

Infarct characterization using CT

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Abstract: Myocardial infarction (MI) is a major cause of death and disability worldwide. The incidence is not expected to diminish, despite better prevention, diagnosis and treatment, because of the ageing population in industrialized countries and unhealthy lifestyles in developing countries. Nowadays it is highly requested an imaging tool able to evaluate MI and viability. Technology improvements determined an expansion of clinical indications from coronary plaque evaluation to functional applications (perfusion, ischemia and viability after MI) integrating additional phases and information in the mainstream examination. Cardiac computed tomography (CCT) and cardiac MR (CMR) employ different contrast media, but may characterize MI with overlapping imaging findings due to the similar kinetics and tissue distribution of gadolinium and iodinated contrast media. CCT may detect first-pass perfusion defects, dynamic perfusion after pharmacological stress, and delayed enhancement (DE) of non-viable territories.

Keywords: Atherosclerosis; cardiovascular disease; computed tomography; coronary arteries; myocardial infarction (MI)

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Introduction

Cardiac computed tomography (CCT) is considered an accurate imaging technique for the evaluation of coronary artery disease (CAD).

CCT may play the role of a non-invasive gatekeeper to invasive conventional coronary angiography especially in patients with suspected CAD (1-5). In particular, CCT is useful in patients at low-intermediate pre-test probability of CAD (6). The tool had an impressive development in the last decade with improvement of the scanner spatial and temporal resolution. Moreover, a significant reduction in radiation dose has been recently achieved (7-10). Such significant improvements determined an expansion of clinical indications even to non-coronary applications (11). Large clinical trials

highlighted the utility and the cost-effectiveness of CCT (12-14). However, the assessment of the morphological pattern of a coronary stenosis should be combined with an evaluation of hemodynamic significance, and eventually related myocardial ischemia, and functional consequences (15). In this clinical context, CCT may integrate additional phases and information in the mainstream examination. CCT and cardiac MR (CMR) may detect and characterize myocardial infarction (MI) with overlapping imaging findings (16).

In this review, we describe the state of the art of CCT in the assessment and characterization of MI focusing on technical aspects, imaging features, and pros and cons in comparison to nuclear medicine and CMR. The review is directed to clinical cardiologists and it can be a focus for radiologists interested in cardiac imaging.

Background

MI is a major cause of death and disability worldwide. According to American Heart Association, CAD caused 1 of every 6 deaths in the United States in 2008 with a remarkable incidence of silent MI (17). According to World Health Organization, the trend of incidence is not expected to abate despite better prevention, diagnosis and treatment (18); nonetheless acute MI prevention and treatment efforts have resulted in favorable declines in the frequency of STEMI and death rates from the major types of acute MI (19).

The heart is a muscle with high energetic demand, which is continuously propelling blood throughout the body. In case of mismatch between oxygen supply and energetic demand, ischemia may follow with a definite sequence of cellular, inflammatory and biochemical effects. MI includes a wide spectrum of pathological stages depending on duration time of ischemia and extension of territories involved. The primary cause of acute MI is the sudden disruption of a coronary unstable atherosclerotic plaque and acute intracoronary thrombosis (20,21). First changes in cells contraction are observed in the first minute of ischemia, however temporary effects are documented after 20 minutes, depending on the robustness and extension of collateral coronary circle (22). After 4 hours from acute event the first gross pathological effects of MI are: edema with increased vascular permeability secondary to inflammation, necrosis (unprogrammed death of cells), and hemorrhage. After 12 hours, the inflammation processes with infiltration of neutrophils start and the myocytes begin to lose nuclei and striations. Within 3 days, the muscle fibers start to disintegrate, the neutrophils die, and the macrophages start to remove the debris of dead cells. Scarring process is defined by the apposition of collagen and ends after two months from the initial event and it is characterized by areas of fibrous tissue (fibrosis) that replace normal cells.

The left ventricle, which is the main target of MI for the primary contribution to heart contraction, can present a reduced functionality with decrease of the ejection fraction. Nonetheless, for a short time period after the beginning of the ischemic process the myocardium is “stunned” in a condition of transient left ventricular dysfunction. A prolonged ischemic state determines the condition of hibernated myocardium, which is partially reversible with revascularization. The restoration of blood flow to the damaged myocardium may also not have positive effects because it may cause an accelerate reperfusion injury due

to the activation of oxygen free radicals, microvascular dysfunction and microvascular obstruction (MO). MO or no-reflow phenomenon is caused by edema and osmotic overload with alterations of endothelial cells and cardiomyocytes.

Macroscopically, the left ventricle may present a more round and dilated shape defined as ventricular remodeling. The ischemic process advances like a wavefront from the endocardium to the epicardium and may become transmural (23). A transmural MI involves the entire thickness of the myocardial wall from endocardium to epicardium. The left ventricle may even rupture with dramatic consequences such as hemopericardium and tamponade. Another later consequence may be the thinning of the ventricular wall and the development of an aneurysm. In some cases MI territories may be infiltrated by adipose cells in a process called lipomatous metaplasia. Rest CT perfusion cannot discriminate between lipomatous metaplasia and a rest perfusion defect with viable myocardium because both appear hypodense in this phase. In this case, delayed enhancement (DE) imaging is useful.

CT technical notes

Myocardial perfusion imaging can be assessed with CCT either in a single-step approach for qualitative evaluation of ischaemic myocardium (24) or in a multi-step approach for quantitative analysis of the myocardial blood supply (25).

Early perfusion defects may be displayed during the first passage of the contrast medium in patients with acute, chronic, and subacute MI. Myocardial territories with impaired perfusion have a reduced distribution of contrast medium. Then, a specific region of hypoattenuation can be depicted even during CCT studies aiming solely at the evaluation of coronary arteries with no additional radiation dose to patients or changes in the scanning parameters. Every CT scanner that is able to perform CCT can be employed to assess first-pass defects (*Figure 1*). Nonetheless, dedicated image filters may improve the delineation of MI areas, which are affected by the hyperattenuating contrast media amount in the left ventricle chamber (26). The contrast in the left ventricle chamber determines beam-hardening artifacts, which may obscure the subtle first-pass subendocardial defects (27,28). The reconstruction of different temporal windows of the cardiac cycle may help to determine if the perfusion defect is true (29).

Dual-energy CT technology may provide image acquisition using more than a single energy X-ray spectrum

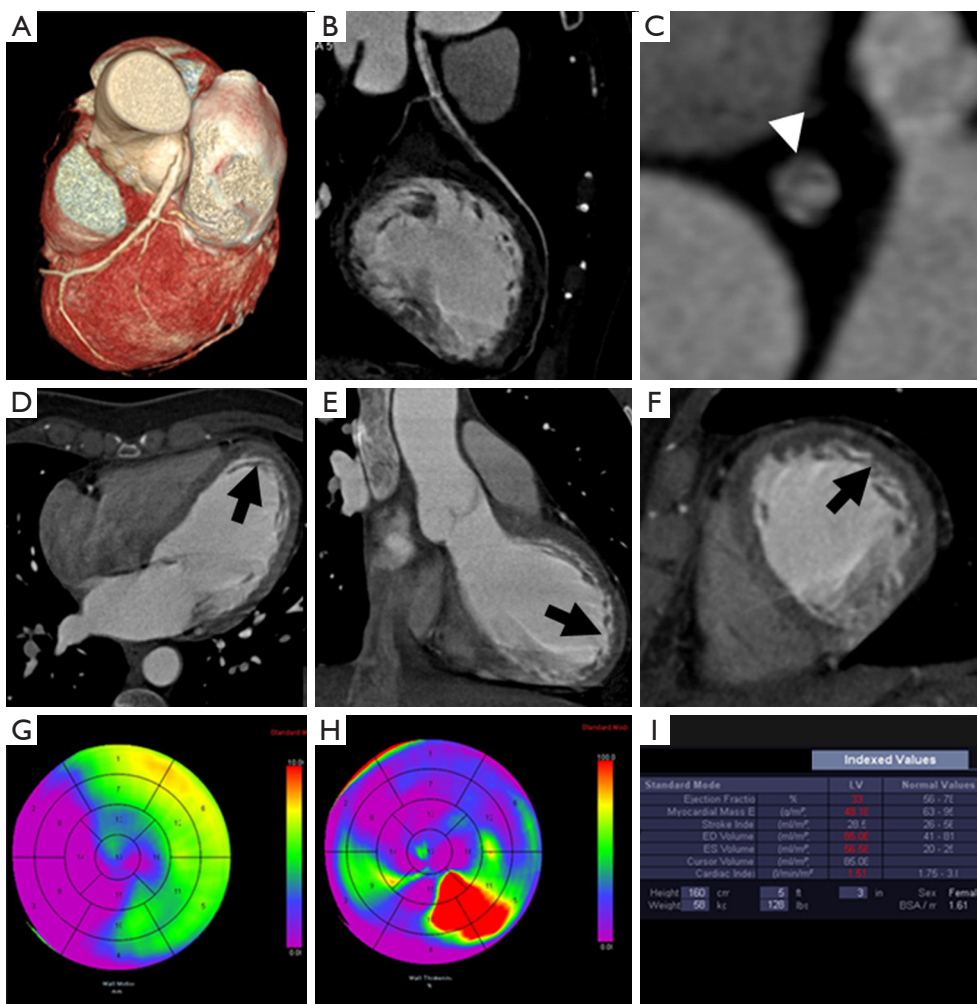


Figure 1 CCT in a female patient with an extensive anterior myocardial infarction of the left ventricle. The patient was revascularized with a left main stenting as depicted in volume rendered (A) and multiplanar (B) images. Intra-stent intimal hyperplasia was displayed (arrowhead, C). Multiplanar images (4-chamber, D; long axis, E; short axis, F) show the first-pass perfusion defects (black arrow) on the subendocardial wall of the left ventricle. The functional bull's eyes depict hypokinetic segments (G) and regional myocardial wall thinning (H). The left ventricular function is considerably impaired (I).

(30,31). Dual-energy CT represents a promising technique for the integrative analysis of coronary artery morphology and myocardial blood supply; furthermore Dual-energy CT is in good agreement with invasive coronary angiography and SPECT (30). Dual-energy technology enables mapping the myocardial iodine distribution, according to the absorption of X-ray spectra at different energy levels. The colour-maps of iodine distribution are based on both energy spectrum datasets and are superimposed into gray-scale multiplanar reformats of the left ventricle. The approach is not requiring additional scanning time or exceeding radiation dose, if compared to conventional

single-energy CCT. Such techniques are usually described as perfusion imaging despite they merely provide a static picture of contrast medium distribution in the myocardium. Moreover, image acquisition covers several segments of the myocardium irrespective of perfusion phase (32,33). In the last years, a dynamic time-resolved scanner technology may exceed the limitations of a static acquisition of data. Such technique provides an effective perfusion imaging with colour-coded maps based on dynamic perfusion CCT performed during adenosine stress at multiple time points of contrast medium distribution through the myocardium (34). Time attenuation curves, perfusion parameters and defects

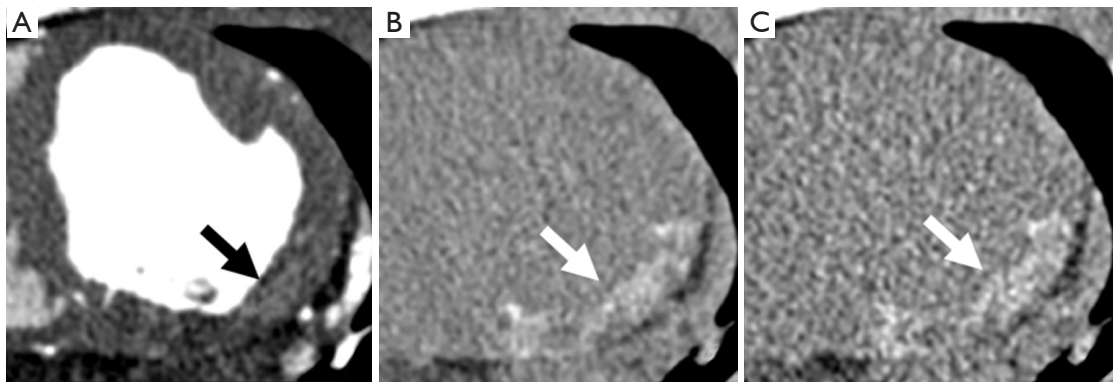


Figure 2 CCT in a porcine model with induced myocardial infarction. First-pass CCT shows early and subtle perfusion defects (black arrow) on the subendocardial lateral wall of the left ventricle corresponding to the perfusion territory of the left circumflex coronary artery (A). Corresponding DE-CCT images performed with standard contrast bolus using a low-dose radiation of 350 mAs (B) and standard 900 mAs (C). DE-CCT shows a good correlation with acute infarct size (white arrow).

may be analyzed. The recent availability of faster CT systems allowed the dynamic time-resolved perfusion imaging, which enables quantitative measurements of tissue blood flow, similarly to cardiac PET with the use of rubidium-82 (35).

CT techniques for imaging of myocardial viability are based on the pathological background of acute MI, whereas the cell damage leads to the loss of cellular membrane integrity and a subsequent increase in the distribution of contrast medium. In this regard, myocardial viability imaging with CCT is based on the same background and technique of CMR with DE (16,36-41). Iodinated contrast media are thought to accumulate in a way similar to gadolinium during CMR. Nevertheless, a plenty of practical factors such as ECG gating technique, tube parameters, and contrast media protocol may affect DE with CT.

First, ECG gating may be retrospective or prospective. The latter may significantly reduce the radiation dose even for DE purposes (9,42). It is reasonable to expect that a DE-CCT may be performed with a low radiation dose of about 1 mSv (10). Second, the noise inherent to CCT may hamper the assessment of areas of MI especially when a single-energy technique is exploited. In this setting, the use of low kilovoltage has been described to improve the detection of areas of DE within the myocardium in animal experiments (43,44), while tube current does not significantly affect the detection of MI territory, image quality or contrast resolution (45). Martini *et al.* also demonstrated that the increase of contrast material volume provides a significant improvement in MI image

quality (46). Nonetheless, the noise may interfere with the accurate delineation of segments showing DE, especially when obese patients are studied. At least 120 mL of contrast medium should be administered with an optimal delayed scan from 5 to 15 minutes (*Figure 2*) (16,40,47) or directly after conventional angiography for reperfusion in the attempt to reduce the contrast media use (41). DE-CCT exploits multiplanar reconstruction or maximum intensity projections, with usual thickness from 5 to 10 mm, strict window width and level (29). CCT may evaluate CAD with an initial angiographic scan and subsequently assess the viability of myocardium with a DE scan.

CCT is not accurate in the prediction of myocardial ischemia if compared with CMR or single-photon emission computed tomography (SPECT) (48). Rest CCT can assess only static perfusion defects of infarcted areas of myocardium, as previously described. In this regard, it is widely accepted that the morphological information on a stenosis must be combined with the functional assessment of the perfusion or wall kinetics during provocative tests (49). A stress test may help to determine if a coronary artery stenosis is responsible of a reduction of myocardial perfusion. The stress may be induced pharmacologically or by exercise. It is well known that stress perfusion abnormalities occur before wall motion dysfunction (50). Therefore, additional scans acquired during pharmacologic stress with adenosine or dipyridamole may detect reversible perfusion defects of myocardium (31,51-53). Therefore, the stress-CCT may be indicated: in symptomatic patients at intermediate risk of

Table 1 Cardiac CT examination phases

Examination type	Target	Examination time	Reading time
Coronary angiography	Morphology	5'	5'
Left ventricle assessment	Function	5'	5'
Rest	Perfusion	5'	5'
Stress	Perfusion	5'	5'
Delayed enhancement	Viability	5'	5'

*, not additional time; phase simultaneous to coronary angiography if retrospective gating is employed; **, additional time of phase.

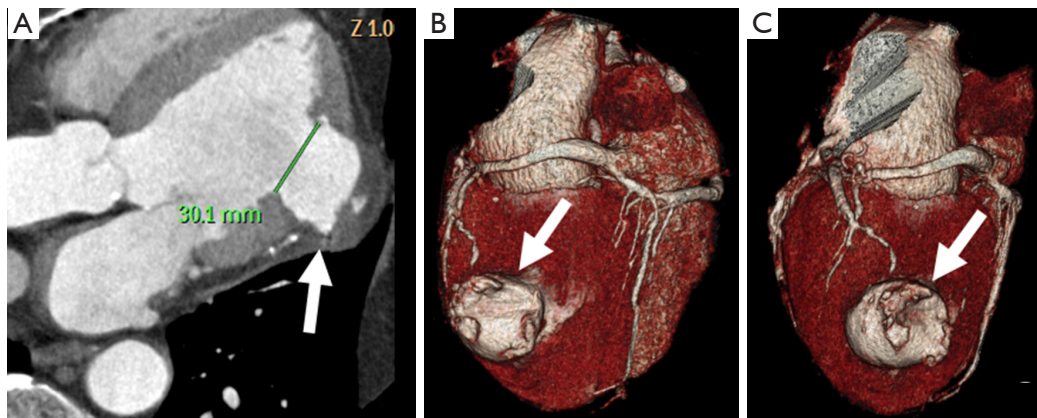


Figure 3 Saccular post-ischemic aneurysm of the left ventricle with layered thrombus depicted by multiplanar (A) and VR images (B,C).

CAD with non-diagnostic or equivocal ECG result or unable to exercise; in patients with a known coronary artery stenosis, to determine the hemodynamic significance; in patients with coronary artery bypass grafts and recurrent thoracic pain (11). However, as for other methods of provocative testing, stress CCT should be used under safety standards (54,55). CCT and SPECT have an important limitation due to high radiation exposure. Furthermore the use of contrast media should be limited and could be a limitation in patients with impaired renal function. In this case clinical examination together with functional evaluation with echocardiography may represent an alternative solution.

In conclusion, a comprehensive protocol of CCT should include: an initial angiographic scan to assess coronary arteries and myocardium at rest; a second scan with a second bolus of iodine contrast medium, before or after the rest scan, at peak of pharmacologic stress (adenosine 140 µg/min/kg of body weight for 2–5 minutes); a DE acquisition, about 5–10 minutes after the contrast injection, for viability imaging (Table 1).

Imaging findings

Improved CT scanner technology with high spatial and temporal resolution may detect MI even with standard CT techniques. Characteristics of chronic MI such as perfusion abnormalities, fatty metaplasia with lower attenuation values (<0 HU), calcifications, remodeling of the left ventricle, focal wall thinning, left ventricular thrombus or aneurysm may be easily depicted (Figure 3) (39,56).

Non-contrast CCT for calcium scoring purpose can already detect chronic MI showing hypoattenuating myocardial regions if compared with nuclear myocardial perfusion imaging with a sensitivity of 92% and a specificity of 72% on a per-patient basis (56,57).

Similarly, contrast-enhanced CCT may detect hypoattenuated areas of MI (58) with a typical ischemic pattern (Figure 4). The distribution is subendocardial or transmural and it is concordant with the ischemic territory as opposed to epicardial or mid-wall distribution of myocarditis pattern (59). Rest dual energy CT provided comprehensive CAD imaging and identified perfusion

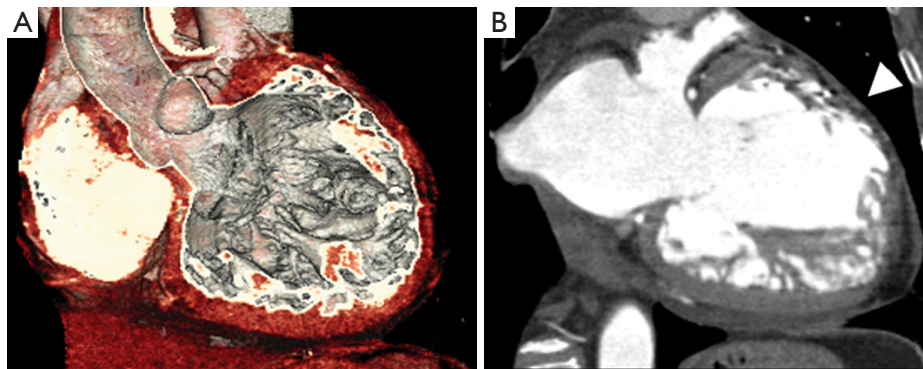


Figure 4 Post-ischemic dilated cardiomyopathy displayed by volume rendered (A) and multiplanar (B) images. An early perfusion defect (arrowhead) on the subendocardial wall of the left ventricle is displayed.

defects in 90% of cases in comparison to SPECT (60). The major drawback is the visualization of small MI (61).

According to iodinated contrast media distribution, CCT may assess ischemic areas and viable myocardium in a way similar to CMR. The loss of membrane integrity of cells determines hyperenhancing areas. However, the DE may reduce from acute to chronic phases of MI because of the reduction of surrounding edema (62). Acute MI is defined by the ischemic area, which may become necrotic if the microvasculature is not recovered. In this setting, percutaneous coronary angioplasty (PTCA) may not lead to a functional recover because of the severe obstruction of the microvasculature. This is called no reflow phenomenon and it is defined by a central core of hypoattenuation within the hyperenhancing region (63). The decrease in infarct size over time is a process that can also be observed with CT (64). In acute MI the area may be hypoattenuated on first-pass and DE-CCT (65), while in chronic MI, reperfused or not, the scar determines a hyper-enhanced region.

Comprehensive protocol of CCT should be tailored to the patient's history and to the findings of the first scan (i.e., if the first scan is normal it is not necessary to perform the stress and the DE; if the patient has an intermediate to high pretest it might be preferred to start with the stress and the rest might be avoided according to the findings).

Diagnostic performance

Perfusion and viability may be assessed with CCT (66-69). In the past decades, areas of suspected MI were mainly investigated by nuclear medicine techniques. SPECT and PET provided relevant diagnostic information with significant therapeutic and prognostic implications (70),

despite some disadvantages such as attenuation artifacts, radiation dose, and limited off-hours availability. CMR may provide similar results in terms of diagnostic accuracy and long-term prognostic value, with the advantage of the lack of ionizing radiation (71,72).

Echocardiography represents a non-invasive diagnostic technique, which provides information regarding cardiac function and hemodynamics. In the acute settings it plays a role in regional wall motion abnormalities evaluation and for ruling out other etiologies of acute chest pain or dyspnea, including aortic dissection and pericardial effusion. Echocardiography can differentiate normal from infarcted myocardium, with the analysis of wall thickening and wall motion (the pattern of dysfunction may be a reflection of the extent of an infarction). Echocardiography plays a role also in the evaluation of complications of an acute MI like ventricular free wall rupture and pseudoaneurysm formation, ventricular septal rupture and mitral regurgitation (73).

In the next years, image fusion and hybrid scanners will combine more effectively structural and functional information regarding the pathological sequence that goes from stenosis to ischemia (74-78).

New concepts and technical solutions of CT scanner enable comprehensive imaging of MI from coronary stenosis to myocardial tissue damage. A plenty of studies demonstrated the high diagnostic accuracy of CCT (Table 2) in the diagnostic workup of patients with suspected CAD (3-5,8,11,79-83) and low to intermediate risk of CAD (6,84). CCT was also validated by several outcome studies that investigated risk stratification and prognostic value in registry data (85-87). Nonetheless, CCT may also provide functional information including regional heart function

Table 2 Diagnostic accuracy of cardiac CT in comparison to CMR and SPECT in the detection of myocardial infarction

Authors	Patients (n)	CT technique	Other technique	Sensitivity (%)	Specificity (%)
Nikolaou, 2005 (66)	30	First pass CCT	DE-CMR	91	79
Habis, 2009 (41)	26	DE-CCT	DE-CMR	90	80
Bauer, 2010 (67)	36	Dual-energy CCT	DE-CMR (3 Tesla)	77	97
Ko 2014, (68)	100	Stress perfusion Dual-energy CCT	Stress perfusion CMR	89	74
Ruzsics, 2009 (30)	36	Rest Dual-energy CCT	Stress-rest SPECT	92	93
Cheng, 2010 (32)	55	Rest Dual-source CCT	Stress-rest SPECT	Rest: 100 Stress: 83.3	Rest: 78 Stress: 90.3
Tanabe, 2016 (69)	53	Stress dynamic CCT perfusion	SPECT (n=25)	Abnormal perfused myocardium: 80 Severe infarction: 95	Abnormal perfused myocardium: 86 Severe infarction: 72
			CMR (n=28)	Abnormal perfused myocardium: 82 Severe infarction: 78	Abnormal perfused myocardium: 87 Severe infarction: 80

CCT, cardiac CT; CMR, cardiac MR; DE, delayed enhancement; SPECT, single-photon emission computed tomography.

and the assessment of MI, ischemia, and viability (88).

Tanabe *et al.* demonstrated that Dynamic CT perfusion has the potential to detect abnormal perfused myocardium and severe infarction assessed by SPECT/CMR using comparable cut-off myocardial blood flow (MBF). Authors retrospectively evaluated fifty-three patients who underwent stress dynamic CTP and either SPECT (n=25) or CMR (n=28) and found that for detecting the abnormal perfused myocardium, sensitivity and specificity were 80% (95% CI, 71–90) and 86% (95% CI, 76–91) in SPECT (cut-off MBF, 1.23), and 82% (95% CI, 76–88) and 87% (95% CI, 80–92) in CMR (cut-off MBF, 1.25) (69).

Even non-contrast CCT for calcium scoring purpose can accurately detect chronic MI showing hypoattenuating myocardial regions if compared with nuclear myocardial perfusion imaging with a sensitivity of 92% and a specificity of 72% on a per-patient basis (57). The presence of a myocardial hypo-enhancement region at rest on CCT has a sensitivity and specificity of around 90% to identify patients with a MI (Figures 5–7) (89,90). Rest dual energy CT provided comprehensive CAD imaging and identified perfusion defects in 90% of cases compared to SPECT (60).

The accuracy in the detection of ischemia was investigated by several studies which compared stress-rest CCT with SPECT and CMR demonstrating a good agreement and similar sensitivity and specificity (30–32,51–

53,91–94). In particular, stress perfusion CCT may refine the diagnostic accuracy of CCT alone (52), with increased sensitivity from 83% to 91% and specificity from 71% to 91%. Nevertheless, the current studies are based on small populations and are often biased by the high prevalence of disease in the recruited patients. On the other side, CCT may detect small perfusion defects because it is a technique with better image resolution than SPECT. Iodinated contrast media are reported to determine a vasodilatory effect and to keep specific kinetics, which may cause local hyperemia and improve the ability to detect small areas of MI (95,96).

PTCA has impressively improved the outcome of patients after MI (97). However, the sequelae of MI can determine left ventricular remodeling with reduced ejection fraction, even after restored coronary flow. Left ventricular remodeling is a major determinant of prognosis (98). In this regard, the infarct size and the distribution over myocardial wall may predict left ventricular remodeling (99,100).

SPECT imaging was considered a standard modality to assess the size of myocardial damage after acute MI with an evaluation of residual cardiac segments with perfusion defects (101,102). SPECT was extensively used for this purpose, however the modality may not recognize small perfusion defect in subendocardial infarcts (103). Gadolinium DE-CMR is the current clinical standard for

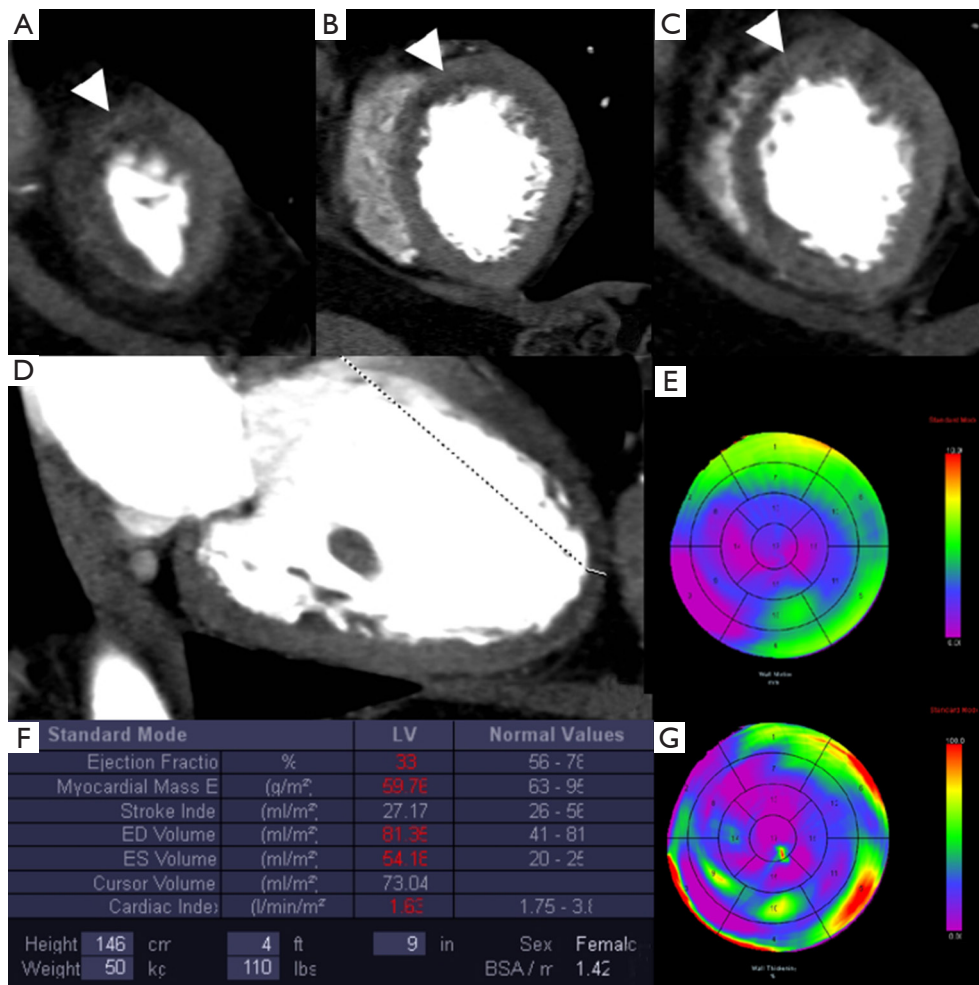


Figure 5 Patient with a previous myocardial infarction in the territory of the left anterior descending artery. Multiplanar images in short axis (A-C) show the early perfusion defects (arrowhead) on the subendocardial wall of the left ventricle in the anterior and anteroseptal segments. In the long axis view (D) the corresponding myocardial wall is thinner than normal. The functional bull's eyes display hypokinetic segments (E) and regional myocardial wall thinning (G). The left ventricular function is impaired (F).

the assessment of left ventricular infarct size (104). CMR may also provide better results in the detection of small infarcts in every clinical condition from acute to chronic settings in comparison to SPECT (105,106). DE-CMR delivers also an excellent prognostic value since it was found to be strongly correlated to the probability of recovered function after revascularization, short and long-term outcome (107,108).

Kim *et al.* demonstrated that segments with a DE of 75% in the myocardial wall don't benefit from revascularization (109). CMR may display several aspects of infarction and reperfusion damage: size, interstitial edema, hemorrhage, periinfarct penumbra, MO (110).

In recent years, CCT has enabled the detection of MI with accurate visualization of infarct size by DE techniques in animal model (38,111) and humans (Figures 8,9) (16). DE may be applied in CCT imaging for the detection of acute and chronic MI with a good accuracy (16,36,112). The dimension of DE territories and perfusion defects are predictive of long-term dysfunction after acute MI (113). Transmural contrast enhancement on CCT without additional administration of contrast media after conventional angiography is a marker of non-viable myocardium (41,114). The pattern of DE may indicate the possibility of functional recovery in patients after MI (115). Moreover, hypoattenuated areas of no-reflow within hyper-

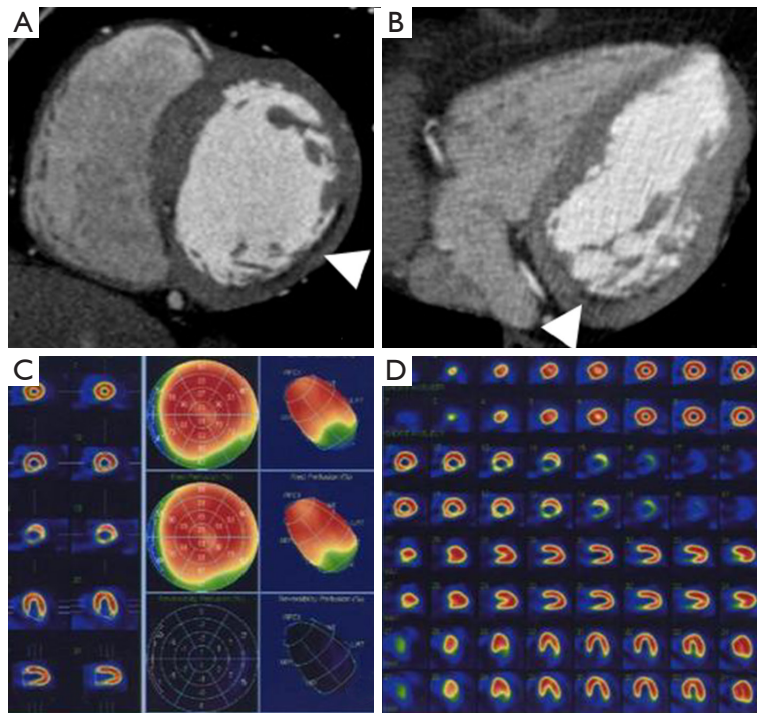


Figure 6 First-pass CCT hypoenhancement (arrowhead) in the basal inferior region (A,B) and corresponding SPECT images showing a perfusion defect (C,D).

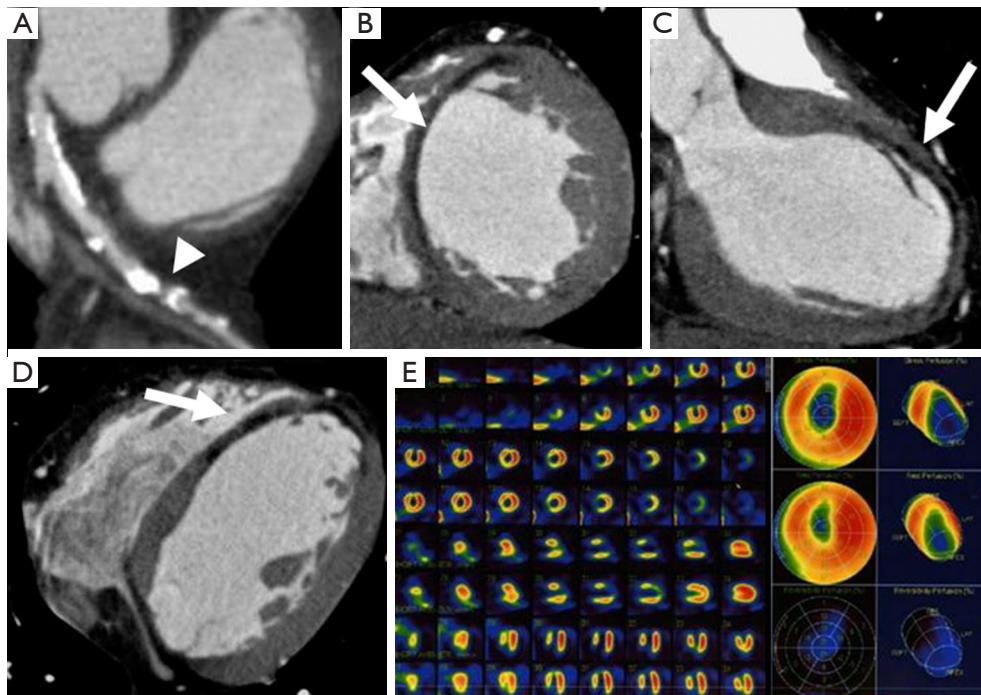


Figure 7 Significant stenosis (arrowhead) of the left anterior descending artery (A) and corresponding first-pass hypoenhancement (arrow) in the anteroseptal segments (B-D), and SPECT images showing a perfusion defect more evident at stress (E).

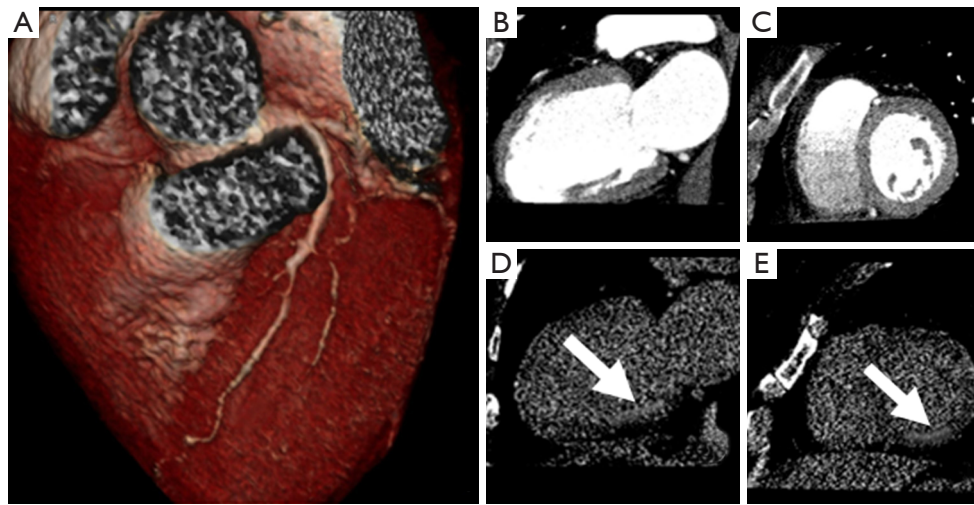


Figure 8 Patient with a previous myocardial infarction in the territories supplied by the circumflex artery (A). First-pass CCT cannot display any early perfusion defects (B; C), while DE-CCT depicts a subendocardial area of late enhancement (arrow) in the basal inferior region (D, E).

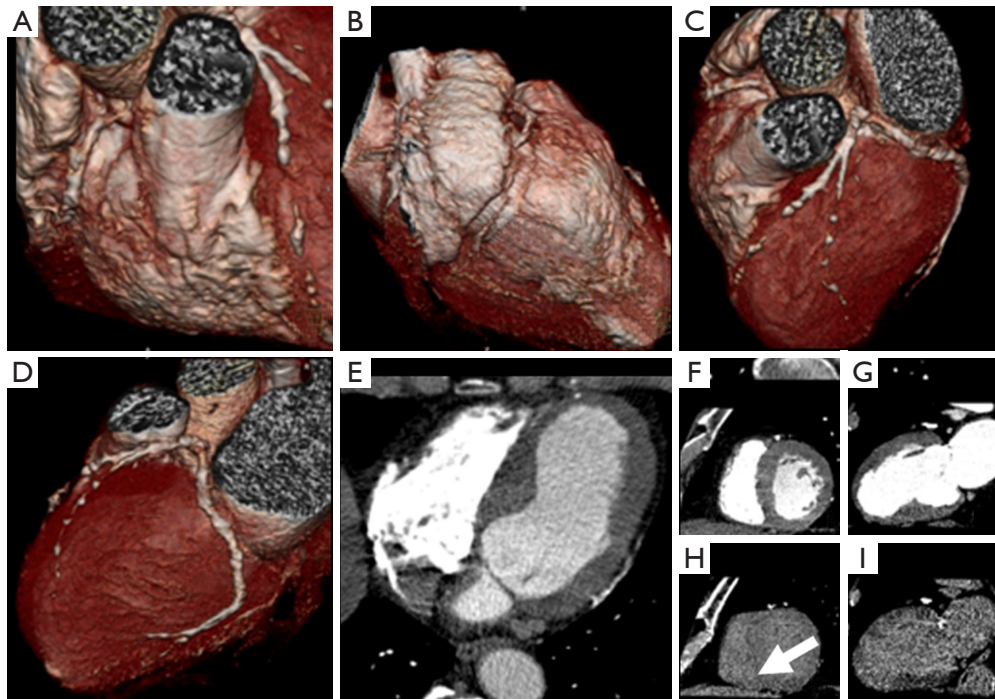


Figure 9 Patient with a previous myocardial infarction in the territory of the left anterior descending artery that is occluded (A-D). The left ventricle is remodeled and aneurysmatic at the apex (E-G). DE-CCT depicts a thin area of subendocardial late enhancement (arrow) in the septum (H,I).

Table 3 Pros and cons of imaging method in myocardial infarction characterization.

Technique	Coronary arteries	Function	Infarcted area	Perfusion stress	Viability	Biological cost	Outcome studies
Echo	–	++	+	++	++	–	++
CCT	+++	+	+	++	++	++	+
CMR	+	+++	+++	+++	+++	–	+++
SPECT	–	++	++	++	++	++	+++

CCT, cardiac CT; CMR, cardiac MR; SPECT, single-photon emission computed tomography. –, limited/absent; +, moderate; ++, high; +++, very high.

enhanced region of DE may be representative of residual perfusion defects after PTCA (116). DE-CCT may evaluate the size of MI immediately after primary PCI without additional contrast media and predict clinical outcome in patients with MI (117). Nevertheless, CCT studies were carried out in small cohorts of patients, although they already have shown promising results.

CCT and CMR employ different contrast media, however they may detect and characterize MI with overlapping imaging findings (16). Gadolinium derived contrast media and iodinated contrast media have similar kinetics and distribution in the normal myocardium and in the infarcted territories. Nevertheless, MI characterization by means of CCT may present some issues related to poor contrast resolution when compared to CMR.

CMR remains the non-invasive reference method for evaluating the extent of post-ischemic and non-viable myocardium. Patients with contraindication to CMR (non-compatible pacemakers, defibrillators, or other metal devices) may more easily undergo dedicated CCT studies. CCT is a fast and 24/7 service usually available in emergency context (118), or in clinical daily routine, including the evaluation of coronary arteries and left ventricular function (119).

Outlook

In the last decade, CCT gained rapid advance and unquestionable success in the non-invasive assessment of coronary arteries. CCT was recently applied to the detection of MI, perfusion, and viability. First, several studies were performed in the animal settings with excellent results. Then, human studies were performed on small patients population to assess the reproducibility of the approach. The first promising results are expected to be confirmed on more numerous patients cohort or on

a multicenter basis for routine clinical application. The following step could be to place these results in a prognostic context in comparison with CMR which, in current-day practice, is considered the most accurate tool for infarct characterization in clinical setting. The health technology assessment should be also completed with cost-effectiveness and economic sustainability study (120,121). A one stop-shop examination with a profile of first-line imaging could be a solution to cut economic and biological costs in the work-up of patients with suspected or known CAD. Beyond the need to obtain more robust data, another requirement for future studies is the correct selection of patient population. A comprehensive protocol of morphological and functional CCT could be used in patients at intermediate-high probability of CAD in order to reduce procedural time and biological costs. Such protocol needs some additional time, which is exceeding the simple evaluation of coronary arteries of CCT angiographic studies (*Table 1*). The additional time should take into account both the patient scan (at least 15 minutes to perform a comprehensive protocol) and the reading time of an experienced radiologist (at least 20 minutes to elaborate a complete report) (122). The reporting time could be in part decreased in the future by the use of automated or semi-automated computer applications. If compared to SPECT and CMR, CCT has several advantages: short examination time, wide availability and patient's acceptance (*Table 3*). In particular, Dual-energy computed tomography might be promising for the integrative analysis of the coronary artery morphology and the myocardial blood supply; DECT resulted in good agreement with invasive coronary angiography and SPECT. Ruzsics *et al.* demonstrated that DECT had 92% sensitivity and 93% specificity, with 93% accuracy for detecting any type of myocardial perfusion defect seen on SPECT (30).

Another relevant issue is that a comprehensive protocol of morphological and functional CCT should be performed

with an additional radiation dose administration. The dose administered with CCT should be at least comparable with that of SPECT in perfusion imaging (34) and viability assessment (123), lower than 10 mSv (9). On the other side, CMR with stress and DE imaging may achieve excellent results in absence of potentially dangerous ionizing radiation, despite coronary arteries still cannot be properly assessed (124).

Another potential matter of interest is the timing of examination according to the phase of MI, because the pattern may differ between acute, subacute, chronic or healing phase. In addition, some patients with MI may also present with non-obstructive CAD (125-128) and therefore a comprehensive morphological and functional assessment of the heart should be pursued. Given that, CCT may be employed also in emergency setting, the tool could be an attractive diagnostic option also in this context (129).

Conclusions

CCT achieved promising results in the detection and characterization of MI, keeping into account that morphological, functional, and perfusional information can be not-invasively obtained. CCT may study the entire atherosclerotic process, including coronary plaque and stenosis, myocardial perfusion and viability. On the other side, some efforts should be spent in order to confirm the results in larger populations and to reduce the use of ionizing radiation as low as possible.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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