chest pain particularly if the ECG and cardiac biomarkers were non diagnostic [43]. CTA has been shown to be accurate and safe to stratify patients with acute chest pain and absence of ECG changes as well as cardiac biomarkers elevation [44-48]. In addition to that Triple-rule-out (TRO) CTA can provide a cost-effective evaluation of the coronary arteries, aorta, pulmonary arteries, and adjacent extra cardiac structures for the patient with acute chest pain. It is most appropriate for the patient who is judged to be at low to intermediate risk for acute coronary syndrome (ACS) and whose symptoms may also be attributed to acute pathologic conditions of the aorta or pulmonary arteries. CCTA has emerged as the standard of reference for identification and characterization of coronary artery anomalies [49] (Table 2). CCTA offers superior definition of the ostial origin and proximal path of the anomalous coronary artery compared with conventional angiography [50-56] (Fig. 4).

Table 2. Classification of coronary artery anomalies

Anomalies of origin
High takeoff
Multiple ostia
Single coronary artery
Anomalous origin of coronary artery from pulmonary
artery (ALCAPA) Origin of coronary artery or branch
from oppositeor noncoronary sinus and an anomalous
(retroaortic, interarterial, prepulmonic, septal) course
Anomalies of course
Myocardial bridging
Duplication of arteries
Anomalies of termination
Coronary artery fistula
Coronary arcade
Extracardiac termination

Greenberg MA, Fish BG, Spindola-Franco H: Congenital anomalies of the coronary arteries. Classification and significance.Radiologic clinics of North America 1989, 27(6): 1127-1146.

2.2 Prognostic Value of CCTA in Coronary Artery Disease

CAC is superior to conventional risk factors in predicting outcomes [57,58]. Use of noncontract CT for calcium scoring was rated as appropriate within intermediate- and selected low-risk patients according to American College of Cardiology Foundation appropriateness criteria guidelines for cardiac CT and MR for risk stratification and primary prevention in a symptomatic individuals [43]. The prognostic value of extensive CAC was demonstrated in a meta-analysis of 3,924 symptomatic patients with a 3.5 year follow-up, the cardiac event rate was 2.6% per year in those with CAC > 0 and 0.5% per year in 0 CAC patients [59].

Recent data suggest that CCTA had incremental prognostic value over traditional risk factors [60]. Prognosis is predicted by coronary anatomy such as left main stenosis ≥ 50%, 3 vessel disease and 2-vessel disease including proximal LAD. The absence of CAD on CCTA conveys an excellent prognosis for symptomatic patients being evaluated for suspected CAD. Werkhoven et al. demonstrated that in patients with suspected CAD and intermediate pretest likelihood, CTA could efficiently make a distinction between patients at low or at high risk for future events [61]. Recently, Chow et al. verified that incremental prognostic value of CCTA could be achieved by the addition of the left ventricular ejection fraction (LVEF) and the total plaque score to CAD severity as determined by CCTA [62].

2.3 Coronary CT Angiography after Revascularization

2.3.1 Bypass grafts

CCTA is increasingly used as a noninvasive modality for the assessment of bypass graft patency and stenosis. Grafts and the anastomosis region of venous and arterial grafts can be analyzed with increased diagnostic yield [63-71] (Fig. 5). Recently published studies have demonstrated a negative predictive value for ruling out high-grade bypass graft stenosis ranging between 96 and 99% [70,71]. However, the distal anastomosis can still be challenging and the degree of stenosis tends to be overestimated [70] (Fig. 6). Additionally the native coronary circulation can be assessed with high diagnostic yield despite previous bypass surgery [71].

2.3.2 Coronary stents

The vast majority of coronary interventions are performed in association with placement of a coronary stent. Most coronary stents are made of stainless steel. Coronary stents usually measure 2.5–4 mm in diameter and are constantly subjected to cardiac motion. Nearly all coronary stents are made of metal and produce typical blooming ("thickening") of the stent struts with an apparent reduction of the visible stent lumen [72].

Detailed analysis of the inner-stent lumen is essential to detect intimal hyperplasia, which is the major mechanism of in-stent restenosis (Fig. 7). Complete stent occlusion could be reliably detected, while high-grade and even subtotal stenosis is frequently not identified. This can be explained by the observation that even vessels with subtotal stenosis often show unimpeded contrast flow or due to retrograde filling via collaterals.

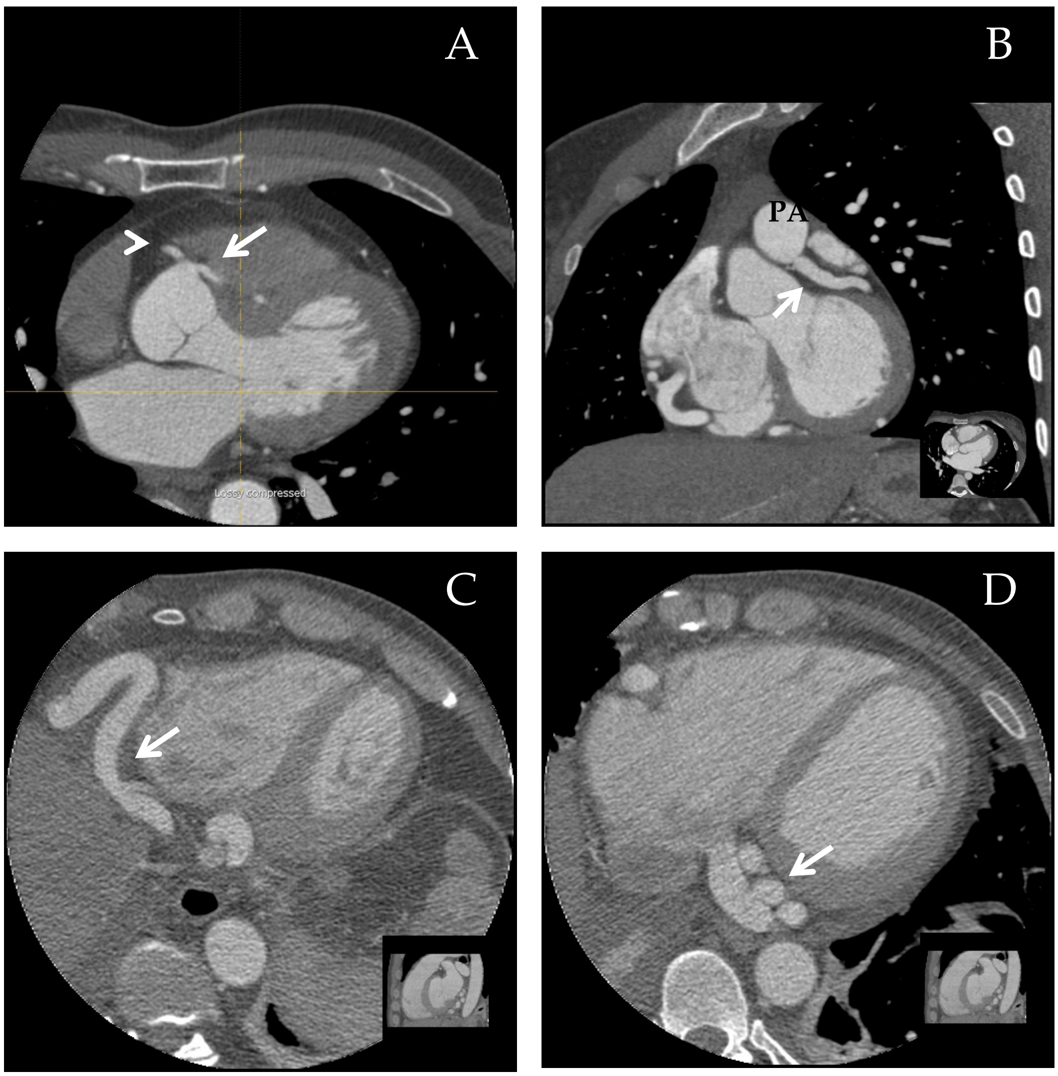

Fig. 4. Coronary artery anomalies. (A) Axial CT image shows a transseptal left descending artery (arrow) that arises from the right coronary artery (arrowhead). (B) Left coronary artery (arrow) arises from pulmonary artery (ALCAPA). Coronary artery fistula in a 44-year-old woman with palpitations (C) CT images show a tortuous and dilated right coronary artery (arrows) terminates into coronary sinus (D)

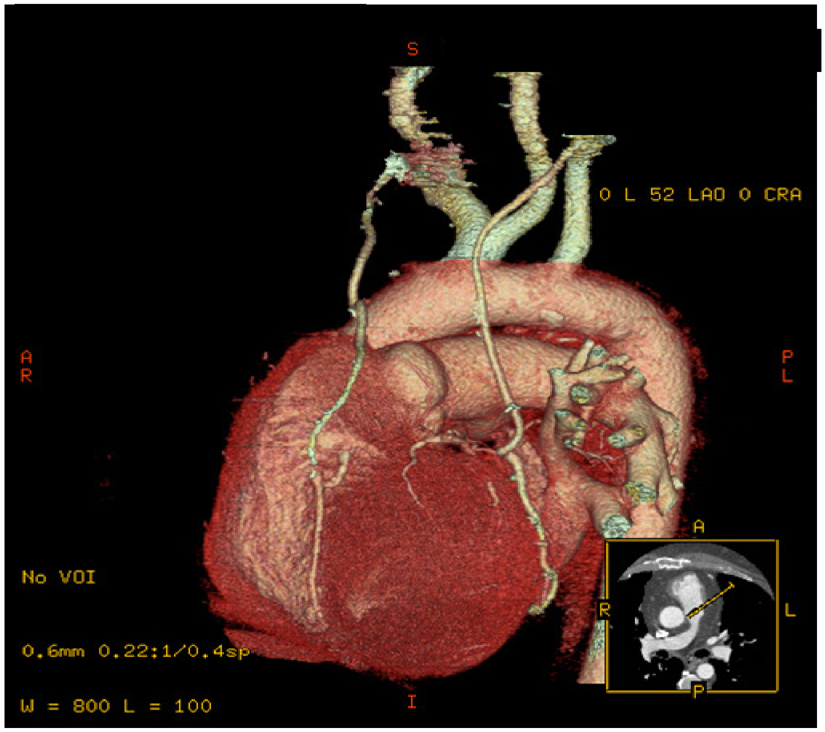

Fig. 5. 64-row MDCT 3D image reconstruction shows two patent arterial grafts coursing to the left anterior descending coronary artery and an obtuse marginal branch

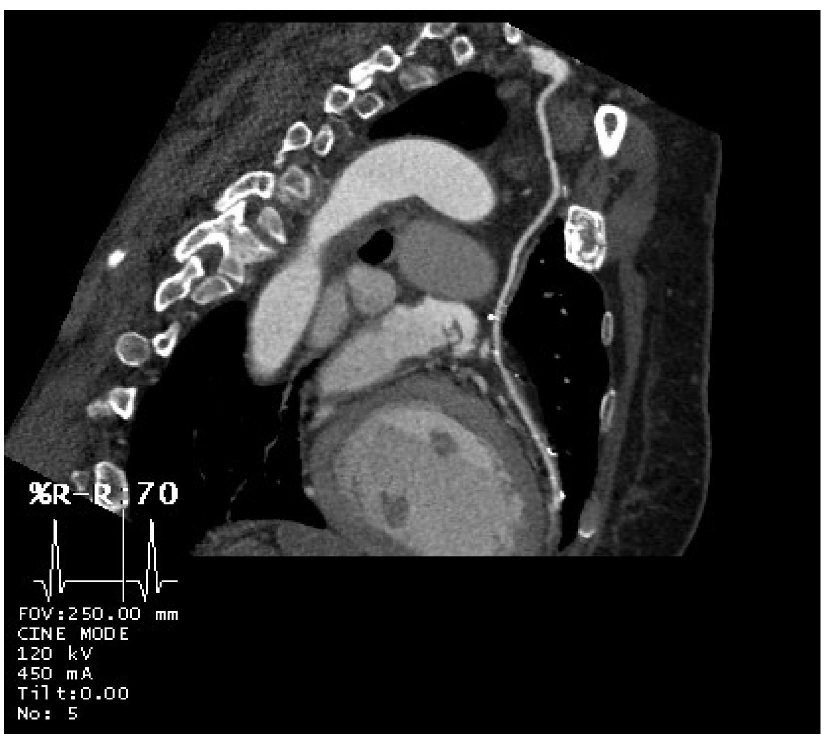

Fig. 6. 64-row MDCT 3D image shows a patent left internal mammary graft to the left anterior descending coronary artery

Recently, two meta-analyses of 16- and 64-row MDCT studies of coronary stents have been published regarding the diagnostic efficiency after stent implantation [73,74]. Overall sensitivity was 91%, specificity was 91% with a positive predictive value of 68%, and a negative predictive value of 98% [74]. Stent material, strut thickness and stent diameter are important factors influencing the ability to achieve diagnostic images. In fact, stents with a diameter ≥4.0 mm can be evaluated with fairly good diagnostic accuracy [75]. The thinner the struts of the usual metal stents are, the fewer artifacts hamper image quality.

2.4 Is Clinical Utility of Cardiovascular CT Limited to CAD?

CCT clinical utility is not limited to the assessment of coronary vasculature, but can yield information about other causes of chest pain such as aortic dissection, or pulmonary embolism. Other applications include assessment of cardiac structure and function, post myocardial infarction complications, and delineation of the pericardium. CT angiography is a useful modality in imaging the aorta and peripheral arterial tree. Furthermore, cardiac CTA became standard of care in pre procedural assessment of trans catheter aortic valve implantation and atrial fibrillation ablation procedures. In addition to that non-contrast studies allow for accurate quantification of coronary calcification, which provides important prognostic information.

2.5 Cardiac CT Angiography Assessment for Cardiac Pathology

Retrospective ECG-gating protocols can provide quantitative data on global and regional left ventricle (LV) and right ventricle (RV) systolic function with excellent correlation to echocardiography and CMRI [76,77]. It can also assess myocardial thickness, cardiac chamber sizes and volumes. Reproducibility of CT in performing right and left ventricular volume and function measurements has been established [78,79]. Further, CCT can effectively evaluate various myocardial diseases, including post myocardial infarction complications (Fig. 8) and other cardiomyopathies [80-82] (Fig. 9). CCT is extremely sensitive to the detection of pericardial thickening and calcification, a finding that can be associated with constrictive pericarditis [83,84] (Fig. 10). Additional applications include assessment of intracardiac shunts, masses, and congenital defects [85-87] (Fig. 11). CCT has a limited role for the evaluation of valvular heart disease (VHD) but CCTA for preoperative evaluation in VHD is increasingly used, and high accuracy for the detection of significant coronary stenosis has been reported [88-90].

3. MYOCARDIAL VIABILITY

The ability to distinguish dysfunctional but viable myocardium from nonviable tissue after acute or chronic ischemia is a potentially important component in the evaluation of patients with CAD and LV dysfunction. Patients with viable myocardium have excellent prognosis after revascularization [91]. Fluorine-18 (fluoro-deoxy-glucose) FDG (positron emission tomography) PET in conjunction with resting perfusion images (N-13 ammonia, rubidium-82 or (single-photon emission computed tomography) SPECT using technitium-99m agents) is one of the established and accurate metabolic imaging techniques used for myocardial viability assessment [92]. The assessment of myocardial viability and infarct morphology with delayed contrast-enhanced MRI has been well validated over the past several years [93]. The recent advent of MDCT technology has expanded its potential for a more comprehensive evaluation of cardiovascular diseases. Delayed MDCT myocardial imaging can accurately identify and characterize morphological features of acute and healed myocardial infarction, including infarct size, transmurality, and the presence of micro vascular obstruction and scar [94,95]. Well-delineated hyper enhanced regions characterize infarcted myocardial tissue by prospective ECG-gated MDCT at lower radiation dose and good resolution [96], whereas regions of micro vascular obstruction by MDCT are characterized by hypo-enhancement on imaging early after MI [94,95]. The mechanism of myocardial hyper-enhancement and hypo-enhancement in acutely injured myocardial territories after iodinated contrast administration is similar to that proposed for delayed gadolinium-enhanced MRI [97]. The better spatial resolution of MDCT as compared to (cardiac magnetic resonance image) CMRI may influence the accuracy of viability assessment, but no study so far has tested this hypothesis.

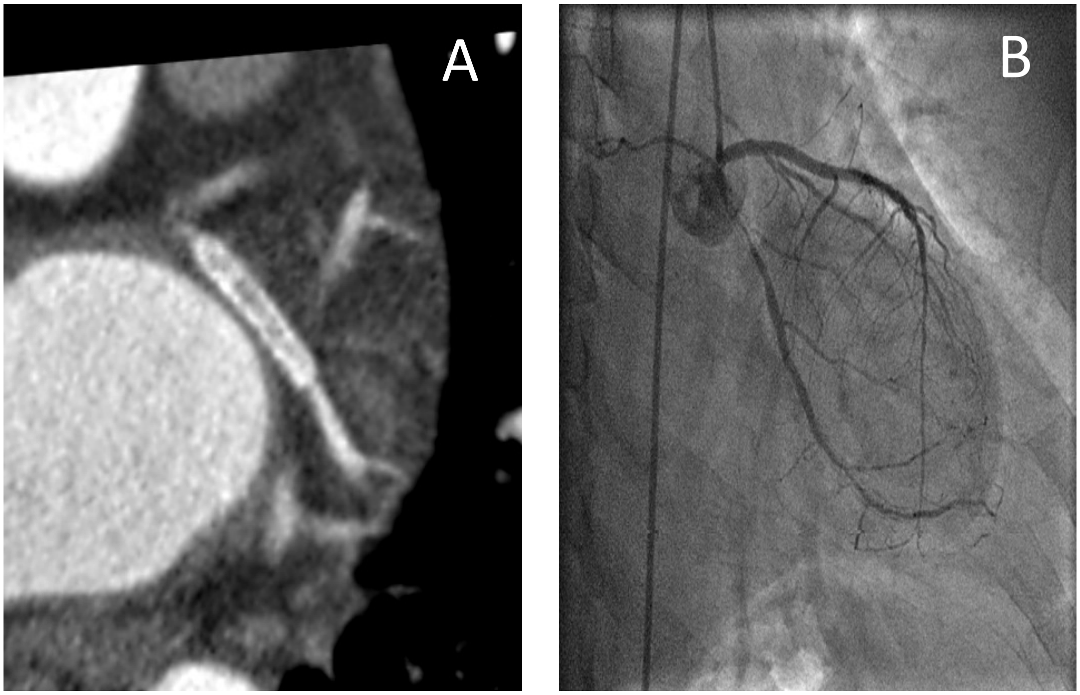

Fig. 7. In-stent stenosis proximal and distal left circumflex coronary artery. (A) 64-row MDCT. (B) Invasive coronary angiography

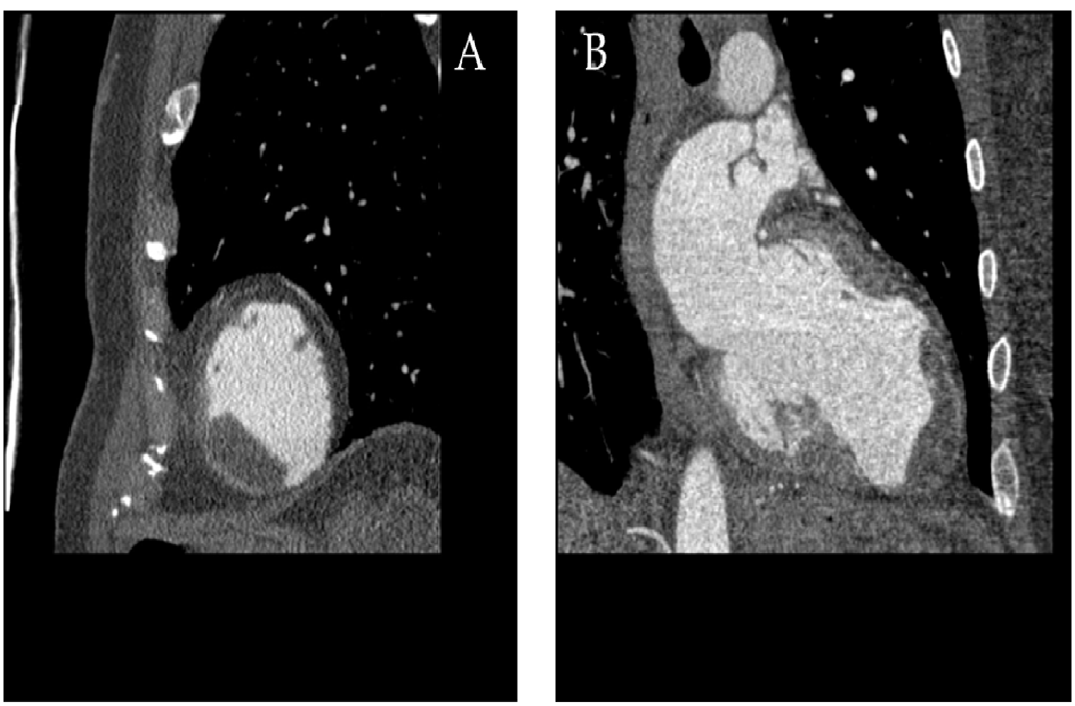

Fig. 8. Fortyfive-year-old woman with a recent myocardial infarction. Short axis (A) and two-chamber (B) views show a left ventricular apical aneurysm with thrombus

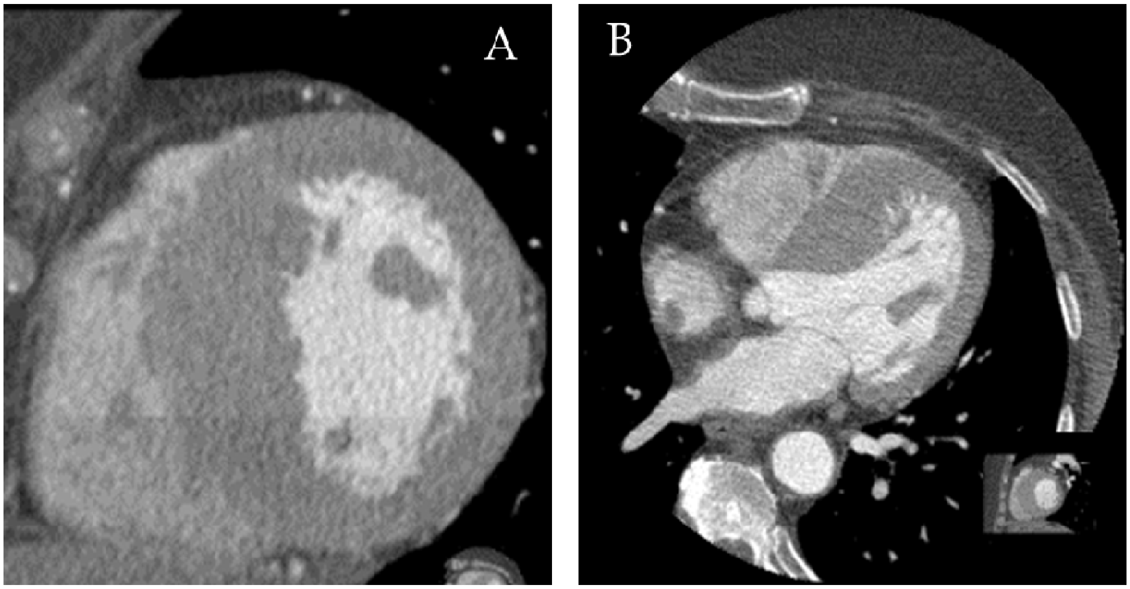

Fig. 9. Short axis and five-chamber view demonstrates abnormal thickening of the mid-and basal interventricular septum. The most common form of hypertrophic cardiomyopathy with or without obstruction

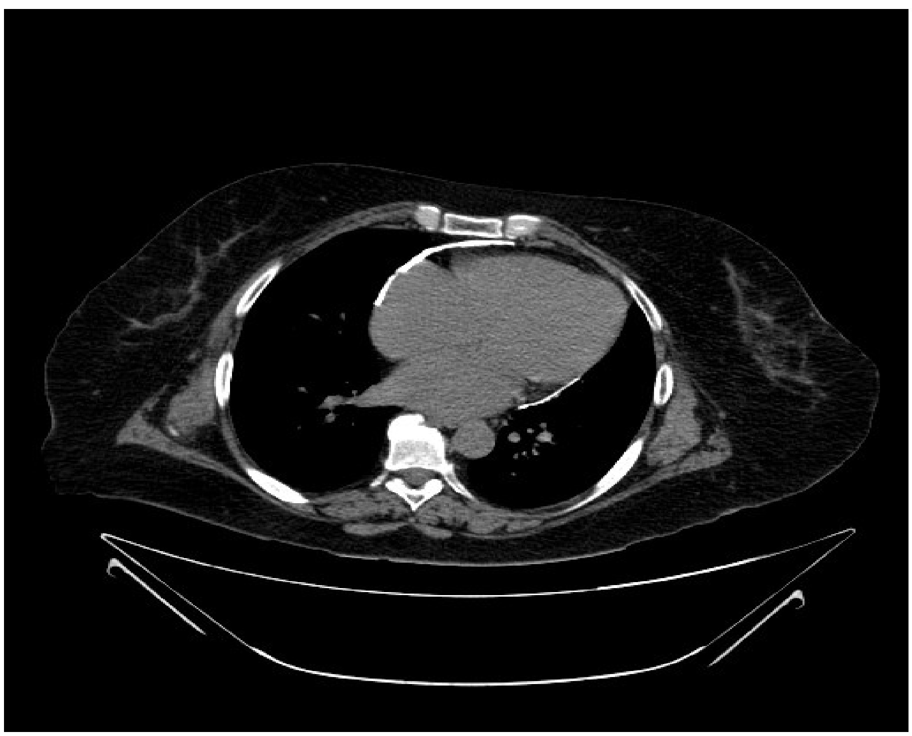

Fig. 10. Non-enhanced contrast CT demonstrates concentric, densely calcified pericardium in a patient with constrictive pericarditis

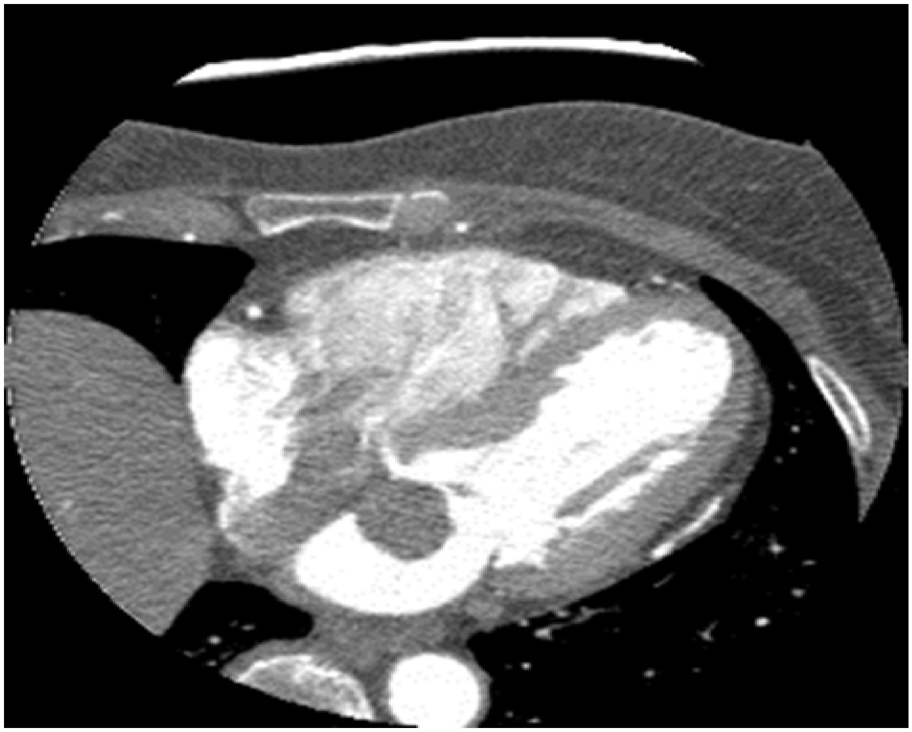

Fig. 11. Fifty two-year-old male with a left atrial mass. The post contrast study shows non-enhancement of the pedunculated mass arises from the region of the fossa ovalis, consistent with left atrial myxoma

4. ISCHEMIA DETECTION

The combination of coronary angiogram with stress-induced myocardial perfusion assessment had to wait until spiral CT technology progressed sufficiently to enable the acquisition of 64 slices simultaneously [98]. Current generation 64-detector scanners still have limited coverage of the heart, resulting in the base of the heart being scanned earlier in time than the apex, making comparisons in signal intensities between the two areas problematic. The greatest limitations to CCTA are the presence of severely calcified coronary segments, stents, or other artifacts that limit luminal visualization. The possibility of quantifying epicardial coronary plaque while also assessing microvascular disease during maximal vasodilatation enables coronary MDCTA to characterize macrovascular atherosclerosis as well as microvascular dysfunction.

5. ELECTROPHYSIOLOGICAL MAPPING AND RADIOFREQUENCY CATHETER ABLATION

Atrial fibrillation ablation requires a detailed understanding of cardiovascular anatomy through 3-D characterization of the relationships between the left atrium, the adjacent cardiac structures, and extra-cardiac structures [99] (Fig. 12). Cardiac CT study serves as a preprocedure roadmap for procedural planning, a 3-D data set for intraprocedure electro anatomic mapping and ablation. CTA characterization of the left atrium and pulmonary veins is achieved through multiple modalities of evaluation including multiplane 2-D views, 3-D volumetric reconstructions, virtual endocardial views, and volumetric quantification of the atria. Workstation software can be used for assessment of pulmonary veins anatomy and ostial diameter. Additionally, atrial anatomy, left atrial appendage thrombus and the relationship of the esophagus and aorta to the posterior left atrium and pulmonary veins can be defined [99,100]. Electro anatomic mapping with CCTA image integration has revolutionized catheter-based therapies by allowing for electrical mapping and ablation to occur on a 3 D map of the patient’s individual endocardial left atrial anatomy.

6. LIMITATIONS and CHALLENGES

High-quality images are the most important requirement for the diagnostic assessment of CCTA. Image quality must be ensured through multiple steps, including patient preparation, the actual CCTA scan protocol, and the synchronization of raw image data with ECG information. Motion artifacts occur in patients with high heart rates, heart rate variability, and the presence of irregular or ectopic heart beats such as premature ventricular contractions (PVCs) contribute to the degradation of image quality (Fig. 13). Multiple studies have demonstrated that the highest image quality of CCTA can be achieved at low heart rates (<65 beats per minute) [101-103]. Adequate patient preparation with medication (e.g. B-blocker) to reduce the heart rate as well as training of the breath-hold commands is mandatory to avoid cardiac and respiratory artifacts. High-attenuation structures, such as calcified plaques or stents may degrade the accuracy of the assessment of stenosis due to beam-hardening artifacts. Several metanalyses demonstrated high-density calcification produces blooming artifacts, which lead to overestimation of the degree of coronary stenosis [104-106]. The specificity of CCTA is reduced in the presence of coronary artery calcium if the Agatston score is >400 [19-37]. The radiation dose associated with CT imaging is a serious concern for both clinicians and manufacturers [22,23]. With increasing application of CCTA in the diagnosis of CAD, the research focus has shifted from the previous emphasis on diagnostic accuracy to the current focus on reduction of radiation dose with acceptable diagnostic images [24,25]. Tremendous progress has been made to reduce the radiation dose by using many of the technologies and strategies however; much effort is still necessary to ensure that CCTA is safely performed in imaging patients with suspected coronary artery disease.

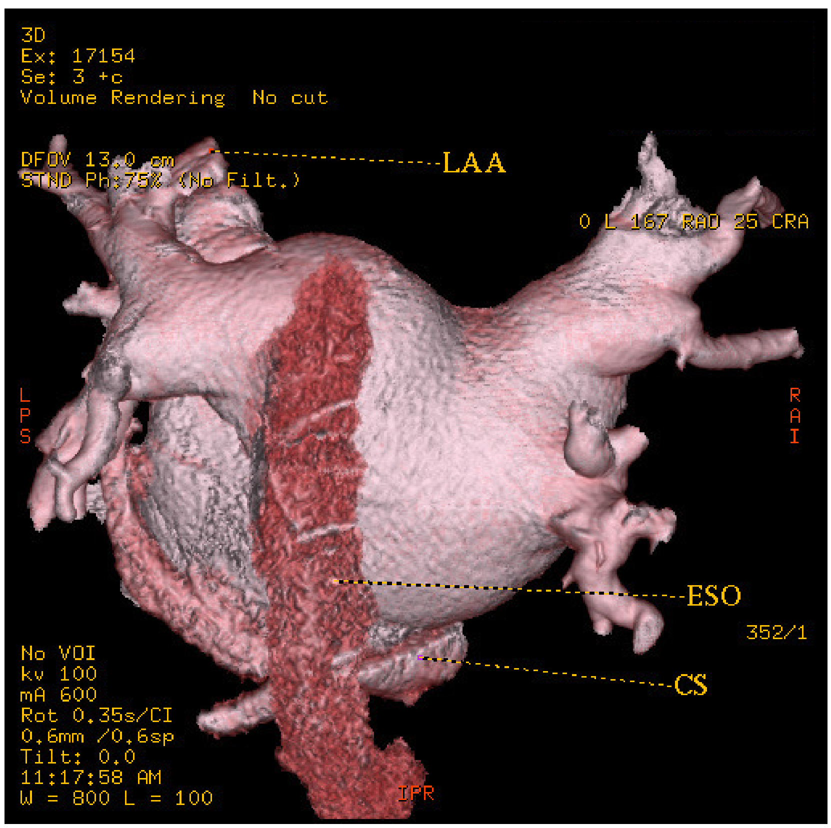

Fig. 12. D reconstructions demonstrating the relationship of coronary sinus (CS) and esophagus (ESO) to the posterior left atrium and left lower pulmonary vein

Fig. 13. (A) Patient imaged at heart rate of 77 beats per minute. Axial image at level of mid right coronary artery demonstrates typical appearance of motion artifact (arrow). (B) Patient with multiple extra systolic beats during image acquisition. Stair-step artifacts (arrows) are caused by irregular rhythm

7. CONCLUSION

CCT/CCTA is a well-established cardiac diagnostic modality, which can be used, in various cardiovascular conditions. Major advantages of CCT/CCTA include reliability, safety and the fact it provides both anatomical and functional information. The reduction of radiation dose with acceptable diagnostic image quality is the focus of current and future research.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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