Case 1
A 46-year-old woman with diabetes mellitus and a body mass index of 32 kg/m² reports repeated episodes of chest pain after moderate activity. Single photon emission computed tomography myocardial perfusion imaging demonstrates no electrocardiographic (EKG) abnormalities and a small fixed perfusion defect in the posterior left ventricle. Prospectively EKG-triggered coronary CT angiography (CCTA), performed with a radiation dose of 3.5 mSv, demonstrates unremarkable coronary arteries with no evidence of stenosis or atherosclerosis (Figure 1).

Case 2
A 63-year-old man with treated hypertension and hyperlipidemia experiences diffuse chest pain and shortness of breath after a long distance flight. Catheter angiography 2 years earlier was normal. At emergency department arrival, his EKG demonstrates no signs of myocardial injury. Cardiac troponin I is 0.04 ng/mL. An EKG-synchronized acute chest pain CCTA examination demonstrates extensive noncalcified plaque of the mid left anterior descending coronary artery causing severe stenosis with signs of acute myocardial hypoperfusion in the anterior and apical left ventricle (Figure 2). The patient undergoes successful revascularization with a drug eluting stent.

CCTA has left the early stages of clinical evaluation and matured into a robust diagnostic technique in both elective and emergent settings. Technological innovations are continuously improving the diagnostic performance and decreasing the radiation dose associated with this test. In this Clinician Update, we provide an updated summary on the state-of-the-art and clinical use of CCTA.

Technical Developments and Radiation Exposure
The integration of CCTA into clinical practice can predominantly be attributed to substantial technical developments over the last years, which have enabled shorter scan times, higher temporal and spatial resolution, and lower radiation requirements. Conventionally, CCTA has been performed using retrospective ECG gating. This technique applies continuous radiation and can involve dose levels of 10 to 20 mSv.1 More recently, prospective EKG-triggering was rediscovered, an old technique gleaned from electron-beam CT, which applies radiation discontinuously. This approach has a mean radiation dose of ≈3.5 mSv,1 which is comparable with the annual background radiation from natural sources. The most current class of CT instruments can image the entire heart within a single beat and a radiation dose of <1 mSv² in patients with slow sinus-rhythm. Further reduction is expected from novel iterative reconstruction techniques, which also address some of the traditional limitations of CCTA, such as imaging artifacts from heavy calcifications and high image noise in obese patients. Enhanced temporal resolution and data postprocessing algorithms of more recent scanner classes furthermore improve the robustness of image acquisition vis-à-vis high and irregular heart rates.

Figure 3 shows that CCTA using contemporary acquisition methods...
now falls within the lower range of radiation doses from coronary artery disease (CAD) imaging tests. This is a consideration for 1-time testing and also for patients who undergo repeated imaging with various modalities and a typical cumulative dose of 16 mSv over 3 years and 64 mSv over 20 years. However, importantly, risks across an adult population from even such comparatively higher levels of radiation are likely too low to be epidemiologically detectable and may be nonexistent. In a patient of the age range in which CAD is a concern, radiation risk is likely a minor consideration in the decision to proceed to imaging, although the appropriateness of indication and the expected benefit in the specific clinical scenario deserve more careful weighing.

Evidence and Guidelines on CCTA

The efficacy of CCTA has been exhaustively demonstrated over the last decade. As a consequence of the robust and low-risk technology, current studies extend the value of CCTA from efficacy to effectiveness.

Stable Chest Pain Syndrome

Current guidelines on the use of CCTA in patients with stable angina are predominantly derived from the favorable results of the initial efficacy trials. A systematic analysis of studies using regular dose and low radiation dose CCTA revealed a pooled sensitivity and specificity of CCTA of 98% and 89%, respectively. The negative predictive value approximates 100%, indicating that CCTA can safely exclude obstructive CAD. These results compare favorably with alternative noninvasive CAD imaging tests.

Findings from cost-effectiveness analyses indicate that with CAD pretest probabilities of 10% to 50%, CCTA is more cost-effective than other imaging modalities.

As a result, current Appropriate Use Criteria recommend CCTA for the diagnostic work-up of patients with stable angina but low to intermediate CAD likelihood, especially in the setting of equivocal prior study results. This indication chiefly encompasses the use of CCTA for clarifying abnormal findings at functional testing. Subjects with significant findings on CCTA are referred for catheter angiography (Figure 4). However, increasing efforts aim at defining the role of CCTA as a

Figure 1. Unremarkable coronary CT angiography study with no evidence of stenosis or atherosclerosis. Cx indicates circumflex artery; D1, first diagonal; LAD, left anterior descending; LM, left main; OM1, first obtuse marginal; and RCA, right coronary artery.
primary gate-keeper in the management of patients with suspected CAD.¹¹

**Acute Chest Pain Syndrome**

A substantial body of evidence is emerging on the use of CCTA in the setting of acute chest pain. CCTA-based strategies for ruling out acute coronary syndrome (ACS) consistently enable safe emergency department discharge of patients in a more expeditious manner than standard of care algorithms.¹²–¹⁴

Also in the acute chest pain setting, the use of CCTA has been shown to be cost-effective,¹⁵ although the exact effect of the specificity of interpretation on downstream resource-utilization needs further study.¹³ CCTA is considered appropriate in patients with acute nonspecific chest pain, low to intermediate CAD risk, normal or uninterpretable EKG, and negative or equivocal cardiac biomarkers. Because a substantial percentage of the emergency department population presents in exactly this manner, this indication is increasing. Typically, the majority of patients will not show any acute pathology and will be recommended for immediate discharge. Subjects with either extensive plaque burden or significant stenosis are referred for subsequent work-up by functional testing or catheter angiography (Figure 5).

### Prognostic Value

There is increasing evidence on the prognostic value of CCTA both in the stable and acute chest pain setting. The presence of obstructive CAD and, more importantly, the amount of coronary atherosclerotic plaque at CCTA is strongly related to cardiac outcomes in patients with chronic and acute chest pain.¹⁶ The absence of CAD, conversely, portends an exceedingly favorable prognosis regarding all-cause and disease-specific morbidity and mortality.

Data on the use of CCTA for risk stratification in asymptomatic subjects are scarce,¹⁷ and substantial further study is needed. Accordingly, this use is currently discouraged outside of clinical trials. Imaging reports will rarely state any prognostic implications of CCTA findings.

### Future Directions of CCTA

A number of large-scale trials (eg, Prospective Multicenter Imaging Study for Evaluation of Chest Pain [PROMISE], International Study of Comparative Health Effectiveness With Medical and Invasive Approaches [ISCHEMIA], Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Diagnostic Examinations [RESCUE])¹⁸ are ongoing.
to study the effectiveness of CCTA in the management of stable angina.

A unique strength of CCTA is the ability to noninvasively visualize, quantify, and characterize atherosclerotic plaque components, enabling in vivo insights into CAD pathobiological mechanisms in various populations. Although currently incompletely understood, identification of high-risk plaque features may provide more precise individual risk estimates. CCTA can noninvasively provide information on CAD burden and on the distribution of obstructive disease in major epicardial vessels, which will increasingly establish this test as a primary gatekeeper to catheter angiography.

At the same time, technical evolution will continue to broaden the ability of CCTA to more comprehensively characterize CAD. Novel approaches include single-adenosine-mediated stress CT acquisitions or sequential stress perfusion imaging to obtain quantitative markers of myocardial perfusion.

Also, computational fluid dynamics for estimating fractional flow reserve from CCTA studies have shown good correlation with invasive measurements in initial investigations.

**Conclusion**

CCTA has matured into a robust cardiac imaging modality with high efficacy and rapidly emerging evidence of effectiveness. Adaptation in clinical practice is increasing. Current guidelines recommend its use in stable and acute chest pain syndrome in low- to intermediate-risk populations. Several large ongoing trials include CCTA in their effort to identify the most effective contemporary CAD management strategies. The characteristics of this test, enabling rapid, noninvasive exclusion of obstructive lesions along with the definition of the distribution, severity, and composition of the atherosclerotic burden, uniquely address current and emerging needs in CAD management. The utilization of this test will likely be less governed by the choice of CCTA versus alternative imaging modalities but rather by the developing consensus on specific clinical scenarios in which imaging is considered appropriate.

**Disclosures**

Dr Schoepf is a consultant for or receives research support from Bayer Healthcare, Bracco Diagnostics, General Electric Healthcare, Medrad, and Siemens Healthcare. The other authors report no conflicts.

**References**


**Figure 5.** Suggested CCTA-based patient management algorithm in the setting of acute chest pain. Modified from Taylor et al with permission of the publisher. Copyright © 2010, Wolters Kluwer. CA indicates catheter angiography; CAD, coronary artery disease; CCTA, coronary CT angiography; MI, myocardial infarction.


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Coronary Artery Computed Tomography Scanning
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