CT of Coronary Artery Disease[1]

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Technical innovation is rapidly improving the clinical utility of cardiac computed tomography (CT) and will increasingly address current technical limitations, especially the association of this test with relatively high levels of radiation. Guidelines for appropriate indications are in place and are evolving, with an increasing evidence base to ensure the appropriate use of this modality. New technologies and new applications, such as myocardial perfusion imaging and dual-energy CT, are being explored and are widening the scope of coronary CT angiography from mere coronary artery assessment to the integrative analysis of cardiac morphology, function, perfusion, and viability. The scientific evaluation of coronary CT angiography has left the stage of feasibility testing and increasingly, evidence-based data are accumulating on outcomes, prognosis, and cost-effectiveness. In this review, these developments will be discussed in the context of current pivotal transitions in cardiovascular disease management and their potential influence on the current role and future fate of coronary CT angiography will be examined.

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The rapid rise of coronary computed tomographic (CT) angiography from a research application to a robust, widely embraced clinical tool over the last decade has very few parallels in medicine. We currently observe a convergence of factors that has the potential of making coronary CT angiography a pivotal cornerstone in cardiovascular disease management, deserving of the highest level of attention of our field. Factors with critical influence on the clinical implementation of coronary CT angiography are related to the scope and importance of cardiovascular disease, rapidly evolving technology, widening use of coronary CT angiography for established indications, emerging new applications, fundamental changes in clinical cardiovascular disease management, and increased emphasis on cost-effectiveness in health care. In this article, we review each of these factors as they relate to the current and future role of coronary CT angiography.

Essentials

- Innovations in scanner technology and acquisition protocols continue to improve the performance and usefulness of coronary CT angiography and enable substantial reductions in radiation exposure associated with this test.
- Compared with invasive coronary catheterization, coronary CT angiography has high accuracy for stenosis detection; the exceedingly high negative predictive value of this test enables reliable noninvasive exclusion of significant coronary artery stenosis.
- The available evidence suggests that the use of electrocardiographically synchronized CT for the assessment of patients with acute chest pain is accurate and safe and can effectively address limitations of the traditional diagnostic work-up.
- Coronary CT angiography enables the noninvasive assessment of the calcified and noncalcified atherosclerotic plaque burden and may play an increasing future role for cardiac risk stratification and therapeutic monitoring.
- Technologies and acquisition protocols are currently under development that aim at combining coronary CT angiography with CT-based methods for the evaluation of myocardial function, perfusion, and viability for the comprehensive assessment of coronary heart disease, with CT as the sole imaging modality.
- Rapidly accumulating evidence-based data increasingly supports that coronary CT angiography, if used according to established guidelines, is cost-effective.

The Scope

We currently are observing a sharp decline in cardiovascular disease mortality, which has been mainly attributed to substantial improvements in primary and secondary prevention and medical (ie, pharmaceutical) disease management (1). However, the fact remains that cardiovascular disease continues to be the most important health problem globally; particularly in the westernized world. In the United States, the current prevalence of coronary heart disease is estimated at 16 000 000 individuals (about 8 700 000 men and 7 300 000 women) among adults older than 20 years of age. The prevalence of myocardial infarction is estimated at 8 100 000. In 2004, coronary artery disease (CAD) caused 451 326 deaths (233 538 male and 217 788 female deaths), of which 156 816 (82 909 men, 73 907 women) were owing to myocardial infarction (1).

Technical Evolution

While electron-beam CT (2,3) for the time of its existence had a role in noninvasive cardiac imaging, primarily as a technique for coronary artery calcium scoring, the rapid rise of cardiac CT was driven by the introduction of multi–detector row CT in 1998. The first generation of four–detector row CT technology enabled electrocardiographically (ECG) synchronized high spatial and temporal resolution imaging of the heart (4), and soon after its introduction was shown to be capable of quantifying coronary artery calcification (5), evaluating coronary artery stenosis (4,6), measuring cardiac function (7), and analyzing atherosclerotic plaque (8). With each subsequent scanner generation, for example, introduction of 16–detector row CT in 2001 (9,10), the proportion of patients that could be successfully imaged with noninvasive coronary CT angiography gradually increased. For example, improvements in temporal resolution reduced the percentage of vessel segments that were not evaluable because of motion artifacts (11), shorter overall scan times enabled higher contrast medium attenuation with lower volumes (11,12), and the gradual implementation of radiation protection techniques lowered the overall patient radiation exposure (13,14).

The recent rapid widespread growth in coronary CT angiography parallels the introduction of 64–detector row CT systems (15) in 2004. These are currently the most commonly used platform for performing cardiac CT. These scanners have a temporal resolution of up to approximately 165 msec and enable image acquisition of the cardiac anatomy within 5–10 seconds of scan time (16). However, while a substantial improvement over previous generations, the temporal resolution of these scanners, even with use of multisegment reconstruction algorithms, which can potentially yield temporal resolution of up to approximately 43 msec at some heart rates (17,18), is still too limited in subjects with high resting heart rates and irregular heart rhythm. As a result, pharmacological rate control above heart rates of 60–70 beats per minute remains a necessity (19,20).

Dual-source CT entered the field in 2006; its design reflects the concepts of an earlier experimental prototype (ie, the "dynamic spatial reconstructor") (21,22). This

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Abbreviations:
CAD = coronary artery disease
ECG = electrocardiogram
LAD = left anterior descending coronary artery
3D = three-dimensional

scanner consists of two x-ray tubes and two detectors mounted perpendicularly in the same gantry (23). Because of this configuration, sufficient projection data for full image reconstruction can be sampled during quarter-rotation scanning as opposed to half-rotation scanning with conventional single-source multidetector CT systems, thus improving the temporal resolution to one-fourth of the gantry rotation time (ie, 330 msec/4 = approximately 83 msec) (23,24). Because of this excellent temporal resolution, high diagnostic accuracy for the detection of coronary artery stenosis at high and irregular heart rates without pharmacological rate control has repeatedly been reported (25,26) (Fig 1).

Technical innovations in cardiac CT are continuing at a rapid rate. Recently, 256-row and 320-row single-source systems, as well as 128-row dual-source CT scanners, have been introduced (27,28). The quest for broader detector arrays is motivated by the thought that complete volume coverage of the heart within a single heartbeat and isophasic datasets may reduce patient radiation (29) and can reduce susceptibility to arrhythmia, thus eliminating the type of ECG-misregistration artifacts that are still occasionally problematic with 64-row CT acquisitions (27,30,31). The availability of detector arrays that are wide enough to cover the entire cardiac anatomy (27,28) also enables new approaches in the assessment of cardiac function. This includes the acquisition of dynamic, time-resolved data on myocardial perfusion and the myocardial blood supply, which previously had been limited by insufficient detector coverage (32).

An alternative strategy, dual-energy acquisition, for evaluating the myocardial blood supply based on static, non–time-resolved coronary CT angiograms has also been proposed with dual-source CT (33,34). First, concepts of dual-energy CT imaging date back more than 2 decades (35–38). However, early experimental efforts ordinarily required the acquisition of two separate CT scans at different kilovoltage levels with subsequent image coregistration, which limited their clinical utility and naturally precluded imaging the beating heart. The recent availability of dual-source CT with its two-tube configuration enables the simultaneous acquisition of high and low x-ray energy spectra with a single CT scan (39). In the heart, dual-energy CT has been shown to permit the analysis of the myocardial blood supply by analyzing the iodine (and thus blood) volume within the myocardium (33,34), exploiting the fact that tissues in the human body and iodine-based contrast media have unique absorption characteristics when penetrated with different x-ray energy levels (see below). The application of the dual-energy approach using first-generation dual-source CT, however, results in decreasing the temporal resolution to 165 msec compared with the available 83 msec when both tubes are operated at the same kilovoltage. Other strategies for the acquisition of multiple energy image data that provide integrative information on coronary artery morphology and the state of myocardial perfusion are currently under investigation and include rapid switching of kilovoltage levels during scan acquisition and multilayer detectors that filter specific photon energies from the x-ray spectrum.

Radiation Dose

Recent reports (40,41) on increasing radiation exposure from diagnostic CT examinations have sparked increasing concern and discussion among the medical community and public at large. A multicenter study reported an average effective radiation

Figure 1

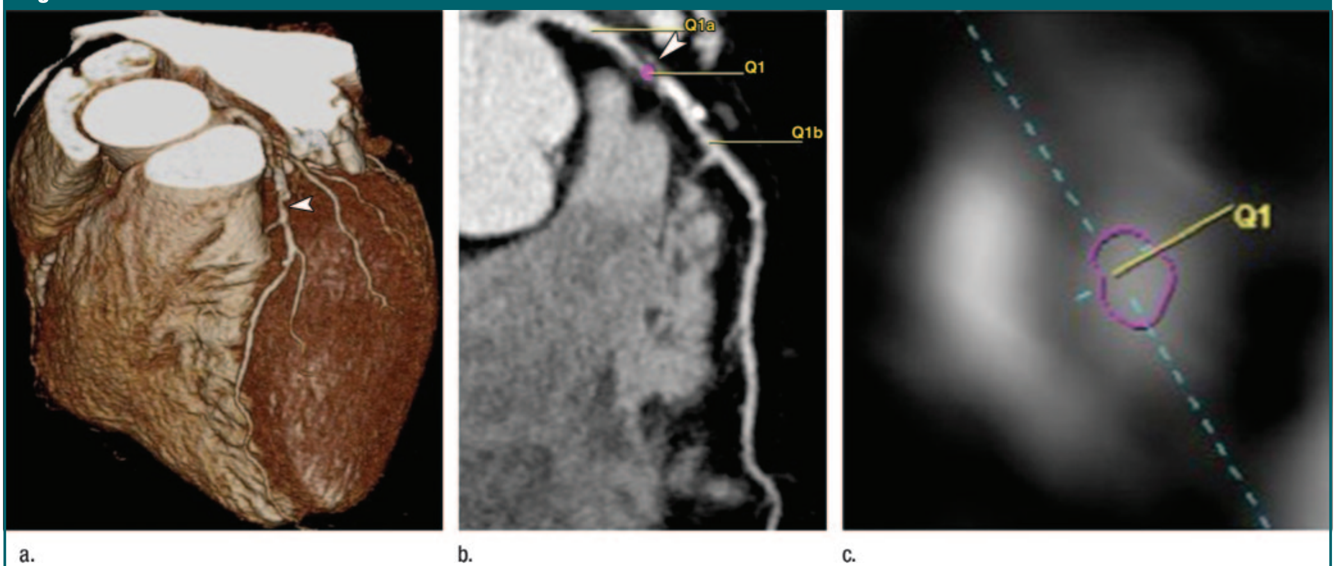


Figure 1: Contrast-enhanced retrospectively ECG-gated dual-source coronary CT angiography in 79-year-old man with atypical chest pain. Average heart rate during scan acquisition was 129 beats per minute (minimum, 103 beats per minute; maximum, 150 beats per minute). **(a)** Three-dimensional (3D) volume rendering from left anterior oblique perspective, **(b)** curved multiplanar reformation, and **(c)** transverse section orthogonal to the vessel lumen demonstrate significant coronary artery stenosis (arrowhead) in the proximal left anterior descending coronary artery (LAD) caused by predominantly noncalcified plaque.

dose equivalent of 12 mSv associated with cardiac CT and demonstrated large variations (5–30 mSv) among participating centers depending on the scanner manufacturer, geographic location, and use of radiation protection regimens (42). As with all imaging studies involving radiation, the individual assessment of the patient's risk-benefit ratio and the responsibility to keep radiation exposure at a minimum is incumbent on us as the stewards of radiation use in medical imaging. Accordingly, all approaches to lowering radiation dose in cardiac CT are welcome and should be carefully considered. There are time-honored approaches such as ECG-dependent tube current modulation (14) and use of lower tube voltage (43,44) in slimmer individuals (Fig 2), which should be used whenever possible.

However, the greatest radiation dose reductions have been reported with the recently rediscovered technique of prospectively ECG-triggered coronary CT angiography (45–47). This technique consists of sequential acquisition of transverse sections with application of radiation only during a predetermined interval in the cardiac cycle (ordinarily diastole). This had been the default method for ECG synchronization of scan acquisition used with electron-beam CT (48). Prospective ECG triggering enables performing coronary CT angiography at a fraction of the effective radiation dose equivalent (ie, 1–4 mSv), when compared with the constant application of radiation used in retrospectively ECG-gated slow-pitch spiral multidetector CT (4) (Fig 3).

The main limitations of prospective ECG triggering to date have been the inability to evaluate cardiac function. More important, this technique has a limited ability to retrospectively (ie, after scan acquisition) change the simultaneous registration of image data with more suitable phases of the cardiac cycle, which is one of the hallmarks of retrospective ECG gating. Also, patients with arrhythmia have traditionally not been eligible for prospectively ECG-triggered examinations, because arrhythmia naturally precludes reliable simultaneous registration of image data with the desired cardiac phase. There are various technical attempts at improving the robustness of this acquisition technique for faster and more irregular heart rates. These include single heart beat volume CT acquisition (27), prolonging the acquisition interval during the RR-cycle to provide more flexibility in choosing the most suitable phase of image reconstruction (49), or adaptive online monitoring of the ECG for the occurrence of extra systoles to ensure image acquisition only during the desired cardiac phase (49). Despite these technical advances, we currently recommend restricting the use of prospective ECG triggering to subjects with stable and slow (ie, < 65 beats per minute) heart rates. This may make it advisable to pharmacologically control heart rate, regardless of the scanner's temporal resolution.

Another recent technical development with potential to lower radiation exposure of CT studies, including cardiac CT, is statistical iterative image reconstruction. Traditional filtered back projection image reconstruction has limitations regarding 3D cone-beam geometry, data completeness, and low radiation dose acquisitions. Iterative image reconstruction approaches provide more flexibility for accurate physical noise modeling and geometric system description (50). Initial experience (50) suggests that these reconstruction methods allow for improvements in image quality and lower image noise and thus appear to be particularly promising for low-radiation dose cardiac CT (Fig 4).

Scanner technology continues to evolve; the heightened awareness of increasing radiation exposure from medical imaging will stimulate the expedited development of systems and acquisition strategies that are capable of imaging the heart at much lower radiation dose than current CT systems, which should, in the future, ameliorate current radiation concerns about cardiac CT.

Figure 2

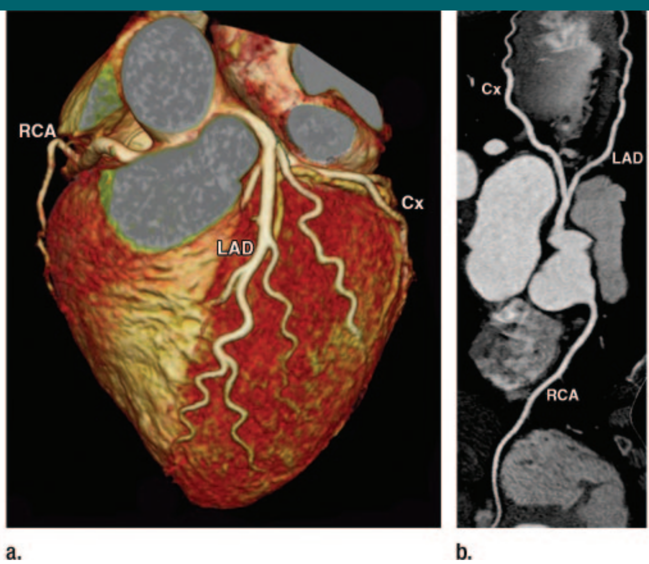


Figure 2: Contrast-enhanced retrospectively ECG-gated coronary CT angiography in 52-year-old woman (height, 1.63 m; weight, 51 kg; body mass index, 19.2) with atypical chest pain. A low-voltage (100-kVp) protocol and ECG dose modulation were used with an effective radiation dose equivalent of approximately 5 mSv (dose–length product = 274 mGy · cm). **(a)** Three-dimensional volume rendering from left anterior oblique perspective and **(b)** automatically generated curved multiplanar reformation show normal coronary arteries. *RCA* = right coronary artery, *Cx* = circumflex coronary artery. The high negative predictive value of a normal or near-normal coronary CT angiogram can reliably exclude coronary artery stenosis as a reason for chest pain and obviate further work-up for CAD.

Framework for Appropriate Use and Indication

As with all diagnostic procedures involving the use of ionizing radiation, the assessment of the risk-benefit ratio for each patient, appropriate patient selection, and indication for coronary CT angiography should guide referring physicians and radiologists in the use of this examination. Initially, patient selection and indications for cardiac CT were variable and largely institutionally driven. However, with more widespread use, the need for defining patient selection and appropriate use has become more apparent. Recently, several documents have been issued by the pertinent professional societies (51–55) that provide more informed guidance on appropriate indications for the use of cardiac CT. These recommendations confirm a number of traditional indications for cardiac CT, such as the assessment of coronary artery anomalies (Fig 5) and bypass grafts. There is consensus that the use of coronary CT angiography is appropriate in symptomatic individuals, especially if symptoms, sex, and age suggest a low to intermediate probability of significant coronary artery stenosis (Fig 6). There is also consensus that coronary CT angiography to date has no role for general screening for coronary atherosclerosis in asymptomatic individuals, because the current levels of radiation are incompatible with the prerequisites of a successful screening test (56,57) and data on the cost-effectiveness of this indication are lacking. The issuance of guidelines and appropriateness criteria by the professional societies has helped to define the indications for coronary CT angiography and curb potential overutilization, although they do not replace the need for individual assessment of the risk-benefit ratio in each patient. In addition, these recommendations only reflect the current status of our understanding of the appropriate use of this test and are subject to change as new data and experience are gathered.

Figure 3

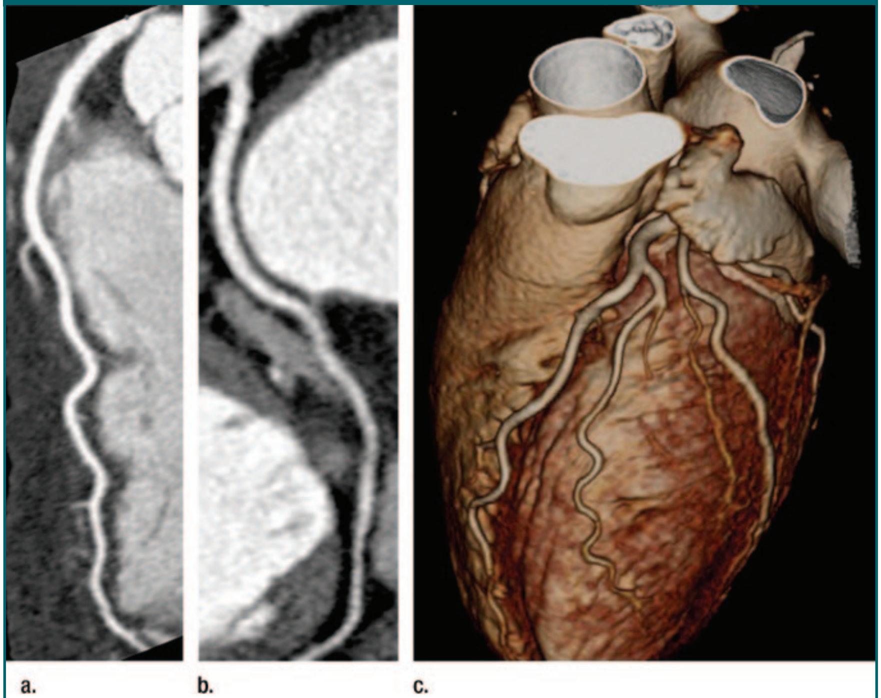


Figure 3: Contrast-enhanced prospectively ECG-triggered 128-section coronary CT angiography performed with 120 kV and 220 mAs in 49-year-old woman (height, 1.65 m; weight, 54 kg; body mass index, 19.8; heart rate, 54 beats per minute) with atypical chest pain, equivocal stress test, and an effective radiation dose equivalent of approximately 2.4 mSv (dose–length product = 135 mGy · cm). Curved multiplanar reformations of **(a)** LAD and **(b)** circumflex coronary artery and **(c)** 3D volume rendering from a left anterior oblique perspective show normal coronary arteries enabling confident noninvasive exclusion of coronary artery stenosis at radiation dose levels that are lower than the average annual background radiation from natural sources.

Comparison with Conventional Coronary Angiography

The early observations using four- and 16-row (6,58–60) CT scanners with regard to the diagnostic performance of noninvasive coronary CT angiography were seminal in demonstrating the potential usefulness of this test for visualizing the coronary artery lumen and vessel wall in subjects suspected of having CAD. Early investigations reported sensitivity, specificity, positive predictive value, and negative predictive value of 75%–90%, 90%–95%, 70%–90%, and 80%–90%, respectively, for the detection of hemodynamically significant stenosis (58,61–63). However, these early results were substantially limited by motion artifacts or extensive calcification. These artifacts frequently necessitated the exclusion of coronary artery segments, vessels, or patients from data analysis in the early descriptions and to some extent overstated the diagnostic performance that was achievable at that time (6,64). Subsequently, more systematic analyses of the performance of coronary CT angiography using four- and 16-row CT in patients suspected of having CAD demonstrated a pooled sensitivity for detecting any stenosis of about 89% (range, 85%–92%), concluding that the sensitivity obtainable with these scanner generations may not be completely satisfactory to reliably rule out coronary artery stenosis (15,65).

The subsequent introduction of 64-row CT technology led to substantial improvements in spatial and temporal resolution that resulted in increased sensitivity and specificity for detecting significant coronary stenosis when compared with conventional coronary angiography. Results of representative studies evaluating the performance of 64-row CT and dual-source CT for detecting hemodynamically significant coronary artery stenosis (Fig 7) are shown in the Table (25,26,66–77). These studies report sensitivity and specificity of 86%–99% and 92%–98%, respectively. Most important, with the exception of a single, recent study (78) that showed lower sensitivity than specificity (85% sensitivity, 90% specificity, 91% positive predictive value, 83% negative predictive value), all investigations performed with current generations of multidetector CT scanners have consistently reported high negative predictive values that approach or reach

100% on a per-patient basis. This exceedingly high negative predictive value, which allows reliable exclusion of significant coronary artery stenosis following a normal or near-normal noninvasive coronary CT angiogram (Figs 2, 3), is the cornerstone for the use of cardiac CT in the management of symptomatic patients suspected of having CAD. In this patient population, a normal or near-normal coronary CT angiogram can effectively obviate further testing (79–82).

Despite the considerable advances in scanner technology and image postprocessing techniques, there are still instances (about 1% of vessels [67]) where results at coronary CT angiography are ambiguous and inconclusive. Causes of ambiguous results include motion artifacts from high and irregular heart rates, excessive image noise in obese patients, heavy vascular calcifications (67,74), and the limited accuracy of coronary CT angiography for measuring stenosis severity (83).

Newer scanner technology has improved the robustness of the examination in patients with high and arrhythmic heart rates (84,85). Similarly, recent technical developments have enhanced our ability to evaluate heavily calcified vessel segments and to determine lesion severity when compared with the earlier results. Promising recent ex vivo work has suggested the potential of dual-energy CT (86,87) in reducing blooming artifacts from heavy calcification and metallic stent struts, which may further improve diagnostic accuracy of coronary CT angiography in these patients. Currently, however, the presence of excessive coronary artery calcium, particularly in combination with motion or low signal-noise ratio, continues to reduce the specificity we can obtain in differentiating clinically significant from nonclinically significant coronary artery lesions. Thus, in symptomatic patients with inconclusive results at coronary CT angiography, further evaluation with noninvasive physiologic testing (eg, nuclear myocardial perfusion imaging, ergometric stress testing) is advised so that hemodynamically significant lesions are not missed and the hemodynamic effect of borderline (ie, 30%–70% luminal narrowing [88]) lesions can be assessed. The percentage of patients in whom results at coronary CT angiography are ambiguous and inconclusive has become successively smaller with each new iteration of multidetector CT technology and can be expected to decrease further with coming technical innovations, such as further improvements in temporal resolution, more sensitive detector materials, and more advanced postprocessing techniques.

Beyond Feasibility Testing

Virtually all investigations that compare the diagnostic performance of coronary CT angiography with invasive catheterization have suffered from verification bias, because results have been obtained in

Figure 4

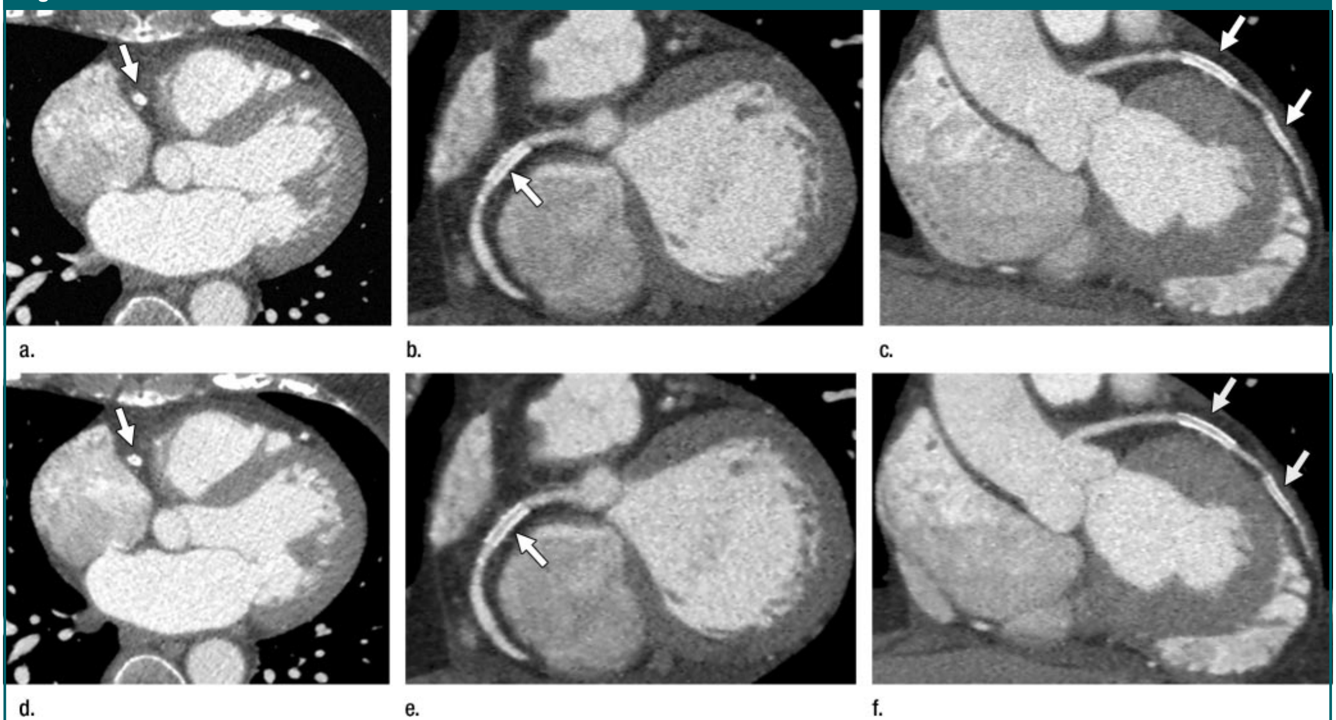


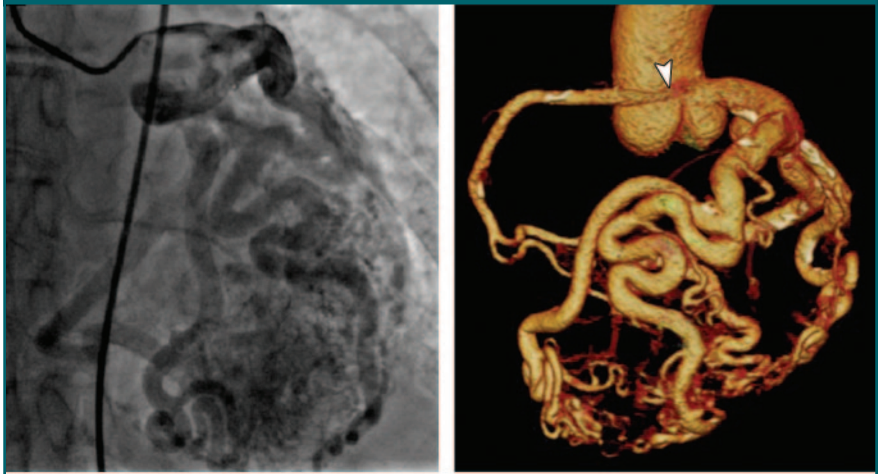
Figure 4: Contrast-enhanced retrospectively ECG-gated dual-source coronary CT angiography in 56-year-old man with body mass index of 34 kg/m^2 after coronary artery stent placement. **(a– c)** Image reconstruction with conventional filtered back projection and **(d–f)** iterative reconstruction with two iterations. **(a, d)** Transverse sections and multiplanar reformations of the **(b, e)** right coronary artery and **(c, f)** LAD show substantial reduction in image noise that corresponds to a potential dose reduction by 50% without loss of resolution, enabling improved visualization of coronary artery stents (arrows).

populations who clinically require invasive work-up and may be different from those in the general population. More recently, the clinical performance in nonselected patient populations has also been investigated (89,90). In a segment-based analysis for detection of significant stenosis (>50%) performed in 40 consecutive individuals, Grosse et al found a sensitivity, specificity, positive predictive value, and negative predictive value of 87%, 99%, 98%, and 95%, respectively. In this study, patient-based analysis demonstrated a negative predictive value of 91% for excluding significant CAD (89). Gaemperli et al (90) prospectively compared the accuracy of 64-section coronary CT angiography with that of technetium 99m tetrofosmin single photon emission computed tomography (SPECT) myocardial perfusion imaging, as the reference standard, for the detection of functionally relevant CAD in 100 consecutive patients. Using a cut-off threshold of 75% or greater area stenosis, these authors found a sensitivity, specificity, negative predictive value, and positive predictive value for the detection of any (fixed and reversible) perfusion defect of 75%, 90%, 93%, and 68%, respectively, on a per-patient basis.

CT for Acute Chest Pain Assessment in the Emergency Department

ECG-synchronized CT is increasingly used to assess patients with acute chest pain for pulmonary embolism, acute aortic syndrome, acute coronary syndrome (the so-called triple rule-out strategy), and other thoracic pathologic conditions with a single examination (52). Even after detailed patient history, physical examination, an ECG, cardiac biomarkers, and cardiac risk stratification (eg, using the Thrombosis in Myocardial Infarction, or TIMI, score [91]), there is a considerable (≈10%) proportion of patients with acute myocardial infarction who are inappropriately discharged from the emergency department. ECG-synchronized CT has been proposed as a means to address this dilemma by rapidly triaging patients for admission, if actionable disease is found, or discharge them on the basis of normal CT findings (92–95).

Figure 5



a. b.

Figure 5: Images in 70-year-old woman with continuous systolic murmur and anterior wall motion abnormality at stress nuclear myocardial perfusion imaging. **(a)** Coronary angiogram (right anterior oblique perspective) was initially obtained and depicted abundant coronary-cameral fistulas; however, the right coronary artery could not be cannulated. **(b)** Contrast-enhanced retrospectively ECG-gated coronary CT angiogram displayed as 3D volume rendering from a left anterior oblique perspective shows the extent of fistulas of the left coronary system and reveals anomalous origin of the right coronary artery (arrowhead) from the left coronary artery cusp.

Figure 6

1. Detection of CAD
    1.1. Acute chest pain in symptomatic subjects
        - Intermediate pretest probability of CAD
        - No ECG changes and serial enzymes negative
    1.2. Evaluation of chest pain syndrome in symptomatic subjects
        - Intermediate pretest probability of CAD
        - ECG uninterpretable or unable to exercise
    1.3. Evaluation of intracardiac structures in symptomatic subjects
        - Evaluation of suspected coronary anomalies
2. Detection of CAD with prior test results
    2.1. Evaluation of chest pain syndrome
        - Uninterpretable or equivocal stress test (exercise, perfusion, or stress echo)
3. Structure and function
    3.1. Evaluation of intra- and extracardiac structures
        - Noninvasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization
    3.2. Morphology
        - Assessment of complex congenital heart disease, including anomalies of coronary circulation, great vessels, and cardiac chambers and valves
        - Evaluation of coronary arteries in patients with new onset heart failure to assess etiology

Figure 6: List of appropriate clinical indications for the performance of coronary CT angiography based on Hendel et al study (54).

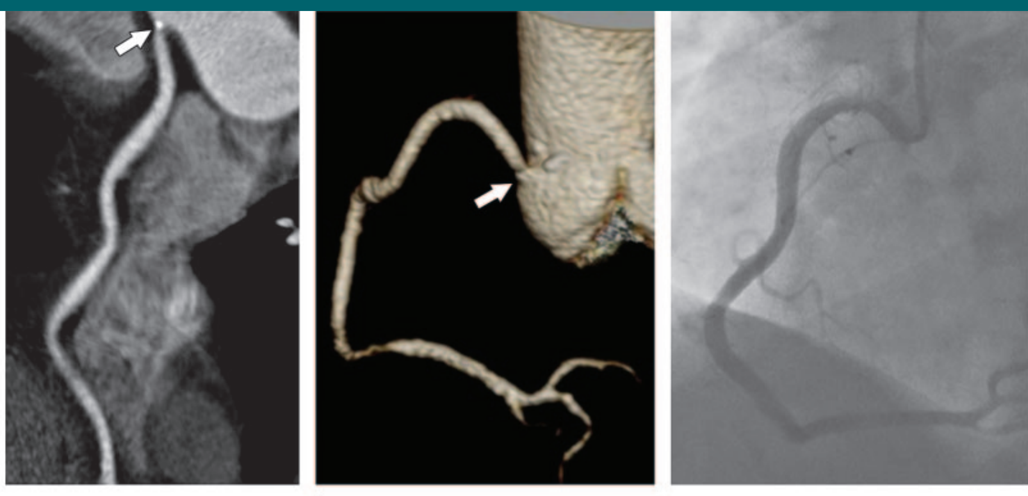
Image acquisition strategies vary depending on whether the scan range includes the entire thorax or is restricted to a dedicated coronary CT angiogram (96). There is also discussion regarding the exact time-point when the CT study should be performed in the work up of patients with acute chest pain. This mainly depends on the risk profile and general presentation of the patient and the local availability of this test. The role of CT in the assessment of acute thoracic disease involving the great vessels such as pulmonary embolism (97–99) and acute aortic syndromes (100,101), as well as other noncardiac causes of acute chest pain, is well established (102). In addition to diagnosing or excluding these diseases, ECG-synchronized CT acquisitions using 64-section CT angiography depict significant coronary artery stenosis, with sensitivity and specificity of 86%–100% and 92%–98%, respectively (66–73,103). CT-based evaluation for significant coronary artery stenosis has been shown to decrease the number of unnecessary hospital admissions without reducing the rates of appropriate admissions (104) by ruling out the absence of acute coronary syndrome (105). The accuracy and safety of CT appear to be at least as good as those of stress nuclear imaging for diagnosing patients with acute coronary syndrome, while time to diagnosis is shortened and costs are potentially reduced (106–108, see below). Finally, coronary CT angiography has been shown to have prognostic value in the acute chest pain setting, with normal findings portending an extremely low risk of future cardiovascular events (109).

Left Ventricular Function

The evaluation of left ventricular function is a crucial component in the assessment of patients with coronary heart disease and has substantial prognostic implications (110,111). CT may also be useful in patients with new decreased left ventricular function to differentiate ischemic from nonischemic causes. Despite the clinical importance of this parameter, CT has never been and likely never will be the primary method for the assessment of cardiac function, even if superiority of CT over echocardiography, scintigraphy, and left ventriculography has been demonstrated (112–114). For the primary assessment of cardiac function, there are less invasive (eg, cardiac ultrasonography [US]) and better (eg, magnetic resonance [MR] imaging [115–117]) technologies available, which should be preferentially used. However, whenever retrospectively ECG-gated coronary CT angiography is performed, the data inherently contain image information across the cardiac cycle, which can be reconstructed and used for analyzing myocardial and valvular motion and for measuring global functional parameters (Fig 8).

While CT-based cardiac function analysis was initially time-consuming and laborious (7), modern postprocessing software allows intuitive cine viewing and rapid quantification of cardiac function parameters (118,119). Initial studies performed with four-row CT underestimated left ventricular ejection fraction (118), primarily due to limited temporal resolution. The increased temporal resolution of 16-row CT improved the accuracy of left ventricular function measurements in comparison with other diagnostic techniques (120–123). The results obtained with modern-era scanners approach the accuracy of cardiac MR imaging (116,117,124) for this application, with slight overestimation of end-systolic volume at multidetector CT when compared with MR imaging, resulting in a systematic underestimation

Figure 7



a. b. c.

Figure 7: Images in 57-year-old man with persistent chest pain despite negative prior conventional angiography findings (heart rate, 79 beats per minute). Contrast-enhanced retrospectively ECG-gated dual-source coronary CT angiogram displayed as **(a)** curved multiplanar reformation and **(b)** 3D volume rendering from right anterior oblique perspective show significant ostial stenosis (arrow) of the right coronary artery due to calcified plaque. This lesion had not been appreciated on **(c)** prior coronary angiogram in straight left anterior oblique projection because the tip of the catheter was advanced beyond the stenosis prior to contrast medium injection.

of left ventricular ejection fraction that ranges from 1% to 7%, especially with earlier generation scanners (118,125–127). In addition to measuring global cardiac function, cine viewing of multiphasic cardiac CT reconstructions enables diagnosis of focal wall motion abnormalities according to the standardized 17-segment model proposed by the American Heart Asssociation (Fig 8) (128). Visual evaluation of wall motion abnormalities at cardiac CT has shown good agreement with cardiac US and MR imaging using four-row (129,130) and 16-row CT (120,131) and has further improved with current scanners (122,132–134). The temporal resolution of CT, however, remains limited compared with that of echocardiography and MR imaging. The recent availability of detector arrays that cover the entire cardiac anatomy, such as 320–detector row scanners (23,24), is expected to further improve the assessment of cardiac function and, more important, permit dynamic time-resolved evaluation of myocardial perfusion, which has, to date, been limited by insufficient detector coverage (28).

Accuracy of 64-Section CT and Dual-Source CT for Detection of Coronary Stenosis in Comparison with Conventional Coronary Angiography (Per-segment Analysis)

Author	Scanner Type	No. of Patients	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Raff et al (67)	64-Section CT	70	86	95	66	98
Leschka et al (66)	64-Section CT	67	94	97	87	99
Mollet et al (69)	64-Section CT	51	99	95	76	99
Fine et al (68)	64-Section CT	66	95	96	97	92
Ropers et al (73)	64-Section CT	81	93	97	56	100
Ehara et al (70)	64-Section CT	69	90	94	89	95
Ong et al (72)	64-Section CT	134	82	96	79	96
Oncel et al (71)	64-Section CT	80	96	98	91	99
Meijboom et al (77)	64-Section CT	360	88	90	47	99
Weustink et al (76)	Dual-Source CT	100	95	95	75	99
Johnson et al (75)	Dual-Source CT	35	88	98	78	99
Leber et al (25)	Dual-Source CT	88	94	99	81	99
Ropers et al (26)	Dual-Source CT	100	92	97	68	99
Brodoefel et al (74)	Dual-Source CT	100	91	92	75	97

Note.—NPV = negative predictive value, PPV = positive predictive value.

Emerging Applications

Coronary Atherosclerotic Plaque Imaging

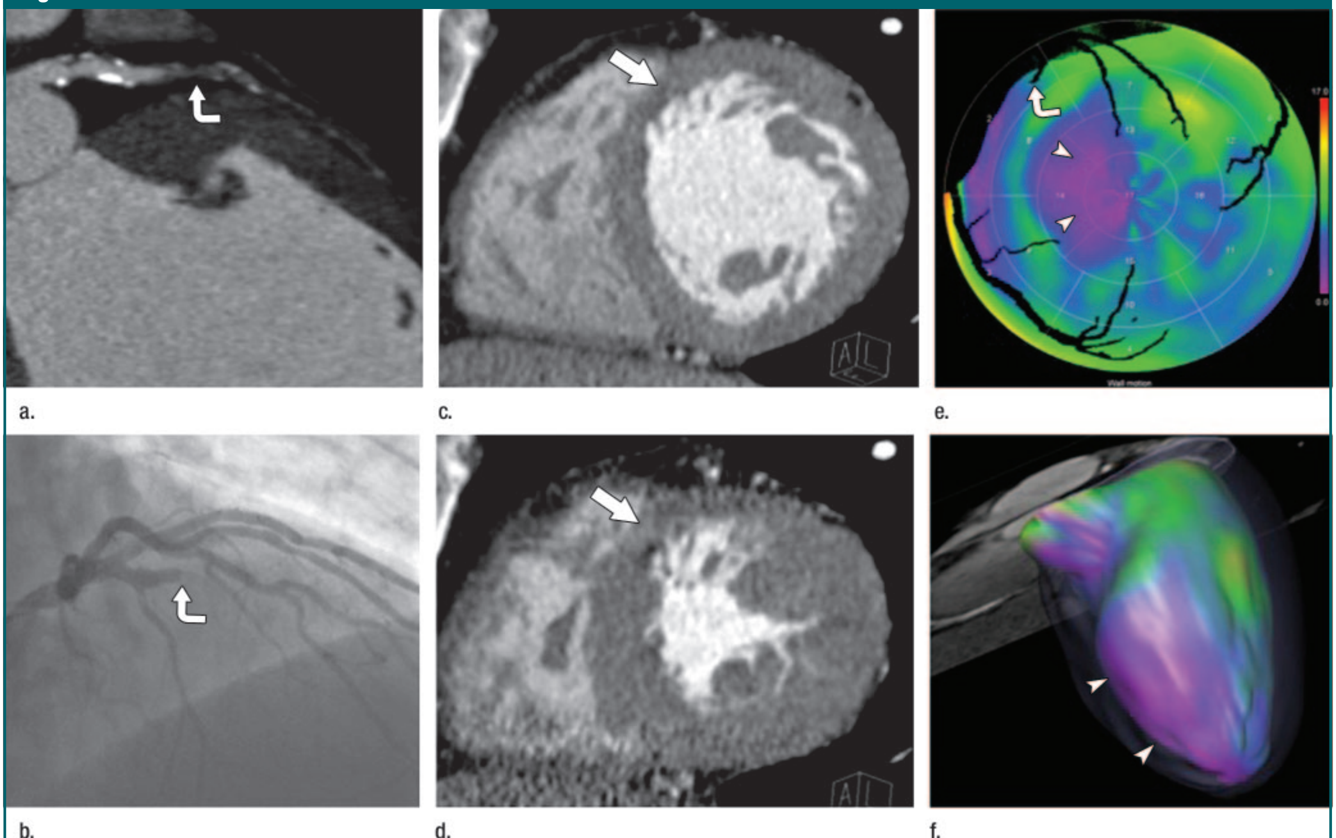
Coronary artery calcium scoring has been used for decades to quantify the calcified atherosclerotic plaque burden (135–137). Despite the recognized limitations of this test (136), it is currently seeing renewed interest as an aid for further cardiovascular risk stratification and risk factor management. Since it has been shown that contrast material–enhanced coronary CT angiography can noninvasively depict calcified and noncalcified atherosclerotic plaque components (138) (Fig 9), there has been intense interest in the evaluation of coronary CT angiography as a tool for risk stratification and for monitoring risk factor management. The rationale behind these efforts is our growing understanding of the relationship between plaque composition and the different clinical manifestations of CAD. It has long been recognized that symptoms of chronic stable angina find their correlate in stenotic, predominantly fibro-calcified lesions (139), whereas the acute coronary syndrome and sudden cardiac death are more likely to be associated with the rupture of previously nonstenotic, predominantly lipid-rich, "vulnerable" plaques (140–142). MR coronary angiography (143) has contributed to our current understanding of these relationships, and coronary artery plaque composition has been studied invasively with intravascular US (144) and more recently with optical coherence tomography (145). The complexity, expense, invasiveness, and limited availability of these modalities make them prohibitive for more widespread clinical application beyond specific clinical scenarios and research. Coronary CT angiography with its high temporal and spatial resolution currently enables coronary artery stenosis detection along with atherosclerotic plaque burden analysis. Significant efforts have been undertaken to investigate and refine plaque detection and characterization based on CT findings (25,146–150). Attenuation-based atherosclerotic plaque characterization at coronary CT angiography has been shown to correlate reasonably well with histologic findings (151). On the basis of ex vivo histopathologic correlation, specific attenuation ranges for different plaque components according to Hounsfield units have been proposed (152).

However, attenuation measurement of coronary artery plaques in vivo is fraught with multiple confounding factors: The small size and irregular shapes of target lesions result in substantial volume averaging. Plaque attenuation is strongly influenced by the contrast medium attenuation in the adjacent coronary lumen (153), and there is substantial overlap in the attenuation ranges of fibrous and lipid-rich plaque types (154). Currently, in routine clinical practice, reliable differentiation of plaque composition beyond that of distinguishing calcified from noncalcified plaque components is very limited. Furthermore, it appears unlikely that in the near future, CT technology will be able to prospectively identify the truly "vulnerable" plaque that is at risk of rupture and cause acute coronary syndrome. Newly developed software algorithms that can volumetrically quantify calcified and noncalcified atherosclerotic plaque components (Fig 10) may permit use of multidetector CT in risk stratification and monitoring therapies designed to manage and reduce risk of major adverse cardiac events (155,156). These algorithms may also help in overcoming previous limitations of plaque burden measurements as noted, for instance, by Leber et al (146), who observed an underestimation of mixed and noncalcified plaque volumes and a trend to overestimate calcified plaque volumes at 64-section CT compared with intravascular US when manual plaque volumetry is used. Furthermore, in this study, the interobserver variability in determining plaque volumes with CT was as high as 37% (146). Newer software applications have reduced interobserver variability (R = 0.885–0.920) for the volumetric assessment of the noncalcified atherosclerotic plaque burden (157).

Myocardial Perfusion and Viability

CT versus other imaging modalities.—There has been ongoing speculation as to whether CT techniques will be able to replace nuclear myocardial perfusion imaging in CAD evaluation and management (158). Several studies have explored the relationship between stenosis at coronary CT angiography and myocardial perfusion defects at nuclear imaging (159–161) and invariably demonstrated relatively weak correlation. On the basis of a figure of merit of 50% or greater stenosis at coronary CT angiography, the sensitivity for detecting reversible myocardial perfusion defects ranged 85%–95% with a specificity of 53%–79% (159,161). Using the same threshold of 50% or greater stenosis, Nicol et al (160) found 87% agreement between coronary CT angiography and myocardial perfusion imaging, whereas this percentage increased to 96% when stenosis of 70% or greater was used. Accordingly, the authors argue that at coronary CT angiography, stenosis of 70% or greater should be used as the criterion to determine functional significance of the lesion (160). The relatively weak correlation between coronary CT angiography and nuclear myocardial perfusion imaging comes as little surprise considering the fundamentally different nature of these tests and the known vari-

Figure 8



a. c. e. b. d. f.

Figure 8: Images in 58-year-old woman with atypical chest pain and abnormal stress test. Contrast-enhanced retrospectively ECG-gated coronary CT angiogram displayed as **(a)** curved multiplanar reformation shows occlusion (arrow) of proximal LAD subsequently confirmed on **(b)** conventional angiogram in right anterior oblique cranial projection. Visual evaluation of **(c)** diastolic and **(d)** systolic multiplanar reconstructions in short-axis view show wall motion abnormality with hypokinesis (arrow) in the anteroseptal left ventricular myocardium. **(e)** A 17-segment polar view map with overlay of the coronary artery tree and **(f)** 3D functional model of the left ventricle also show hypokinetic segments (arrowheads) and normal wall motion in the remainder of the myocardium; **e** with vessel overlay illustrates the anatomic relationship of LAD occlusion (arrow) to myocardial segments with wall motion abnormalities (arrowheads).

ability in the hemodynamic effect of stenotic lesions on myocardial perfusion (90). Nuclear myocardial perfusion imaging is a pure physiologic test aimed at evaluating the myocardial blood supply and provides similar information as exercise stress testing, rest-stress cardiac US, and myocardial perfusion MR imaging. Coronary CT angiography per se is primarily an anatomic, morphologic test to evaluate coronary artery luminal integrity and typically provides information that has traditionally been obtained with coronary angiography. Both, physiologic and anatomic tests are important in the work up of patients suspected of having CAD, for detecting stenosis, and for gauging the hemodynamic effect of lesions on myocardial perfusion. Coronary CT angiography can replace coronary angiography in the appropriate clinical scenario but is a priori complimentary to, and not competitive with, physiologic testing.

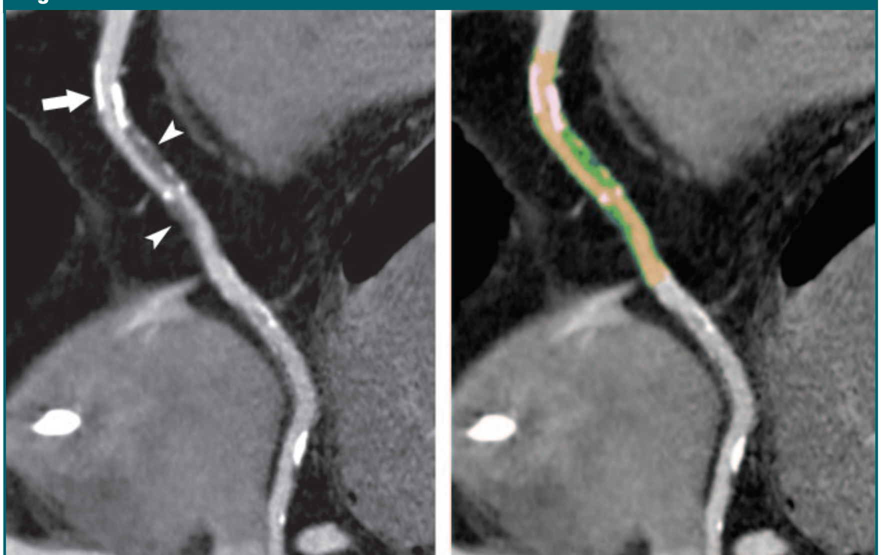
Myocardial perfusion: CT development.—Myocardial perfusion is one of the most important prognostic indicators for patient outcome in the management of CAD (162). The comprehensive assessment of myocardial perfusion from physiologic testing and morphologic evaluation of the coronary arteries by means of image fusion of nuclear imaging and coronary CT angiography has been shown to provide incremental diagnostic value over either technique alone (90,159,163,164). However, obtaining diagnostic information on coronary artery morphology and the status of myocardial perfusion with a single, stand-alone examination remains a coveted goal. Accordingly, there are a number of ongoing investigative efforts to supplement the information on vascular luminal integrity obtained from coronary CT angiography with the assessment of myocardial perfusion and viability. These efforts have their origins in the era of electron-beam CT (165) and the very early days of four-row CT when it was shown in animal models of acute myocardial infarction (166) that hypoattenuating myocardial segments reflect perfusion defects. Recently, these initial observations have been applied in the clinical setting to patients with acute and chronic myocardial infarction (167,168). For example, Nikolaou et al (168) reported a 91% sen-

Figure 9

a. b. c.

Figure 9: Images in 70-year-old woman with atypical chest pain. Contrast-enhanced retrospectively ECG-gated coronary CT angiogram displayed as **(a)** curved multiplanar reformation and **(b)** 3D volume rendering in angiographic setting seen from a caudal left anterior oblique projection show significant stenosis (arrow) in the mid LAD subsequently confirmed on **(c)** conventional coronary angiogram in the same projection. The cross-sectional nature of coronary CT angiography reveals the completely noncalcified nature of the culprit lesion (arrow in **a**).

Figure 10



a. b.

Figure 10: Contrast-enhanced retrospectively ECG-gated coronary CT angiography in 63-year-old man with atypical chest pain. **(a)** Curved multiplanar reformation shows 50% stenosis of the mid right coronary artery caused by predominantly noncalcified plaque (arrowheads), as well as more proximal nonobstructive calcified plaque (arrow). **(b)** Color-coded characterization and volumetry of atherosclerotic plaque components performed by using a dedicated plaque analysis and quantification algorithm. Low-attenuation, medium-attenuation, and calcified plaque components are differentiated and displayed in dark green, light green, and pink, respectively. Intravascular contrast material is displayed in orange.

sitivity, 79% specificity, and 83% accuracy for the CT detection of myocardial infarct. More recently, initial reports have shown good correlation between dual-energy CT (see above) and SPECT nuclear myocardial perfusion imaging for detecting decreases in the myocardial blood supply (33) (Fig 11). Since dual-energy CT data can be postprocessed in different ways to provide routine morphologic information on vascular luminal integrity, as well as the status of the myocardial blood supply (Fig 11), this modality allows detection of obstructive CAD while simultaneously providing information on the hemodynamic effect of detected lesions on myocardial perfusion from a single dual-energy CT acquisition.

Efforts are underway to apply the principles of nuclear rest-stress myocardial perfusion imaging for CT applications. Preclinical studies (32,169) investigating CT image acquisition under adenosine-induced stress demonstrate the feasibility of detecting reversible ischemia and accurately measuring myocardial blood flow during first-pass contrast-enhanced CT. On the basis of this preclinical evidence and emerging human investigations, it is conceivable that adenosine stress CT may provide similar information about the status of the myocardial blood supply as does stress nuclear myocardial perfusion imaging, while at the same time enabling the assessment of coronary artery morphology (Fig 12). George et al (170) recently performed a pilot study using adenosine stress 64- and 256-row CT in 40 patients with abnormal myocardial perfusion SPECT findings. They compared the combination of coronary CT angiography and rest-stress CT myocardial perfusion imaging to detect hemodynamically significant stenosis, with the combination of rest-stress SPECT and quantitative coronary angiography as the reference standard. These authors reported 86% sensitivity, 92% specificity, 92% positive predictive value, and 85% negative predictive value on per-

Figure 11

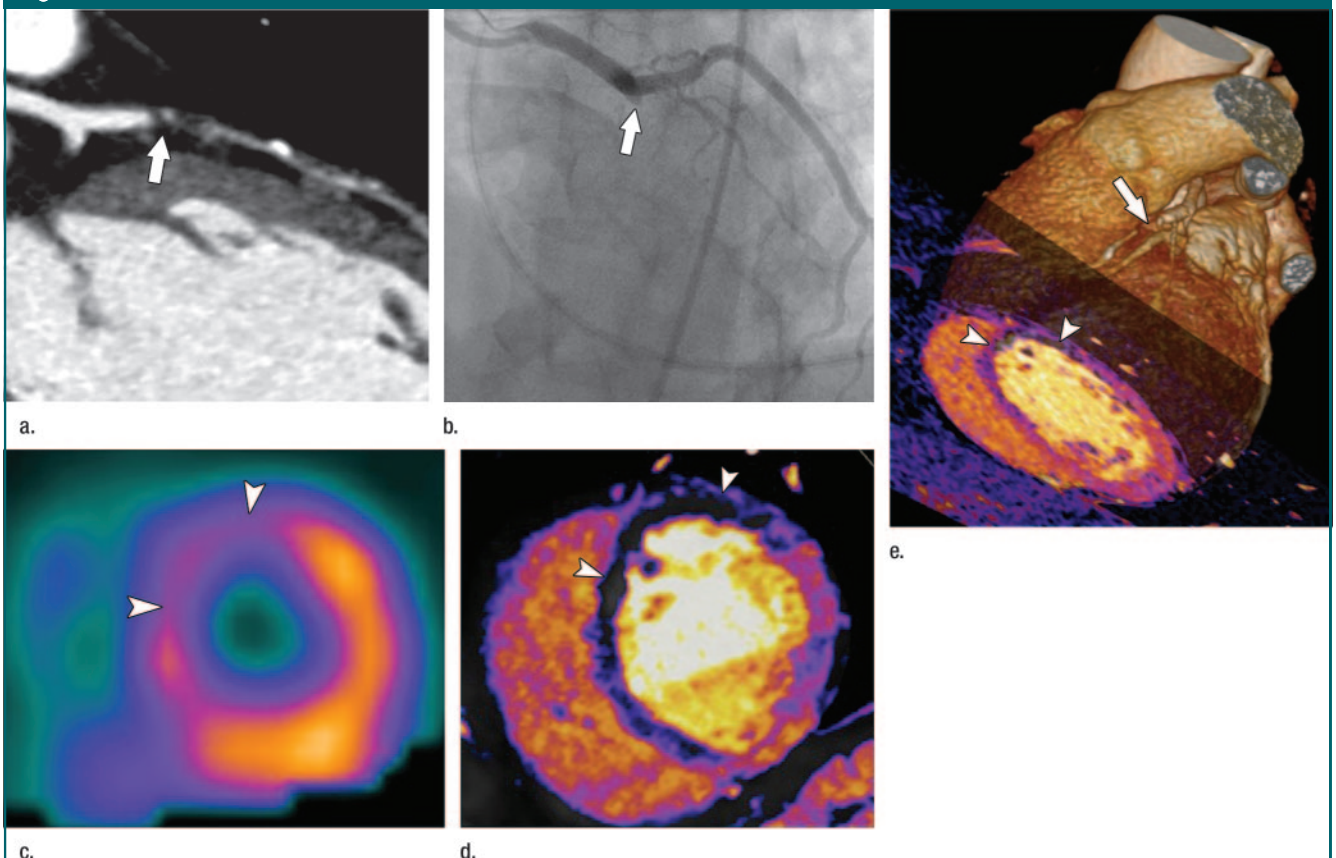


Figure 11: Images in 58-year-old woman with atypical chest pain and prior abnormal stress test. Contrast-enhanced retrospectively ECG-gated dual-source coronary CT angiogram obtained with dual-energy technique and displayed as **(a)** curved multiplanar reformation shows occlusion (arrow) of the mid LAD, which is subsequently confirmed at **(b)** invasive coronary catheterization in left anterior oblique caudal projection. **(c)** Prior rest perfusion SPECT in short-axis view shows corresponding fixed perfusion defect (arrowheads) in the anteroseptal myocardium. Dual-energy reconstruction of the same CT scan displayed in **(d)** short-axis view and as **(e)** 3D volume rendering from a caudal left anterior oblique perspective show corresponding lack of iodine-based contrast material in the anteroseptal left ventricular wall (arrowheads in **d**); **e** illustrates the anatomic relationship of LAD occlusion (arrow) to myocardial segments with decreased blood supply (arrowheads).

Figure 12

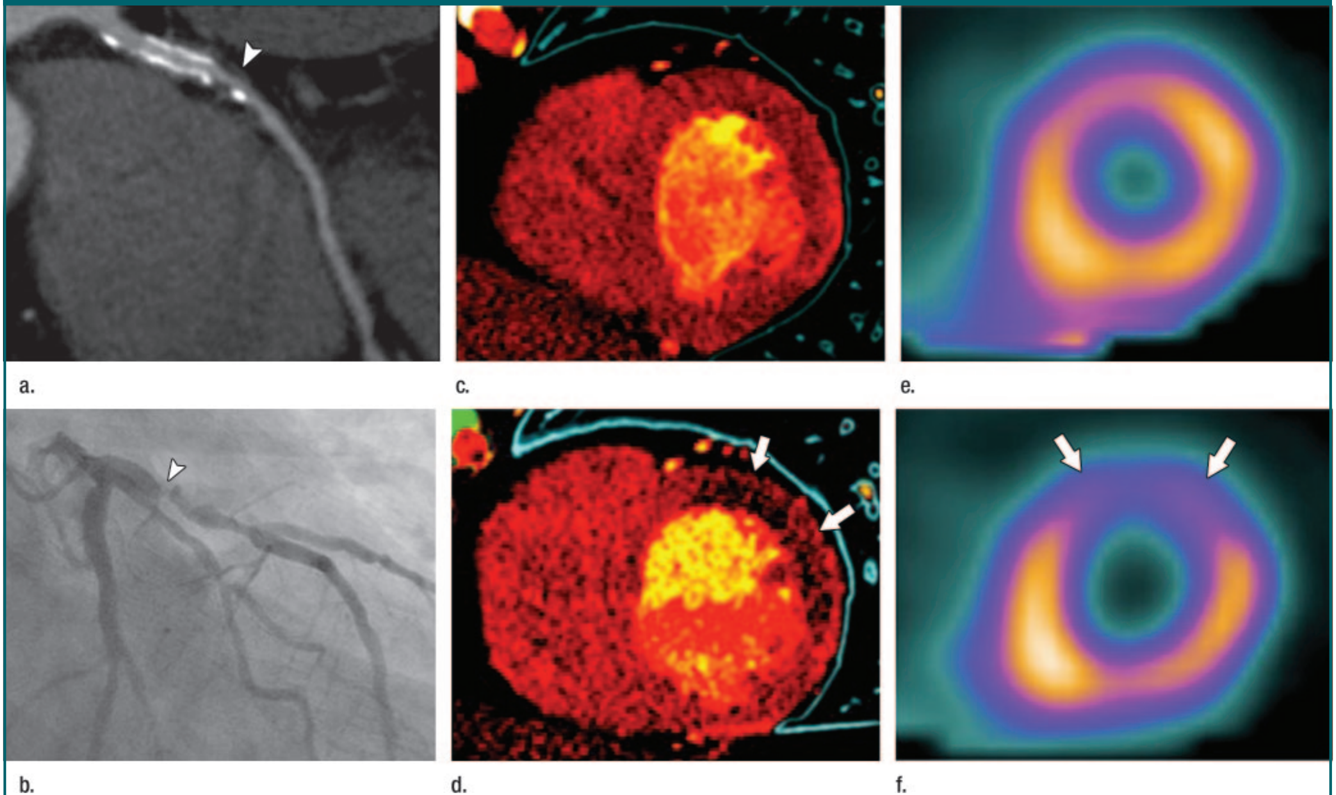


Figure 12: Contrast-enhanced retrospectively ECG-gated rest-stress dual-source coronary CT angiography performed with dual-energy technique at rest in 58-year-old man with prior LAD stent implantation, atypical chest pain, and abnormal stress test. **(a)** Curved multiplanar reformation of the rest CT scan shows patent LAD stent but complex, predominantly noncalcified lesion (arrowhead) just distal to the stent, subsequently confirmed at **(b)** conventional angiography in right anterior oblique cranial projection. **(c)** Dual-energy reconstruction of the same rest CT scan displayed in short-axis view shows unremarkable left ventricular iodine distribution at rest. **(d)** Repeat dual-energy CT scanning during adenosine-induced hyperemia shows decreased blood supply (arrows) in the anterolateral left ventricular myocardium. Findings are in good correlation with prior SPECT myocardial perfusion images acquired at **(e)** rest and **(f)** stress, which show reversible perfusion defect in the same myocardial area (arrows).

patient analysis and 79% sensitivity, 91% specificity, 75% positive predictive value, and 92% negative predictive value on per—vessel territory analysis. In this study, the estimated mean effective radiation dose was 21.6 mSv for combined rest and stress 256-row CT imaging and 16.8 mSv for 64-row stress CT examinations.

Myocardial viability.—The determination of myocardial viability with nuclear imaging (171) and MR imaging (172) is playing an increasing role in predicting the success of revascularization therapy. Myocardial viability has traditionally been assessed by using nuclear techniques (173,174), and more recently, MR imaging, which is now considered the clinical reference standard (172,175,176). Delayed contrast-enhanced imaging with MR detects accumulation of gadolinium-based chelates in areas of myocardial necrosis after infarction (177). The same principle may apply to cardiac CT (Fig 13), since iodine-based intravenous contrast material has similar kinetics as gadolinium. It has repeatedly been shown in animal models that CT can depict iodine accumulation in areas of irreversibly damaged myocardium (178,179). CT has been shown to correlate well with delayed-enhancement MR imaging during the different stages of infarction, enabling assessment of reperfused infarction during acute, subacute, and chronic stages (180,181) and accurate determination of transmural involvement (182). In humans, delayed-enhancement CT also correlates well with delayed-enhancement MR imaging, even though CT systematically underestimates the true infarct size as compared with MR imaging (168,183–185).

So far, there is no universal agreement on the most suitable protocol for delayed-enhancement CT imaging. Some studies indicate that the highest difference in contrast attenuation between a normal and infarcted myocardium occurs 5 minutes after intravenous iodinated contrast material injection (178); however, intervals of up to 15 minutes after contrast material injection have been proposed. Low kilovoltage (eg, 80 kVp) protocols for delayed-enhancement CT imaging have been shown to result in better iodine contrast differentiation (186). The calculated additional radiation exposure from performing delayed enhancement CT for assessment of myocardial viability is approximately 3.8 mSv in female and 2.8 mSv in male patients (183).

The efforts at further refining cardiac CT into a technique that can assess coronary artery anatomy, function, perfusion, and viability are likely to continue and intensify. The effectiveness of these efforts in challenging the role of traditional physiologic testing remains to be seen. However, patient evaluation with a single, noninvasive modality is likely to provide safer and cheaper evaluation with less radiation than the routine combination of nuclear myocardial perfusion imaging and conventional angiography currently needed to obtain this information.

Coronary CT Angiography in a Changing Health Care Environment

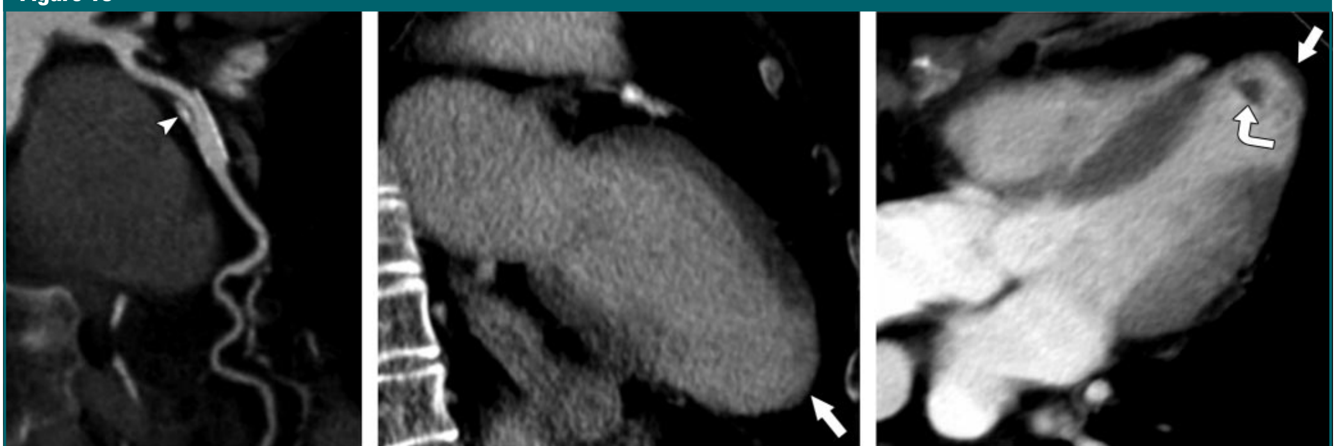
Emerging Data about Outcome and Prognosis

As coronary CT angiography is increasingly becoming a clinical tool in widespread use, we note substantial growth of the evidence base regarding outcomes and prognostic value of this test. There is evidence that the extent and severity of CAD defined at coronary CT angiography predicts all-cause mortality. In a consecutive cohort of more than 1000 symptomatic patients older than 45 years of age, disease markers obtained at coronary CT angiography could identify increased risk for all-cause death, whereas a negative coronary CT angiogram portended an extremely low risk (79). In another cohort of 100 patients undergoing coronary CT angiography, the extent and severity of CT markers of CAD during 16-month follow-up was closely associated with the occurrence of major cardiac events, while the excellent prognosis in patients with a normal test result was confirmed (82). A recent study (81) documented the safety of ruling out coronary artery stenosis solely on the basis of a normal coronary CT angiogram and showed a concomitant reduction in conventional coronary catheterizations. In a cohort of more than 1000 consecutive symptomatic outpatients who were initially managed solely on the basis of coronary CT angiography findings, there were only two patients in whom significant stenosis was detected at subsequent coronary catheterization during 6-month clinical follow-up (187). Clinical outcomes over a 9-month follow-up in almost 2000 patients who underwent coronary CT angiography were no different from those of a matched cohort of more than 7000 patients undergoing SPECT (188). The results of these studies are consistent with the high negative predictive value of a normal coronary CT angiogram, which has been consistently demonstrated in the early investigations and strongly supports the potential role of coronary CT angiography as a frontline test in the diagnostic algorithm of CAD.

Evolution of Cardiovascular Disease Management

The paradigm for CAD management is undergoing pivotal transitions. For the longest time, percutaneous coronary intervention with coronary artery stent placement had been one of the most rapidly growing procedures in medicine, while the number of coronary artery bypass surgeries was steadily declining (1). Controversy remains as to whether patient outcome is better with percutaneous or with surgical revascularization (189–193). With the availability of ever more refined and potent pharmaceutical

Figure 13



a. b. c.

Figure 13: Contrast-enhanced retrospectively ECG-gated dual-source coronary CT angiography in a 49-year-old woman with previous inferoapical infarct and prior LAD stent placement. **(a)** Curved multiplanar reformation shows mild proximal in-stent re-stenosis (arrowhead) of the LAD stent due to intimal hyperplasia. Multiplanar reformations of delayed, low-radiation-dose repeat CT acquisition after 6 minutes displayed as **(b)** two-chamber long-axis and **(c)** three-chamber views show delayed enhancement (straight arrow) of the infarcted inferoapical myocardium, as well as formation of a layered apical thrombus (curved arrow) as an incidental finding.

agents, however, medical therapy is emerging as a formidable contender to invasive therapies for CAD management. One of the most publicized recent testimonies to this development is the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial (194). This investigation and prior work (195–197) support the notion that the outcome of patients with chronic angina does not differ with optimal medical treatment compared with percutaneous coronary intervention. Although the design and conclusions of these trials have predictably been challenged (198,199), the paradigm of optimal medical treatment as the core of CAD management is increasingly gaining support. For the first time since their introduction, we see slowed growth or even decline of coronary artery stent-placement procedures (200). Use of medical therapy as part of a program of primary and secondary prevention and improvements in screening and risk stratification have widely been credited with the current sharp downward trend in cardiovascular disease mortality (1). Efforts are ongoing to further improve this approach by identifying new markers and developing new strategies for ever finer risk stratification and disease prevention. The current renaissance of coronary artery calcium scoring is reflective of the desire for more sensitive methods of identifying at-risk individuals and for customizing the aggressiveness of risk modification. As outlined above, coronary CT angiography is the only noninvasive modality that enables appreciation of the entire coronary atherosclerotic plaque burden (Fig 10). The atherosclerotic plaque burden is the substrate of all coronary events, for example, stable angina in the presence of heavily calcified stenotic lesions (142) or acute coronary syndrome due to sudden rupture of predominantly noncalcified plaque (201). The current evidence base does not justify the use of coronary CT angiography for population-based screening of asymptomatic individuals for coronary atherosclerosis (54). However, the above considerations along with ongoing technical refinement (eg, lower radiation dose) and emerging data (82,202) on the prognostic implications of plaque composition at coronary CT angiography may suggest that select asymptomatic high-risk (ie, those with a dismal combination of multiple risk factors) individuals could benefit from finer risk stratification by determining the extent and phenotype of their entire coronary atherosclerotic disease burden to help determine the appropriate level of aggressiveness of medical risk management and its success (203).

Cost-effectiveness

Initial reports demonstrate that coronary CT angiography is particularly cost-effective in symptomatic subjects with low and intermediate pretest probability of obstructive disease (204), which supports this indication as appropriate (51–55). In their study, Dewey et al (204) concluded that for patients with a 10%–50% pretest likelihood of CAD, coronary CT angiography was the most cost-effective approach, whereas in individuals with a likelihood for disease above 60%, conventional catheterization remains the most effective first line test. Several investigations highlighted the cost-effectiveness advantage of coronary CT angiography over nuclear myocardial perfusion imaging (80,188). A recent analysis of Medicare category III transaction codes showed a reduction of 27% in adjusted total health care costs and of 33% in disease-specific expenditures when coronary CT angiography was used instead of SPECT (188).

In the assessment of patients with acute chest pain, all analyses available to date demonstrate substantial savings when CT is integrated in the diagnostic algorithm (107,108,205,206). Compared with the standard of care work-up, significant reductions in the length of hospital stay and cost-savings ranging from the hundreds to thousands of dollars per patient have been reported (107,108). Khare et al (206) used a computer model to estimate the cost-effectiveness of coronary 64-section CT angiography in the emergency department compared with an observation unit stay that included stress ECG or stress echocardiography for the evaluation of low-risk patients with chest pain in the emergency department. According to their analysis, the thresholds where coronary CT angiography constituted a cost-saving strategy compared with the conventional work-up were the cost of CT of less than \$2097, the cost of observation unit care of more than \$1092, and a prevalence of CAD of less than 70% (206), again emphasizing the impact of pretest likelihood on cost-effectiveness. In a randomized controlled trial of coronary CT angiography for evaluation of acute chest pain, Goldstein et al (107) investigated 203 individuals with acute chest pain in the emergency department. The authors found that CT evaluation reduced the time to diagnosis compared with the standard of care (3.4 hours vs 15.0 hours) and lowered costs (\$1586 vs \$1872). The use of CT in the triage of patients with acute chest pain has been shown to be particularly cost-effective in women, who traditionally present a greater challenge for the diagnostic work-up of acute chest pain than men (205). For example, Ladapo et al observed that coronary CT angiography was cost-saving in women under a wide variety of model assumptions (205).

Thus, rapidly accumulating evidence-based data increasingly support that coronary CT angiography, if used according to established guidelines (54), is cost-effective. The increasing recognition of the utility of this test as a core component in the work-up and management of CAD can benefit patients and the health care system as a whole.

Conclusion

In summary, current technical limitations, especially the association of coronary CT angiography with relatively high levels of radiation, will be increasingly addressed by ongoing refinements in technology. Along with an increasing evidence base, guidelines for appropriate indication are in place and are evolving to ensure appropriate use, curb overutilization, and ensure cost-effectiveness. New technologies and new applications are constantly being explored and are widening the scope of coronary CT angiography over mere coronary artery assessment to the complete analysis of cardiac morphology, function, perfusion, and viability. Considering all of the above, we believe that there can be no doubt over the rapidly expanding role and growing importance of coronary CT angiography.

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