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**EACVI DOCUMENT**

# Clinical applications of cardiac computed tomography: a consensus paper of the European Association of Cardiovascular Imaging—part I

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Cardiac computed tomography (CT) was introduced in the late 1990's. Since then, an increasing body of evidence on its clinical applications has rapidly emerged. From an initial emphasis on its technical efficiency and diagnostic accuracy, research around cardiac CT has now evolved towards outcomes-based studies that provide information on prognosis, safety, and cost. Thanks to the strong and compelling data generated by large, randomized control trials, the scientific societies have endorsed cardiac CT as pivotal diagnostic test for the management of appropriately selected patients with acute and chronic coronary syndrome. This consensus document endorsed by the European Association of Cardiovascular Imaging is divided into two parts and aims to provide a summary of the current evidence and to give updated indications on the appropriate use of cardiac CT in different clinical scenarios. This first part focuses on the most established applications of cardiac CT from primary prevention in asymptomatic patients, to the evaluation of patients with chronic coronary syndrome, acute chest pain, and previous coronary revascularization.

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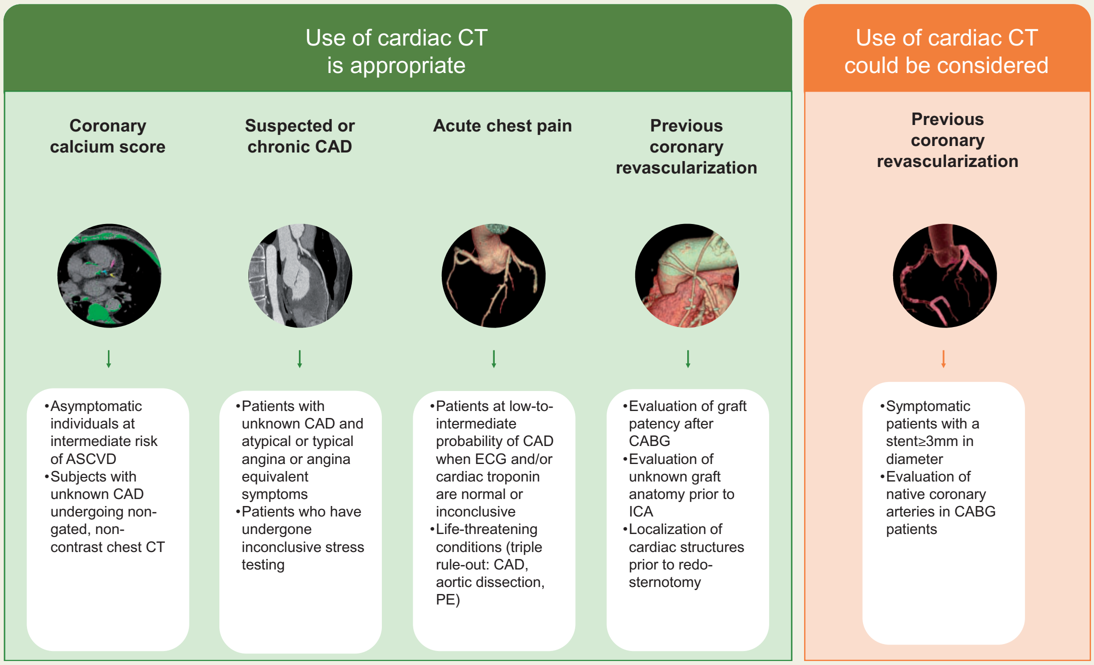
## Graphical Abstract




Clinical applications of cardiac CT. For more details, please see *Table 1*, which summarizes the main applications of cardiac CT. ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery by-pass graft; CAD, coronary artery disease; CT, computed tomography; ECG, electrocardiogram; ICA, invasive coronary angiography; PE, pulmonary embolism.

**Keywords** coronary computed tomography angiography • coronary calcium • acute chest pain • chronic coronary syndrome • coronary stent • coronary artery bypass graft

# Introduction

Since its introduction in the late 1990's, the technology of cardiac computed tomography (CT) has evolved rapidly, and in parallel, an increasing body of evidence regarding clinical applications has been generated. This European Association Cardiovascular Imaging (EACVI) consensus document aims to provide a summary of the current evidence and to give indications on the appropriate use of cardiac CT in different clinical scenarios. The first part of the document focuses on the most established applications of cardiac CT in the field of coronary artery disease (CAD), from primary prevention in asymptomatic patients, to the evaluation of patients with chronic coronary syndrome, acute chest pain, and previous coronary revascularization. The second part reviews the role of cardiac CT in the evaluation of atherosclerotic plaque, cardiomyopathies, structural heart disease, and congenital heart disease. In addition, it summarizes emerging CT technologies and imaging biomarkers, such as computational fluid dynamics, perfusion imaging, pericoronary adipose tissue attenuation, as well as radiomics and artificial intelligence.

## Methodology

The topic of this document was approved by the EACVI Scientific Document Committee. The writing committee comprises acknowledged experts in the field of cardiac CT. The writing committee discussed and approved the table of contents. This includes either well-established applications of cardiac CT or novel tools that have shown promising results for a potential implementation in the clinical arena. The evidence-based literature was searched in the electronic databases Medline/PubMed, Embase, and the Cochrane Library and afterwards reviewed by G.P. and A.R., with the restriction to English language. Both retrospective and prospective studies were considered eligible. Case reports, letters to the editor, and comments were excluded. The final decision on inclusion was reached by consensus between the two screening authors. Based on the collected data, the screening authors wrote the first draft of the manuscript which was then circulated among all co-authors. Thereafter, each section was carefully reviewed by the entire writing committee until a consensus was reached for each potential application of cardiac CT. Thus, this consensus document reports the current and emerging clinical applications of cardiac CT agreed by the panel of experts and grounded on the best available evidence at present, as summarized in *Table 1* and in the *Graphical Abstract*.

# Brief overview of CT technology

The first attempts to visualize the heart by CT took place in the early 1980s, but artefacts due to cardiac motion and long scan times prevented the acquisition of diagnostic-quality images.[1,2] In the following years, rapid advances in CT hardware and software algorithms, such as slip-ring technology and the introduction of multidetector arrays and more powerful X-ray tubes, provided the necessary technical

**Table 1 EACVI key points on the clinical applications of cardiac CT**

Cardiac CT technology

- Sixty-four slice CT represents the minimum requirement for cardiac imaging in routine clinical practice. State-of-the-art CT scanners allow for optimal image quality whilst limiting radiation exposure.
- Low-dose scanning protocols should be adopted whenever possible.

Coronary calcium score

- For calcium imaging, image acquisition, and reconstruction settings are standardized. Deviations from the standard protocols (i.e. using lower tube potential, iterative reconstructions) are discouraged.
- It is appropriate to measure calcium score in asymptomatic individuals at intermediate likelihood of ASCVD. In this group of subjects, calcium score could improve risk classification and could help guide statin primary preventive therapy.
- Repeat calcium imaging could be appropriate in asymptomatic subjects without detected coronary calcium and not taking statins, at a time interval of 5 years.
- It is appropriate to semi-quantitatively report the presence of coronary calcium in all subjects without known coronary artery disease undergoing non-gated, non-contrast chest CT scan.

CCTA in symptomatic patients with suspected or chronic coronary syndrome

- CCTA is appropriate as first-line diagnostic test for the evaluation of patients with no previously known CAD and atypical or typical angina or angina equivalent symptoms.
- CCTA is appropriate in patients who have undergone inconclusive stress testing.
- Based on the CT technology available, CCTA could not be recommended in situations which may hamper image quality like extensive coronary calcifications, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands.

CCTA in symptomatic patients with acute chest pain

- CCTA is appropriate as a first-line diagnostic test for the evaluation of patients with acute chest pain at low-to-intermediate likelihood of CAD when ECG and/or cardiac troponin are normal or inconclusive.
- CCTA is appropriate before deciding on an invasive approach in patients with no recurrence of chest pain, normal ECG findings, and normal level of cardiac troponin, but still with a suspected ACS.
- CCTA is appropriate to detect other life-threatening conditions in patients with acute chest pain when tailored acquisition and injection protocols for 'triple rule-out' (i.e. CAD, pulmonary embolism, and aortic dissection) are used.
- CCTA could be indicated to identify the presence of stable CAD after ACS has been ruled-out.

CCTA in the evaluation of patients with previous coronary revascularization

- CCTA should not be routinely used in patients with previous coronary revascularization by percutaneous coronary intervention.
- CCTA could be useful for the evaluation of symptomatic patients with a stent ≥3 mm in diameter. Optimized acquisition protocols aimed to reduce blooming effect and image noise as well as to optimize spatial resolution should be adopted.
- CCTA is appropriate for the evaluation of graft patency after CABG.
- CCTA could be useful for the evaluation of native coronary arteries in patients with previous CABG, although this is frequently challenging.
- CCTA is appropriate for the evaluation of unknown graft anatomy prior to ICA.
- CCTA is appropriate for the localization of cardiac structures (e.g. left internal mammary artery) in patients prior to redo-sternotomy.

ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery by-pass graft; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CT, computed tomography; ECG, electrocardiogram; ICA, invasive coronary angiography.

advances to reliably image the heart.[3–5] Currently, CT scanning systems with 64 slices are considered the minimum requirement to perform cardiac imaging.[6] New generation CT systems include dual-source CT and wide detector CT systems.[7,8]

Coronary CT angiography (CCTA) is acquired with electrocardiogram (ECG) synchronization, either retrospective gating or prospective triggering, to avoid motion-related factors, after intravenous injection of iodinated contrast agent. Since this document is not primarily intended as a comprehensive review of CT technology, essential definitions of technical terms related to cardiac CT are provided in Supplementary data online, *Table S1*. In addition, the reader is referred to the manuscript 'Society of Cardiovascular CT (SCCT) guidelines for the performance and acquisition of coronary computed tomographic angiography' for a more comprehensive overview of CCTA-related technical factors, including hardware, software, and acquisition protocols.[6]

The radiation dose from cardiac CT is an ongoing concern due to its dose-dependent association with cancer induction.[9] However, the PROTECTION (PROspective multicenter registry on radiaTion dose Estimates on cardiac CT AnglOgraphy iN daily practice) VI survey showed that exposure from cardiac CT decreased by 78% in the last decade, whilst image quality was preserved.[10] In this report, the authors showed that reduced tube voltage and ECG-triggered axial acquisition were the main dose saving strategies applied. For a comprehensive review on available strategies for radiation dose reduction in cardiac CT the Reader is referred to the specific report released by EACVI, Cardiovascular Committee of European Association of Nuclear Medicine, and the European Society of Cardiovascular Radiology in 2018[11] and to the 2011 SCCT guidelines on radiation dose.[12]

## Key points

- Sixty-four slice CT represents the minimum requirement for cardiac imaging in routine clinical practice. State-of-the-art CT scanners allow for optimal image quality whilst limiting radiation exposure.
- Low-dose scanning protocols should be adopted whenever possible.

## Coronary calcium score

For coronary calcium imaging, acquisition, and reconstruction settings are standardized. Data are acquired using prospective ECG triggering in late diastole (70–80% R-R interval) and without contrast material administration using 120 kV tube voltage. Image analysis is performed using the Agatston method.[13] The Agatston score can be reported either as an absolute value or as a percentile in comparison to age-, sex-, and ethnicity-matched individuals.[14] Considering that tube potential affects calcium attenuation and Hounsfiled Unit (HU) values, the standard 120 kV tube voltage setting should not be changed during the acquisition of a coronary calcium scan.[15] Similar considerations apply when iterative reconstructions are used instead of filtered back projections.[16] Although the Agatston score has shown great clinical utility, an improved score that accounts for calcium density and regional distribution may improve reproducibility and risk stratification.[17] A representative example of calcium score acquisition, analysis, and interpretation is summarized in *Figure 1*.

The rationale of measuring coronary calcium relies on the fact that its presence in the coronary arteries is a specific marker of subclinical atherosclerosis. In particular, calcium score provides an accurate measurement of the coronary calcific plaque burden, as confirmed by previous histopathological studies.[18,19] Whilst calcific plaques are generally stable and unlikely to rupture, the calcium score also provides a surrogate of the total coronary plaque volume and the burden of less stable plaque types, accounting for its relationship with future myocardial infarction (MI).

## Coronary calcium score and primary prevention in asymptomatic patients

### Prognostic utility and improved risk assessment of coronary calcium score over traditional risk factors

Major adverse cardiovascular events (MACE) rate increases proportionally with increasing severity of coronary calcifications stratified by Agatston calcium score categories 0, 1–99, 100–399, and ≥400.[20,21] While asymptomatic individuals with 0 coronary calcium present a persistent very low risk across several studies,[22] subjects with coronary calcium ≥ 1000 have a mortality rate comparable to high-risk secondary prevention patients.[23] Notably, even minimal calcium score has been associated with an increased rate of cardiovascular events and all-cause mortality when compared to 0 calcium score.[24,25]

### Coronary calcium score and current clinical use

Calcium score improves risk stratification over and above conventional clinical scores in the cardiovascular risk assessment of asymptomatic patients.[21,26,27] Furthermore, results from large observational studies suggest that calcium score might help identify asymptomatic individuals

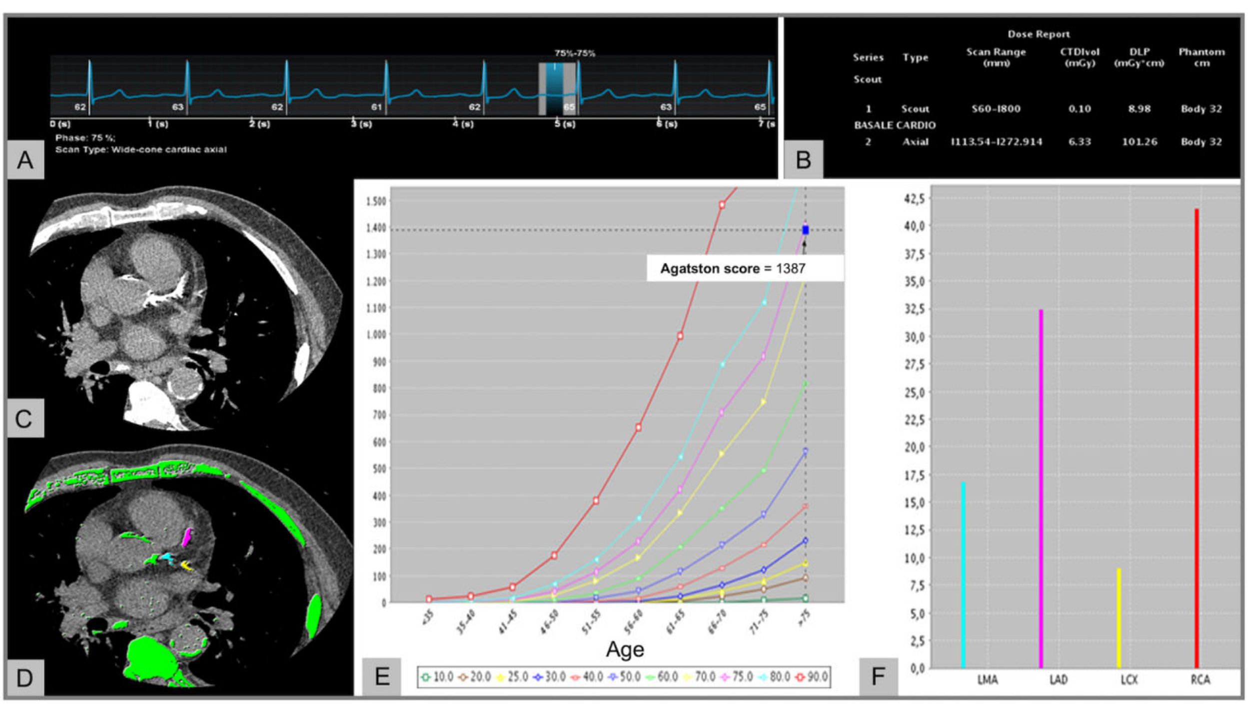



**Figure 1** Coronary artery calcium assessment. (*A*) A non-enhanced, ECG-triggered axial CT scan was acquired in a 78-year-old man to measure the calcific plaque burden. (*B*) Tube potential was set to 120 kV resulting into a total DLP of 101.26 mGy*cm. (*C* and *D*) Image analysis was performed using a dedicated software, which automatically identified structures with a density ≥130 HU and highlighted them in green. Subsequently, coronary arteries were manually segmented (LM: turquoise, LAD: pink, LCX: yellow). (*E* and *F*) Total Agatston score (*E*) and per-vessel Agatston score (*F*) were calculated and correlated to age-matched cohorts to stratify patient's risk. ECG, electrocardiogram; CT, computed tomography; DLP, dose length product; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main.

who will and will not benefit from statin[28] and aspirin[29,30] primary preventive therapy. With regards to statin therapy, current guidelines consider it reasonable to measure coronary calcium in patients at intermediate likelihood of atherosclerotic cardiovascular disease (ASCVD),[31–35] as detailed in *Table 2*. Nevertheless, management based on calcium score is not recommended by any of the guidelines due to the lack of evidence from randomized clinical trials. Only recently, the population-based ROBINSCA (Risk Or Benefit IN Screening for Cardiovascular disease) trial showed that the use of calcium score classified fewer asymptomatic men and women at increased risk as compared to the SCORE (Systematic Coronary Risk Evaluation) model, thus reducing the need for preventive treatment.[36] The follow-up data of this trial will help clarify the clinical role of calcium score.

### Coronary calcium progression and serial scanning

Although atherosclerosis is a dynamic process and coronary calcium can either remain stable or increase over time, repeat calcium imaging is rarely performed. Nevertheless, a repeat scan seems to be of additional value in patients with 0 coronary calcium who deferred statin therapy.[37] Based on data showing a mean time to conversion to positive coronary calcium of 4.1 ± 0.9 years, the suggested scan interval is 5 years.[38] Conversely, there are no convincing data supporting repeat calcium imaging in individuals with 0 coronary calcium following statin therapy. Indeed, statins appear to increase not decrease calcium scores due to their stabilization effect on atherosclerotic plaque type.[39]

## Coronary calcium in non-gated chest CT scans

Recently, Leigh *et al.*[40] demonstrated that calcium score derived from non-gated chest CT was significantly correlated with cardiovascular outcomes in both smokers and eligible patients for lung cancer screening. In line with these findings, recent guidelines from the SCCT/Society of Thoracic Radiology recommended provision of at least semi-quantitative calcium scoring for all subjects without known CAD undergoing non-gated, non-contrast chest CTs.[33]

## Coronary calcium score in symptomatic patients

The '2019 European Society of Cardiology (ESC) guidelines for the diagnosis and management of chronic coronary syndrome' suggested the potential role of coronary calcium to improve the estimation of clinical likelihood of obstructive CAD (i.e. coronary stenosis >50%), in addition to sex, age, and symptoms.[41] As such, data from a large cohort of symptomatic patients showed that incorporating coronary calcium score into pre-test assessment of the likelihood of CAD allowed the reclassification of more than one-half of patients into a lower risk category for obstructive CAD, with no need for further testing.[42] Nevertheless, current evidence does not support its use as a diagnostic tool to rule-out obstructive CAD since it does not provide information on stenosis severity.[41]

**Table 2 Role of coronary calcium in primary prevention guidelines**

| Guideline | Clinical score for risk assessment | Target group | Evaluation of CAC | Class of recommendation/ level of evidence |
|---|---|---|---|---|
| 2017 SCCT Expert Consensus: Clinical Indications for Coronary Artery Calcium Scoring in Asymptomatic Patients[35] | PCE (10-year risk of ASCVD) | Asymptomatic individuals (40–75 years old) without clinical ASCVD in the 5–20% 10-year ASCVD risk group or selected adults in the <5% ASCVD group (i.e. those with a family history of premature coronary artery disease) | Is reasonable | Not provided |
| 2018 ACC/AHA Guideline Management of blood cholesterol[32] | PCE (10-year risk of ASCVD) | Asymptomatic individuals (40–75 years old) at intermediate risk (≥7.5% to <20% 10-year ASCVD risk) without diabetes and with LDL-C levels ≥70–189 mg $dL^{-1}$ or selected adults at borderline risk (5% to <7.5% 10-year ASCVD risk) | Is reasonable | Class IIa LoE: B |
| 2019 ACC/AHA Guideline: Primary Prevention of Cardiovascular Disease[31] | PCE (10-year risk of ASCVD) | Adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk) or selected adults at borderline risk (5% to <7.5% 10-year ASCVD risk), if risk-based decisions for preventive interventions remain uncertain | Is reasonable | Class IIa LoE: B |
| 2021 ESC Guidelines: Cardiovascular Disease Prevention in Clinical Practice[34] | SCORE2 and SCORE-OP (10-year risk of CVD) | Individuals with calculated risks around treatment decision thresholds | May be considered | Class IIb LoE: B |

ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; ESC, European Society of Cardiology; LDL, low-density lipoprotein; LoE, level of evidence; PCE, pool cohort risk equations; SCCT, Society of Cardiovascular Computed Tomography; SCORE2, systematic coronary risk estimation 2; SCORE2-OP, systematic coronary risk estimation 2—older person.

## Key points

- For calcium imaging, image acquisition, and reconstruction settings are standardized. Deviations from the standard protocols (i.e. using lower tube potential, iterative reconstructions) are discouraged.
- It is appropriate to measure calcium score in asymptomatic individuals at intermediate likelihood of ASCVD. In this group of subjects, calcium score could improve risk classification and could help guide statin primary preventive therapy.
- Repeat calcium imaging could be appropriate in asymptomatic subjects without detected coronary calcium and not taking statins, at a time interval of 5 years.
- It is appropriate to semi-quantitatively report the presence of coronary calcium in all subjects without known CAD undergoing non-gated, non-contrast chest CT scan.

# CCTA in symptomatic patients with suspected or chronic coronary syndrome

## Diagnostic accuracy of CCTA for detection of obstructive CAD

The rationale for the use of CCTA in patients with suspected or chronic CAD is based on its ability to non-invasively visualize coronary stenosis as shown in *Figure 2*. Three landmark multicentre trials on the diagnostic accuracy of CCTA as compared to invasive coronary angiography (ICA) for the detection of obstructive coronary stenosis consistently reported high sensitivity values ranging from 85% to 95%[43–45] and a negative predictive value approaching 100%.[43–45] Although CCTA showed a tendency to overestimate stenosis severity in highly calcific plaques due to motion and blooming artifact,[46] it remains more accurate than functional testing in the ruling-out of anatomically defined obstructive coronary stenosis (i.e. lumen narrowing >50% or >70%) on ICA.[47,48]

## Prognostic accuracy of CCTA

Multiple studies have demonstrated the excellent outcomes associated with a normal CCTA, with annualized event rates ranging between 0.02% and 0.3% for short-,[49] intermediate-,[50–52] and long-term outcomes.[53] In addition, the CONFIRM (Coronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry highlighted that both the presence and severity of CAD were strongly correlated with worse prognosis.[54] Of note, the detection of non-obstructive CAD on CCTA, which is generally missed by conventional stress testing, has been associated with an adjusted hazard ratio for MACE between 1.6 and 7.1 compared to individuals with no identifiable plaque,[51,55–57] with an average annualized event rate of 1.6%.[58] In both, the SCOT-HEART (Scottish Computed Tomography of the Heart Trial) and PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trials, as many MIs were observed in patients with non-obstructive as obstructive CAD.[59–61] According to the evidence that cardiovascular risk is most closely associated with the coronary atherosclerotic plaque burden as detected by CCTA rather than the presence of an obstructive stenosis or indeed cardiovascular risk factors,[59–61] the systematic reporting of both obstructive and non-obstructive plaque is therefore suggested as indicated by the Coronary Artery Disease-Reporting and Data System (CAD-RADS) document.[62]

## Randomized clinical trials of CCTA

Up to now, there have been five major randomized control trials (RCTs) investigating the outcomes after CCTA in patients with stable chest pain,[63–69] as detailed in *Table 3*. In the following sections, we report the main findings of these RCTs with regards to (i) major clinical endpoints, (ii) clinical management, and (iii) cost-effectiveness.

### Major clinical endpoints

The PROMISE and SCOT-HEART trials were two large comparative effectiveness trials that randomized large samples of patients with suspected stable CAD to CCTA.[63,64] The PROMISE trial compared CCTA to functional imaging and used a composite primary endpoint including all-cause mortality, MI, hospitalization for unstable angina, or major complications from cardiovascular procedure.[63] Although no differences were found between the study arms regarding the primary outcome, rate of MI, and death at 12 months were lower in patients who underwent CCTA. Furthermore, the rate of patients who did not have obstructive CAD at subsequent ICA was 28% for CCTA and 52% for functional testing ($P = 0.02$).[63] By comparison, the 5-year follow-up of the SCOT-HEART demonstrated that an approach guided by CCTA vs. standard care decreased the occurrence of MI and CAD mortality by 41%.[65] These findings were confirmed by a large meta-analysis including 7403 patients undergoing CCTA and 7414 patients undergoing usual care with various functional testing strategies.[70] The use of CCTA was associated with a significant lower rate of MI (risk ratio: 0.69, 95% confidence interval, 0.49–0.98; $P = 0.038$) but no differences were observed concerning mortality.[70] The mechanism of this clinical benefit has been attributed to the higher and better-targeted use of downstream preventive therapy and better control of cardiovascular risk factors amongst patients randomized to CCTA.[71,72]

### Clinical management

Several studies investigated the impact of CCTA on ICA practice.[73–76] The CONSERVE (Coronary Computed Tomographic Angiography for Selective Cardiac Catheterization) trial showed that 77% of patients initially referred to ICA avoided invasive evaluation when undergoing CCTA, with no difference in clinical outcomes (similar MACE event rates of 4.6%) compared to patients directly referred to ICA.[73]

### Cost effectiveness

The PROMISE analysis found that near-term ($\Delta = 254$\$) and long-term cost differences ($\Delta = 627$\$) for both anatomic and functional testing were not significant.[77] By comparison, the use of CCTA in the SCOT-HEART trial was associated with a modest increase in costs ($\Delta = 462$\$) at 6 months, which derived from the upfront procedural costs and not from additional inpatient and outpatient services.[72] Longer term economic analysis has not yet been performed in this

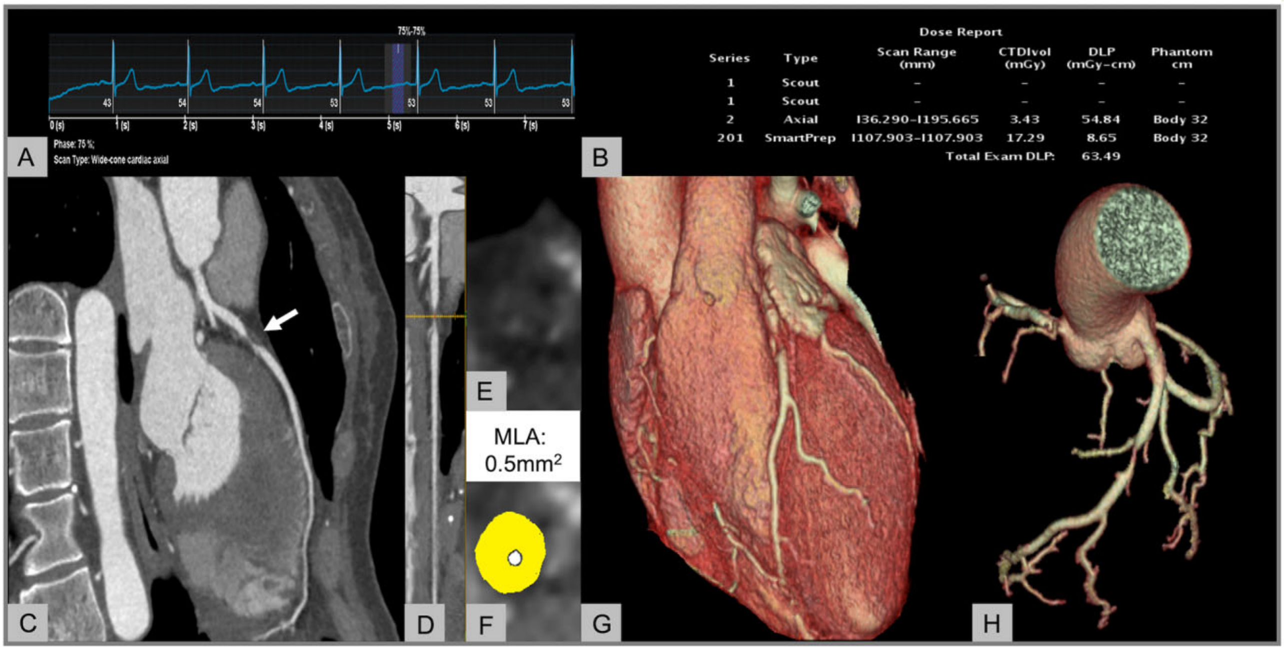



**Figure 2** CCTA in symptomatic patients with suspected CAD. (*A* and *B*) A 56-year-old man underwent CCTA due to atypical chest pain after non-diagnostic exercise test. Single-phase, prospectively ECG-triggered axial CCTA was performed using a wide-detector CT scanner which allowed the coverage of the whole heart in a single beat (*A*), with a total DLP of 63.49 mGy*cm (*B*). (*C–H*) A non-calcific plaque (arrow) was detected in the proximal LAD as shown on curved MPR (*C*), straight MPR (D), cross-sectional views of the vessel (*E* and *F*) and volume rendering reconstruction (*G* and *H*). The yellow overlay in (*F*) indicates the non-calcific plaque and the associated severe stenosis (70–99%) resulting into a MLA of 0.5 mm$^2$. CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CT, computed tomography; DLP, dose length product; ECG, electrocardiogram; LAD, left anterior descending artery; MLA, minimal lumen area; MPR, multiplanar reconstruction.

trial. In the CRESCENT (Cardiac CT Versus Exercise Testing in Suspected Coronary Artery Disease) trial, a CCTA-guided approach yielded cost savings of 16% compared to exercise ECG at 1-year follow-up due to lower rates of follow-up non-invasive diagnostic testing (53% in the exercise ECG arm vs. 25% in the selective CCTA arm; $P < 0.0001$).[67]

## Role of CCTA in the current guidelines

CCTA has been incorporated as a first line, non-invasive diagnostic test for the management of patients with stable chest pain in both the National Institute for Healthcare Excellence (NICE)[78] and ESC guidelines,[41] with difference concerning the use of pre-test probability (PTP).

The 2016 NICE guidelines in the UK recommend CCTA as a first-line diagnostic test in patients with atypical and typical angina (or ECG findings of CAD in the absence of symptoms), regardless of PTP. No further imaging is recommended in patients with non-cardiac chest pain. Functional testing is reserved for patients with known CAD or when CCTA results are inconclusive.[78]

The '2019 ESC guidelines for the diagnosis and management of chronic coronary syndrome' recommend CCTA (Class 1) as an initial test to evaluate chest pain in patients in the lower range of PTP of CAD.[41] CCTA is generally not recommended in situations which may hamper the diagnostic quality of the scan, such as irregular heart rate, extensive coronary calcifications, significant obesity, and inability to cooperate with breath-hold commands, since these factors have been associated with decreased diagnostic accuracy of CCTA.[43,79–82]

### Key points

- CCTA is appropriate as a first-line diagnostic test for the evaluation of patients with no previously known CAD and atypical or typical angina or angina equivalent symptoms.
- CCTA is appropriate for patients who have undergone inconclusive stress testing.
- Based on the CT technology available, CCTA could not be recommended in situations which may hamper image quality like extensive coronary calcifications, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands.

# CCTA in symptomatic patients with acute chest pain

## Diagnostic accuracy of CCTA in patients presenting with acute chest pain

The rationale of using CCTA in the emergency department (ED) is the possibility of accurately ruling-out acute coronary syndrome

**Table 3 Randomized controlled trials of CCTA in patients with stable chest pain**

| Trial | PROMISE[63] | SCOT-HEART[65] | CRESCENT I[67] | CAPP[68] | Min et al.[69] |
|---|---|---|---|---|---|
| Sample size | 10 003 | 4146 | 350 | 500 | 180 |
| Comparator | Functional testing | Standard care | Functional testing | EST | Myocardial perfusion imaging |
| Primary endpoint | Death, nonfatal MI, hospitalization for unstable angina, and major procedural complications | Death from coronary heart disease or nonfatal MI | Absence of chest pain complaints after 1 year | Difference in the change in scores within the Seattle Angina Questionnaires from baseline to 3 months | Angina-specific health status |
| Duration of follow-up | 2.1 years | 4.8 years | 1.0 years | 1.0 years | 55 days |
| Main findings | No difference in clinical outcome | Reduced rate of fatal and non-fatal MI in the CCTA arm | Fewer patients randomized to cardiac CT reported anginal complaints | Less symptoms at 3- and 12-month follow-up in the CCTA arm | No difference in symptoms |
| Hazard ratio (95% confidence interval) of MACE | 1.04 (0.83–1.29) | 0.59 (0.41–0.84) | 0.32 (0.13–0.81) | N/A | N/A |
| Rate of ICA, CCTA vs. comparator | 12% vs. 8% | 23% vs. 24% | 12% vs. 11% | 27% vs. 21% | 13% vs. 8% |
| Rate of coronary revascularization, CCTA vs. comparator | 6% vs. 3% | 13% vs. 12% | 9% vs. 7% | 15% vs. 7% | 8% vs. 1% |

CAPP, Cardiac CT for the Assessment of Pain and Plaque; CCTA, coronary computed tomography angiography; CRESCENT, Cardiac CT Versus Exercise Testing in Suspected Coronary Artery Disease; CT, computed tomography; EST, exercise stress electrocardiography test; ICA, invasive coronary angiography; MACE, major adverse cardiovascular events; MI, myocardial infarction; N/A, not available; PROMISE, Prospective Multicenter Imaging Study for Evaluation of Chest Pain; SCOT-HEART, Scottish Computed Tomography of the Heart Trial.

(ACS), with early and safe discharge of patients without further diagnostic testing or hospital admission. In the past years, several observational studies have demonstrated the feasibility of CCTA in patients presenting to ED with acute chest pain and low-to-intermediate PTP[83–88] as shown in *Figure 3*. In this setting, CCTA showed high negative predictive value but limited positive predictive value for the subsequent diagnosis of ACS and MACE. Recent results support the use of CCTA as gatekeeper to ICA and for risk stratification in patients with an established diagnosis of non-ST segment elevation MI, although randomized controlled trial data is awaited.[89]

## Randomized clinical trials of CCTA

The main RCTs investigating CCTA in patients with acute chest pain and low to intermediate PTP[90–98] are listed in *Table 4*. Overall, accuracy and safety for excluding or diagnosing ACS were comparable between CCTA and myocardial stress perfusion imaging.[91,92,95,97,98] Nevertheless, implementing CCTA in the diagnostic work-up of patients with chest pain allowed for a reduction in time-to-diagnosis, length of hospital stay,[91–94,96,97] and hospital costs[90–93] as well as facilitating discharge from ED.[92,94,96] Importantly, all studies highlighted that the presence of normal coronary arteries on CCTA was associated with a good prognosis and low event rate of subsequent cardiac events at short-term follow-up. However, a large meta-analysis, which included 6285 patients admitted with acute chest pain, found no difference in all-cause mortality, MI, or MACE between CCTA and standard of care.[99]

The majority of the above-mentioned RCTs were performed prior to the introduction of high-sensitivity troponins which are increasingly being used to help rule-in or rule-out MI in the ED. An exception was the BEACON (Better Evaluation of Acute Chest Pain with Coronary Computed Tomography Angiography) study, which showed no reduction of in-length of stay or hospital admission in the CCTA arm.[90] Similar results were confirmed by ROMICAT (Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography) II[100] and RAPID-CTCA (Rapid Assessment of Potential Ischaemic Heart Disease with CTCA)[101] trials. Nevertheless, CCTA remains of value when troponin and ECG evaluation are inconclusive, in excluding other life-threatening conditions in patients presenting with acute chest pain, such as pulmonary embolism or aortic dissection,[102] and in detecting subclinical CAD once ACS is ruled out in order to adjust medical therapy and/or lifestyle factors.[102]

## Role of CCTA in the current guidelines

This evidence is reflected in the guidelines from scientific societies, which designated CCTA as appropriate for the evaluation of acute chest pain patients at low-to-intermediate PTP.[103–106]

The '2014 American College of Cardiology/American Heart Association (AHA/ACC) guideline for the management of patients

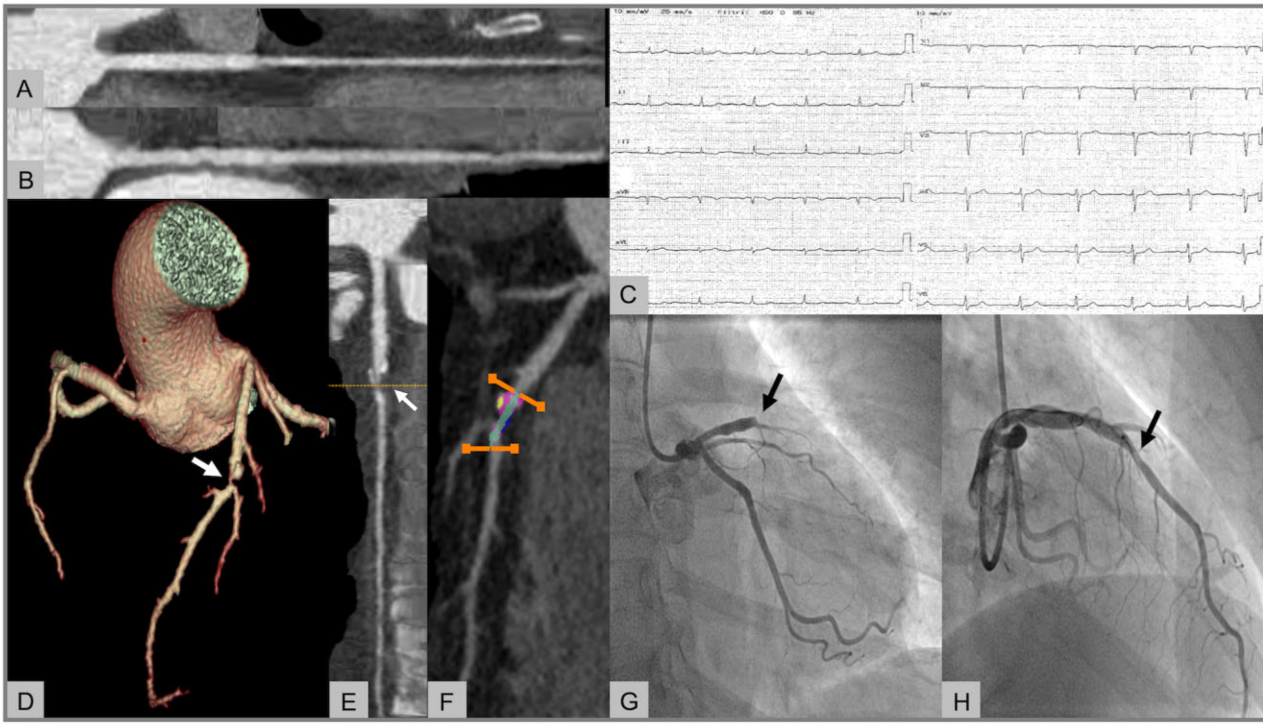



**Figure 3** CCTA in symptomatic patients with acute chest pain. (*A–F*) A 47-year-old woman with a history of hypertension was admitted to the emergency department for atypical chest pain. While physical exam and ECG were unremarkable (*C*), blood test results showed mild increase of hsTnI. No significant delta and/or ST-T changes were detected on serial assessments. CCTA showed no disease of LCX (*A*) and RCA (*B*) and demonstrated sub-occlusion of the mid LAD due to partially calcific plaque, as shown in the volume rendering reconstruction (*D, arrow*) and straight MPR (*E, arrow*). Dedicated plaque analysis software identified the fibroadipose (pink) and calcific (yellow) components of the plaque (*F*). (*G* and *H*) Invasive coronary angiography confirmed the sub-occlusion of mid LAD (*G, arrow*), which was treated with PCI+DES (*H, arrow*). CCTA, coronary computed tomography angiography; DES, drug eluting stent; ECG, electrocardiogram; hsTnI, high-sensitive troponin I; LAD, left anterior descending artery; LCX, left circumflex artery; MPR, multiplanar reconstruction; PCI, percutaneous intervention; RCA, right coronary artery.

with non-ST-elevation acute coronary syndrome' stated that CCTA can result in a more rapid and cost-effective diagnosis than stress myocardial perfusion imaging in low-risk patients with chest pain. Nevertheless, no specific recommendation was provided.[103]

The '2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation' recommended CCTA (Class IA) as an alternative to ICA to exclude ACS when there is a low-to-intermediate likelihood of CAD and when cardiac troponin and/or ECG are inconclusive.[106] Furthermore, these guidelines suggest CCTA (Class IB) in patients with no recurrence of chest pain, normal ECG findings, and normal level of cardiac troponin, but still with a suspected ACS, before deciding on an invasive approach.[106]

## Role of CCTA in ruling-out pulmonary embolism and aortic dissection

The newest developments in CT technology allow a comprehensive assessment of CAD, aortic dissection, and pulmonary embolism by covering the entire thorax and enhancing simultaneously coronary, aortic, and pulmonary vascular tree (i.e. 'triple-rule out protocol') with only minimally increased radiation exposure and contrast administration.[107]

### Key points

- CCTA is appropriate as a first-line diagnostic test for the evaluation of patients with acute chest pain at low-to-intermediate likelihood of CAD when ECG and/or cardiac troponin are normal or inconclusive.
- CCTA is appropriate before deciding on an invasive approach in patients with no recurrence of chest pain, normal ECG findings, and normal level of cardiac troponin, but still with a suspected ACS.
- CCTA is appropriate to detect other life-threatening conditions in patients with acute chest pain when tailored acquisition and injection protocols for 'triple rule-out' (i.e. CAD, pulmonary embolism, and aortic dissection) are used.
- CCTA could be indicated to identify the presence of stable CAD after ACS has been ruled-out.

**Table 4** Randomized controlled trials of CCTA in patients with acute chest pain

| Trial | Goldstein *et al.*[92] | CT-STAT[91] | Litt et al.[96] | ROMICAT II[94] | PROSPECT[95] | CT-COMPARE[93] | BEACON[90] | PERFECT[98] | Nabi *et al.*[97] |
|---|---|---|---|---|---|---|---|---|---|
| Sample size | 197 | 699 | 1370 | 1000 | 400 | 562 | 500 | 411 | 598 |
| Comparator | SPECT | SPECT | Standard of care | Standard of care | SPECT | Treadmill exercise ECG | Standard of care, including high-sensitivity troponin | SPECT or stress echocardiography | SPECT |
| Primary endpoint | Safety (freedom from major adverse events over 6 months), diagnostic efficacy (clinically correct and definitive diagnosis), and cost of care | Time to diagnosis | Safety (absence of MI and cardiac death during the first 30 days after presentation) | Length of hospital stay | Cardiac catheterization not leading to revascularization within 1 year | Diagnostic performance and hospital cost at 30 days | Number of patients identified with significant CAD requiring coronary revascularization | Time to discharge, change in medication, and frequency of downstream testing, cardiac interventions, and cardiovascular re-hospitalizations | Length of hospital stay |
| Duration of follow-up | 6 months | 6 months | 30 days | 28 days | 40 months | 12 months | 30 days | 1 year | 6 months |
| MACE rate at follow-up, CCTA vs. comparator | 0% vs. 0% | 0.8% vs. 0.4% | 1.1% vs. 1.1% | 0.4% vs. 1.2% | 4.5% vs. 7.5% | 0.9% vs. 0.4% | 10% vs. 9% | 1.5% vs. 0.4% | 4.6% vs. 3.0% |
| Length of stay (hours), CCTA vs. comparator | 3.4 vs.15 | 2.9 vs. 6.2 | 18 vs. 24.8 | 8.6 vs. 26.7 | 28.9 vs. 30.4 | 13.5 vs. 19.7 | 6.3 vs. 6.3 | 48 vs. 49 | 19.7 vs. 23.5 |
| ED discharge, CCTA vs. comparator | 88% vs. 96% | 88% vs. 89% | 50% vs. 23% | 47% vs. 12% | N/A | N/A | 65% vs. 59% | N/A | N/A |

BEACON, Better Evaluation of Acute Chest Pain with Coronary Computed Tomography Angiography; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CT-COMPARE, CT Coronary Angiography Compared to Exercise ECG; CT-STAT, Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment; ECG, electrocardiogram; ED, emergency department; MACE, major adverse cardiovascular events; MI, myocardial infarction; N/A, not available; PERFECT, Prospective First Evaluation in Chest Pain; PROSPECT, Prospective Randomized Outcome trial comparing radionuclide Stress myocardial Perfusion imaging and ECG-gated coronary CT angiography; ROMICAT, Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography; SPECT, single photon emission computed tomography.

# CCTA in the evaluation of patients with previous coronary revascularization

## Coronary stent imaging

Imaging coronary stents with CCTA is more challenging than the evaluation of native coronary arteries. According to the most recent meta-analysis including studies performed with ≥64-slice CCTA, pooled data showed a sensitivity of 90% and a specificity of 94% in the detection of in-stent restenosis, defined as diameter narrowing greater than 50% on ICA.[108] Of note, stent size, composition, and configuration are the main determinants affecting diagnostic accuracy in the evaluation of intracoronary stent patency as shown in *Figure 4*. In particular, sensitivity of CCTA has been found to be better in stents with a diameter ≥3 mm compared to smaller diameters (94% vs. 89%), in stents with metal struts <100 µm compared to thickener stents (96% vs. 84%), and in simple stents compared to bifurcation stents (95% vs. 88%).[108] Currently, due to these limitations, the role of CCTA remains controversial for stent imaging.[109] Nevertheless, the recent introduction of new detector technology,[110] iterative reconstruction,[111] and monochromatic imaging[112] has shown promising results in mitigating some of these concerns.

## Coronary artery by-pass graft imaging

In contrast to coronary stent imaging, evaluation of coronary artery bypass grafts (CABG) is usually more accurate than assessment of native coronary arteries, thanks to their larger calibre and lower sensitivity to cardiac motion. A recent meta-analysis including 1975 patients and 5364 grafts showed an excellent diagnostic performance of CCTA in the detection of graft stenosis or occlusion when compared to the reference standard ICA, with a sensitivity of 96%, a specificity of 96%, and a negative predictive value reaching 99%.[113] A representative example of the role of CCTA in the evaluation of graft patency is shown in *Figure 5*. The other key part of the diagnostic work-up of patients

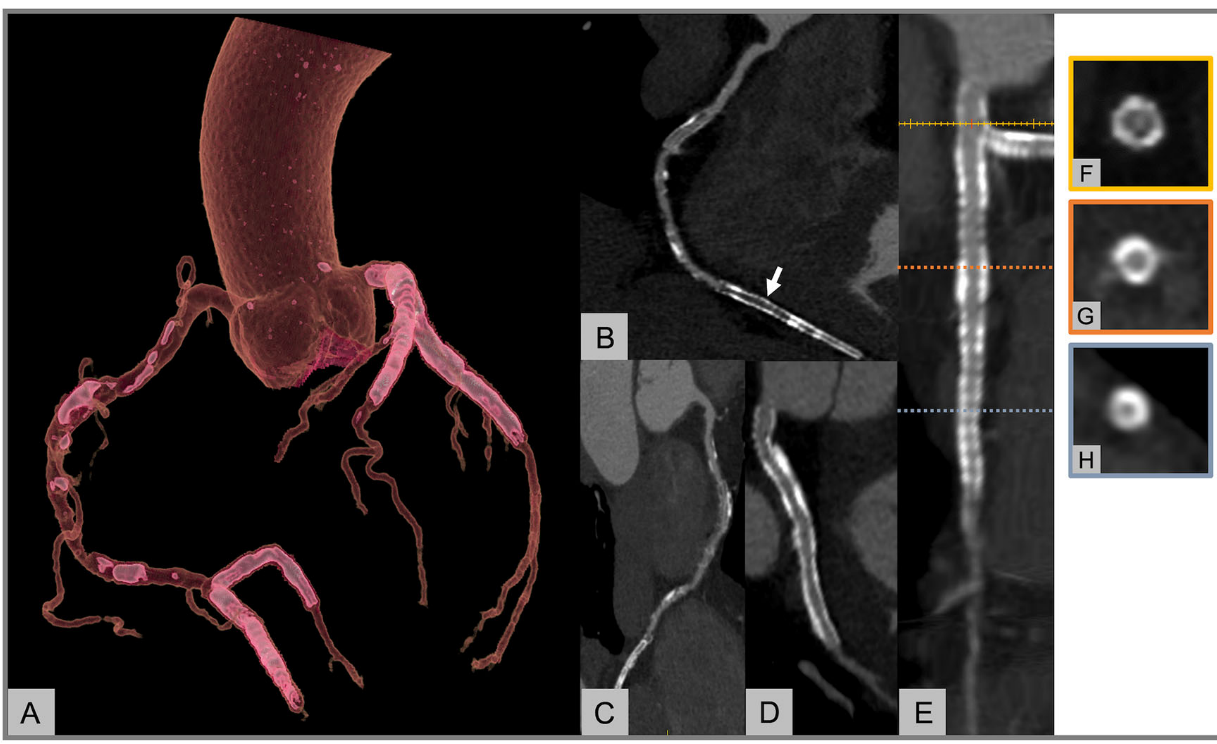



**Figure 4** CCTA in patients with multiple coronary stents. (*A*) A 58-year-old man underwent CCTA due to recent onset of atypical chest pain. The patient had prior multiple stenting as shown in the volume rendering reconstruction of the coronary tree. (*B–D*) Curved MPRs of RCA-PDA (*B*), RCA-PL (*C*) and LCX (*D*). The stent lumen on the PDA artery (*B, arrow*) appears homogenously hypodense indicating stent occlusion. (*E–H*) Straight MPR of LM-LAD (*E*) and cross-sectional images of distal LM (*F*) as well as proximal (*G*) and distal (*H*) LAD. CCTA demonstrated a dark rim in the distal LM stent documenting the presence of in-stent restenosis (*F*). While the stent in the proximal LAD (*G*) was assessable and judged as patent, the small size of the stent in the distal LAD (*H*) precluded the evaluation of the lumen. CCTA, coronary computed tomography angiography; LAD, left anterior descending Artery; LCX, left circumflex artery; LM, left main; MPR, multiplanar reconstruction; PDA, posterior descending artery; PL, posterolateral branch; RCA, right coronary artery.

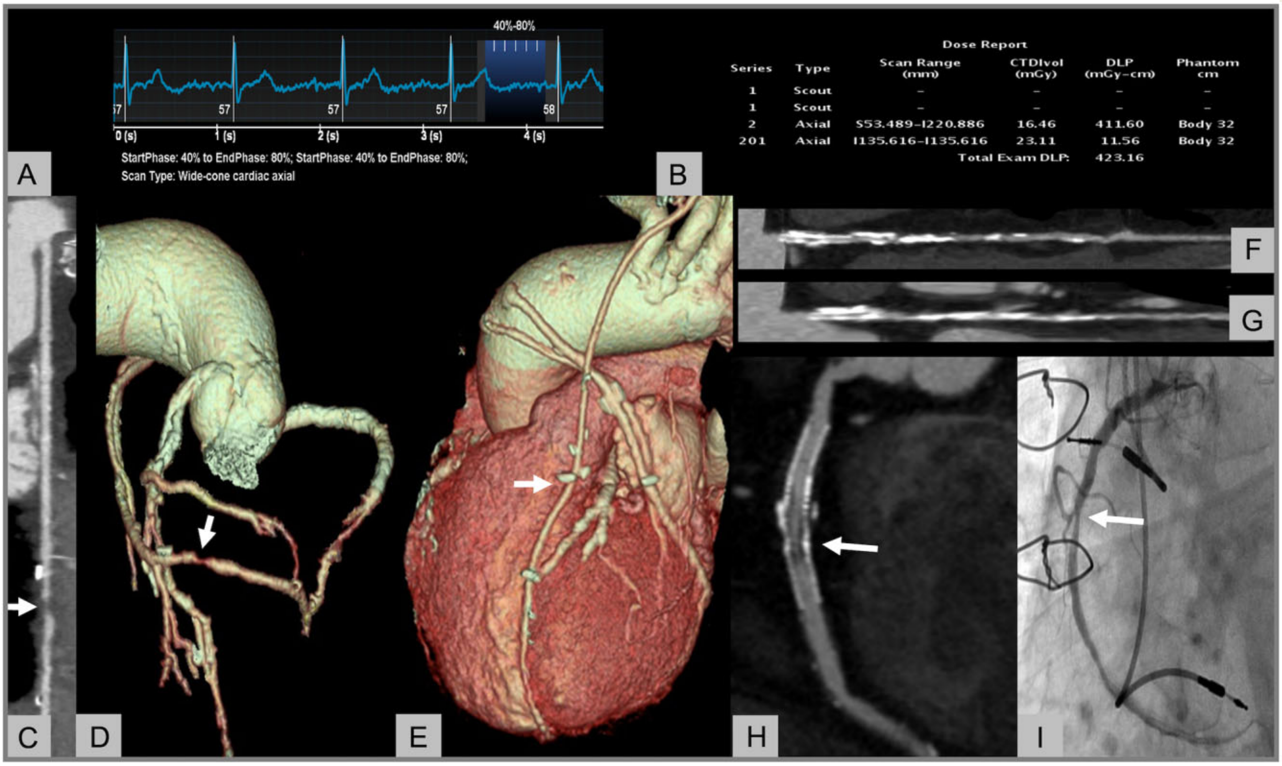



**Figure 5** CCTA in patients with previous CABG. (*A* and *B*) A 70-year-old man with previous CABG surgery (LIMA-LAD, SVG-OM1, SVG-OM2) and PCI + DES on RCA underwent CCTA for recent onset of atypical chest pain. An ECG-triggered axial acquisition (40–80% of the R-R interval) was performed by using a wide-detector CT scanner, covering a volume from the inferior margin of the heart to the top of the lung apices (*A*). The total DLP was 423.16 mGy*cm (*B*). (*C* and *D*) Venous graft to OM2: straight MPR (*C*) and volume rendering reconstruction (*D*) of the venous graft to OM2 showed sub-occlusion (arrow) of the distal anastomosis (OM2) whereas the graft conduit was patent. (*E*) LIMA graft: the LIMA graft to LAD and the distal anastomosis (distal LAD) were both patent as demonstrated by the volume rendering reconstruction. (*F–I*) Native coronary vessels: LM (*F*), LAD (*F*), and LCX (*G*) were diffusely calcified as shown in the corresponding straight MPRs. In addition, the curved MPR image of the RCA demonstrated a severe in-stent restenosis (*H, arrow*), which was confirmed by ICA (*I, arrow*). CABG, coronary artery bypass graft; CCTA, coronary computed tomography angiography; CT, computed tomography; DES, drug eluting stent; DLP, dose length product; ECG, electrocardiogram; ICA, invasive coronary angiography; LAD, left anterior descending artery; LIMA, left internal mammary artery; LM, left main; LCX, left circumflex artery; OM1, first obtuse marginal artery; OM2, second obtuse marginal artery; MPR, multiplanar reconstruction; PCI, percutaneous intervention; RCA, right coronary artery; SVG, single venous graft.

with recurrent angina after CABG is the assessment of native, non-grafted vessels as well as distal, post-anastomotic arteries, given that both can be involved in CAD progression. These coronary segments are often highly calcified due to advanced atherosclerosis and often difficult to assess with CCTA, although several studies have reported an acceptable diagnostic accuracy for stenosis detection, with sensitivities and specificities of 83–100% and 77–100%, respectively.[114,115] The combined evaluation of both graft and native coronary disease severity provides information on the completeness of coronary revascularization and atherosclerotic plaque burden and, therefore, on the long-term prognosis in terms of cardiovascular death and non-fatal MI.[116] Finally, in addition to the evaluation of graft and vessel patency, CCTA can reliably identify the unknown anatomy, number of grafts prior to ICA, and their location prior to redo-sternotomy.[117]

## Viability imaging with CT

Like gadolinium, iodine-based CT contrast agents are extracellular contrast materials. Therefore, in both acute and chronic MI they accumulate in the infarct zone due to an increased distribution volume.[118] Several studies have shown the feasibility of late iodine CT enhancement imaging in the detection of MI reporting good agreement with the reference standard cardiac magnetic resonance.[119,120] Despite this, CT suffers from inferior contrast resolution and lower contrast-to-noise ratio as compared to cardiac magnetic resonance, thus precluding its use in larger patients.[121] More details on late iodine CT enhancement imaging are provided in the second part of this consensus document.

## Key points

- CCTA should not be routinely used in patients with previous coronary revascularization by percutaneous coronary intervention.
- CCTA could be useful for the evaluation of symptomatic patients with a stent ≥3 mm in diameter. Optimized acquisition protocols aimed to reduce blooming effect and image noise as well as to optimize spatial resolution should be adopted.
- CCTA is appropriate for the evaluation of graft patency after CABG.
- CCTA could be useful for the evaluation of native coronary arteries in patients with previous CABG, although this is frequently challenging.
- CCTA is appropriate for the evaluation of unknown graft anatomy prior to ICA.
- CCTA is appropriate for the localization of cardiac structures (e.g. left internal mammary artery) in patients prior to redo-sternotomy.

## Summary

Coronary calcium is a specific marker of sub-clinical atherosclerosis providing strong prognostic information in asymptomatic patients not on statin therapy. CCTA identifies both obstructive and non-obstructive coronary stenoses non-invasively and is now recommended as a first-line diagnostic test for the evaluation of patients with atypical and typical angina symptoms. CCTA can also be used to assess patients presenting with acute chest pain and low-to-intermediate PTP and in assessing graft patency. Its role remains controversial for the evaluation of coronary stents, especially if stent diameter is <3 mm.

# Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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