Growing Evidence for Coronary Computed Tomography Angiography as a First-line Test in Stable Chest Pain

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Abstract: Coronary computed tomography angiography (CCTA) is a validated technique for the evaluation of patients with suspected coronary artery disease, showing high accuracy compared with invasive coronary angiography and high negative predictive value. CCTA is also well positioned as a first-line test for the evaluation of stable chest pain. This purpose of this review is to examine the evidence behind CCTA in the setting of stable chest pain, with attention to 5 key strengths of a CCTA-based approach: (1) effective gatekeeping to cardiac catheterization, (2) selective discrimination for revascularization and tailored medical therapy, (3) advanced risk stratification, (4) improvement in outcomes, and (5) support from multisociety guidelines. Given the expansion of CT technologies to include functional strategies for evaluating ischemia both with and without vasodilators, CCTA is poised to become the comprehensive examination for stable chest pain and anginal equivalent cardiopulmonary symptoms.

Key Words: cardiac computed tomography, coronary computed tomography angiography, Stable chest pain

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KEY POINTS

- Coronary computed tomography angiography (CCTA) is a robust strategy for the evaluation of stable chest pain, and should be incorporated into diagnostic algorithms on the basis of the 2016 NICE, 2013 ESC, or 2012 ACC/AHA guidelines.
- CCTA should be considered to guide the therapeutic management of patients with stable chest pain.
- Functional strategies such as CT myocardial perfusion (CTP) and fractional flow reserve CT (CT-FFR) should be considered for further evaluation of ischemia in patients with intermediate stenosis on CCTA.

Cardiovascular disease is the leading cause of death in the world. Globally, deaths due to ischemic heart disease increased by 16.6% from 2005 to 2015 and accounted for 15.2 million deaths in 2015.[1] CCTA is a validated technique for the evaluation of patients with low to intermediate pretest probability for coronary artery disease (CAD), showing high accuracy compared with invasive coronary angiography (ICA) and high negative predictive value.[2–4] Large-scale registry data also underscore the prognostic value of CCTA for identifying obstructive and nonobstructive CAD.[5] Although recent randomized trials show a cost benefit and faster time-to-discharge using CCTA in the emergency department,[6–8] CCTA is also well positioned as a first-line test for the evaluation of stable chest pain. The purpose of this review is to examine the evidence behind CCTA in the setting of stable chest pain, with attention to 5 key strengths of a CCTA-based approach: (1) effective gatekeeping to cardiac catheterization, (2) selective discrimination for revascularization and tailored medical therapy, (3) advanced risk stratification, (4) improvement in outcomes, and (5) support from multisociety guidelines.

CCTA IS AN EFFECTIVE GATEKEEPER TO CARDIAC CATHETERIZATION

Previous work by Patel et al[9] has shown that only 37.6% of elective cardiac catheterizations reveal obstructive CAD. This suggests a low diagnostic yield ICA. As such, better strategies for risk stratification are needed to increase the diagnostic yield of cardiac catheterization in clinical practice. An ideal gatekeeper to cardiac catheterization would prevent unnecessary catheterizations, and correctly identify indicated invasive procedures. In light of its ability to provide a reliable anatomic roadmap of the coronary arteries and also serve as a noninvasive functional test, CCTA is well suited as a gatekeeper to the cath laboratory.

CCTA is the only noninvasive imaging modality that can provide an accurate anatomic view of the coronary arteries. Several previous studies have shown high accuracy of CCTA, particularly high sensitivity and negative predictive value for obstructive CAD.[3,4,10] For example, in the ACCURACY study,[4] the sensitivity, specificity, positive predictive value, and negative predictive value of 64-row cardiac CT for detecting > 70% stenosis were 91%, 84%, 51%, and 98%, respectively, using quantitative coronary angiography as the reference standard. In the CORE64 trial,[3] the receiver operating characteristic (ROC) area for cardiac CT was 0.93 using quantitative coronary angiography as the reference standard. CCTA also similarly predicted revascularization within 30 days as invasive angiography (ROC area 0.84 vs. 0.82 for CCTA and QCA, respectively).

More recently, CCTA has shown promise as a noninvasive functional test, potentially offering a higher level of precision for intermediate coronary stenosis for which there is no clear definition of who would benefit from revascularization. As a stand-alone imaging approach, noninvasive functional testing for myocardial ischemia, either in the

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TABLE 1. Summary of Functional Strategies With CT

Technique	Types	Strengths	Limitations
CTP	Static or dynamic Single or dual energy	Functional evaluation of coronary stenosis (hemodynamic significance) Reclassification of stenotic lesions Can perform well in heavily calcified lesions or stents More cost effective than SPECT	Additional radiation Additional contrast Higher cost than conventional CCTA alone Not widely available Requires expertise Not ideal in balanced ischemia
CT-FFR	Heartflow (off-site) Vendor-based algorithms (on-site)	Functional evaluation of coronary stenosis (hemodynamic significance) Can be derived from a routine CCTA without changing protocol No additional radiation or contrast Reduces number of negative invasive coronary angiographies Overall, lower cost compared with ICA-guided care Improved outcomes Can evaluate balanced ischemia Useful in multivessel or serial lesions Has potential for evaluating biomechanical features of plaques	Not widely available Requires good-quality image acquisition Not ideal in stents, bypass grafts, or extensive calcium Commonly sent off-site for postprocessing with long turnaround times Potentially additional cost involved with the most commonly available algorithm Lower accuracy in those with borderline CT-FFR values (0.7-0.8) Lower performance in nonculprit lesions of recent STEMI

form of exercise stress electrocardiography, stress echocardiography, single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), or stress cardiac magnetic resonance (CMR), has limited sensitivity and specificity for obstructive CAD, with ~16% false positives and 16% false negatives irrespective of the imaging approach.[11] Simultaneous visualization of coronary anatomy and ischemia/functional testing may offer the best chance to reach an acceptable level of precision to improve patient care, leveraging the strong negative predictive value of CCTA in low to intermediate risk patients and the higher specificity and positive predictive value of functional imaging in intermediate to high risk patients. Two emerging functional CT strategies include CTP and CT-FFR (Table 1).

CTP is a MPI technique that measures the amount of iodine contrast present within the myocardium, allowing one to create an attenuation map of the left ventricle analogous to a SPECT perfusion map.[12] Stress CTP was originally pioneered by George et al[13] in 2006 and has since been validated against SPECT,[14] stress CMR, and invasive FFR.[15] In the multicenter CORE320 trial,[12] CCTA plus stress CTP was compared against the combination of SPECT MPI and ICA. The presence of coronary stenosis > 50% on CCTA plus a perfusion defect on CTP predicted flow-limiting stenosis defined by stenosis > 50% on ICA plus a perfusion defect on SPECT (ROC, 0.87). Using revascularization as the reference standard, CCTA-CTP also performed similar to ICA-SPECT (ROC, 0.72 vs. 0.76, $P = 0.13$).[12] Compared with CCTA alone, Magalhaes et al[16] reported the combination of CCTA and stress CTP improved specificity of flow-limiting stenosis from 63% to 79% among patients with no previous CAD. In a substudy of CORE320 that compared stress CTP head-to-head against SPECT MPI,[17] stress CTP showed higher sensitivity for CAD in patients with left main and multivessel disease while maintaining similar specificity, suggesting that CTP may be a better gatekeeper to revascularization.

CT-FFR is a computational fluid dynamics modeling technique that can be applied to a CCTA dataset for estimating lesion-specific functional information of a coronary stenosis without requiring any protocol modifications.[18] FFR-CT has high diagnostic performance when compared against invasive FFR as the reference standard. For example, in DISCOVER-FLOW,[18] CT-FFR yielded 82% specificity and 74% positive predictive value, with incremental improvement in accuracy over CCTA alone (84% vs. 59%). In the follow-up NXT[19] validation study comparing CT-FFR against invasive FFR in 251 patients with CCTA stenosis between 30% and 90%, CT-FFR yielded 81% accuracy and 79% specificity. More importantly, CT-FFR correctly reclassified 68% of false-positive patients as true negatives, highlighting the potential role of CT-FFR as a gatekeeper to cardiac catheterization. In the PLATFORM trial, a strategy involving CT-FFR reduced the number of ICAs showing no obstruction by 83%.[20] In a meta-analysis by Danad et al,[21] CT-FFR showed high sensitivity (85% to 93%) and moderate specificity (65% to 75%) compared with invasive FFR, and the authors concluded that CT-FFR in combination with CCTA could significantly improve diagnostic specificity provided the coupling of anatomic and functional measures.

CCTA CAN GUIDE REVASCULARIZATION AND THERAPEUTIC DECISION-MAKING

Another advantage of CCTA for the evaluation of stable chest pain is its utility for guiding therapeutic decision-making and revascularization in the setting of stable ischemic heart disease (SIHD). The goals of revascularization are to improve survival among patients at high risk, and to improve symptoms among patients already receiving optimal medial therapy. Proper selection for revascularization is important as these procedures may do more harm than good for certain patients. Previous work by Chan et al[22] showed that 12% of nonacute PCIs are considered "inappropriate" by multisociety guidelines and 72% of "inappropriate" cases show low-risk ischemia on noninvasive stress testing.

Over the past several decades, numerous trials have examined the clinical benefits of revascularization in the setting of SIHD. In the COURAGE trial,[23] 2287 patients with SIHD were randomized to either PCI or optimal

medical therapy, and PCI did not reduce the hard endpoints of death or myocardial infarction. However, PCI did reduce angina during long-term follow-up at 1 year and 3 years, but not at baseline or at 5 years. Critics of the COURAGE trial point to a much higher compliance rate for optimal medical therapy than can be expected in clinical practice. In addition, PCI was associated with greater reduction in myocardial ischemia on nuclear MPI compared with optimal medical therapy alone, and the rate of death or myocardial infarction was lower among patients with ischemia reduction $\geq 5\%$ versus no ischemia reduction. In the FAME2 trial,[24] patients with stable CAD who were scheduled for PCI (documented FFR ≤ 0.80) were randomized 1:1 to either PCI plus medical therapy versus medical therapy alone, and revascularization was associated with lower combined death, myocardial infarction, and urgent revascularization at 12 months, suggesting that invasive FFR-guided PCI improves outcomes.

Recent randomized trials suggest an advantage of CCTA for more appropriate selection of patients who require revascularization over functional testing. In the SCOT-HEART trial,[25] CCTA led to a change in planned investigations among 15% of patients compared with 1% of patients in the functional testing arm ($P < 0.001$), including planned investigations such as ICA that were cancelled, and new investigations ordered. In the PROMISE trial (PROspective Multicenter Imaging Study for Evaluation of chest pain), there was a modest trend toward increased revascularizations among patients undergoing CCTA compared with functional testing, with a hazard ratio of 1.293 ($P = 0.005$). Similar trends were also observed in SCOT-HEART[25] and Min et al.[26] However, CCTA reduced the number of ICA studies showing normal coronaries, with a hazard ratio of 0.396 in SCOT-HEART[27] and 0.800 in PROMISE.[28] In parallel, CCTA increased the diagnostic yield for obstructive CAD at catheterization, with a hazard ratio of 1.293 ($P = 0.005$). With respect to medical therapy, SCOT-HEART showed a change in treatment among 23% of patients in the CCTA arm compared with 5% in the standard-of-care arm. This included increases in the use of preventive therapy (statins, aspirin) when atherosclerosis was identified and cancellations of preventive and antianginal therapy with normal coronaries. Min et al[26] also demonstrated an increased use of aspirin and statins among patients undergoing CCTA. These results are not surprising as CCTA, unlike functional testing, has the ability to identify nonobstructive atherosclerosis and prompt earlier preventive measures.

CCTA IS A VALUABLE TEST FOR RISK STRATIFICATION AND PROGNOSIS

Although functional testing only identifies patients with advanced stenosis, CCTA can identify patients with both nonobstructive and obstructive CAD. The unique ability of CCTA to stratify patients across the full spectrum of coronary plaque burden allows it to serve as a useful tool for risk stratification. Data from the CONFIRM registry show that patients with nonobstructive and obstructive CAD have incrementally higher rates of mortality, whereas the absence of atherosclerosis is associated with a very favorable prognosis.[5] In fact, patients with extensive nonobstructive CAD have higher rates of adverse cardiovascular events than patients with less extensive, but obstructive disease (14.5% vs. 13.6%), underscoring the prognostic value of plaque burden only available with CCTA.[29]

Anatomic testing with CCTA also allows for the evaluation of plaque morphology. This includes identification of high-risk plaque features such as positive remodeling, low-attenuation plaque, spotty calcification, and the napkin-ring sign. In a sample of 3158 patients who underwent CCTA and were followed prospectively, Motoyama et al[30] showed that high-risk plaque was an independent predictor of acute coronary syndrome beyond significant stenosis. Similarly, in a sample of 4415 outpatients with stable chest pain from the PROMISE trial, Ferencik et al[31] showed that high-risk plaque on CCTA was independently predictive of future MACE, and that adding high-risk plaque to the atherosclerotic cardiovascular disease risk score and significant stenosis led to a continuous net reclassification improvement of 0.34. In a recent systematic review and meta-analysis of 13 studies comprising 13,977 patients, Nerlekar et al[32] reported that the presence of 2 or more high-risk plaque features on CCTA carried the highest risk of future MACE, with a pooled hazard ratio of 9.17 ($P < 0.001$).

CCTA IMPROVES OUTCOMES

Recent large, randomized-controlled trials suggest an improvement in clinical outcomes for the evaluation of stable chest pain with a CCTA strategy compared with functional testing (Table 2). In PROMISE (PROspective Multicenter Imaging Study for Evaluation of chest pain),[28] 10,003 symptomatic patients with stable chest pain were randomized to CCTA or functional testing, which included exercise stress electrocardiography, stress echocardiography, or nuclear MPI. In SCOT-HEART (Scottish Computed Tomography of the HEART),[27] 4146 outpatients with suspected angina due to CAD were randomized to CCTA plus standard-of-care or standard-of-care alone. The CAPP trial[33] (Cardiac CT for the Assessment of chest Pain and Plaque) randomized 500 patients with stable chest pain to CCTA or exercise stress electrocardiography, and Min et al[26] randomized 180 patients to CCTA or nuclear MPI.

Using a pooled population of 14,817 patients from the aforementioned trials, Bittencourt et al[34] carried out a meta-analysis of clinical outcomes after the evaluation of SHID by CCTA. The results were significant for a 31% relative risk reduction in the rate of MI using a CCTA strategy. In a post-hoc analysis of the SCOT-HEART trial that excluded the median time to treatment alteration (50 d), there was a 50% reduction in fatal and nonfatal MI within the CCTA group ($P = 0.020$). In the PROMISE trial, a CCTA strategy also yielded a lower number of deaths and nonfatal MI within a 12-month follow-up period in the PROMISE trial ($P = 0.049$).[28] However, CCTA performed similar to functional testing with respect to the primary endpoint of composite all-cause mortality, MI, hospitalization for unstable angina, and major complications of cardiovascular procedures and testing ($P = 0.75$). In a separate case-control observational study by Budoff et al,[35] 4244 symptomatic patients who underwent CCTA were matched with 1706 patients who underwent standard-of-care at a university cardiology clinic. After a mean follow-up of 80 months, the mortality rate was significantly lower in the CCTA group (4.2% vs. 10.8%, $P < 0.001$). Multivariate analysis further showed a 32% risk reduction with CCTA ($P = 0.0001$).

The effects of CCTA on subsequent symptoms are mixed. In SCOT-HEART, no difference in symptoms at 6 weeks was observed between CCTA with standard-of-care and standard-of-care alone.[25] PROMISE also identified no

TABLE 2. Randomized-controlled Trials of CCTA Versus Functional Testing: Summary of Design and Key Findings

Trial	Study Design	Key Findings
PROMISE[25]	10,003 patients CCTA vs. functional (exercise stress ECG, stress echo or nuclear MPI) Median follow-up 25 mo	No significant difference in the primary composite endpoint over 2 y (all-cause mortality, MI, unstable angina, postprocedural complications) (3.3% vs. 3%, $P=0.75$) Lower (by 33%) secondary endpoint of number of deaths and nonfatal MI in 12 mo with CCTA ($P=0.049$) Higher diagnostic yield on cath with CCTA (72.1% vs. 47.5%) Fewer false-positive invasive caths with CCTA (3.4% vs. 4.3%, $P=0.022$) No significant difference in symptoms over 2 y Higher cost at 90 d by $254 with CCTA Increased revascularization with CCTA (6.2% vs. 3.2%, $P<0.001$)
SCOT-HEART[23,24]	4146 patients CCTA plus standard of care vs. standard of care (exercise ECG) alone Median follow-up 1.7 y	Higher reclassification of diagnosis of angina because of CAD at 6 weeks with CCTA (23% vs. 1%, $P<0.0001$) Higher reclassification of diagnosis of CAD with CCTA (27% vs. 1%, $P<0.0001$) Higher change of planned investigations with CCTA (15% vs. 1%, $P<0.001$) Higher change of treatment with CCTA (23% vs. 5%, $P<0.001$) No difference in symptom severity at 6 weeks or subsequent hospital admission for chest pain Almost-significant decrease in fatal, nonfatal MI over 1.7 y (38% lower, $P=0.0527$) Post hoc analysis (excluding median time to treatment alteration) 50% reduction in fatal and nonfatal MI with CCTA (17 vs. 34, $P=0.020$), > 50 d after implementation of preventive therapy Lower MACE at 20-mo follow-up with CCTA Higher cost with CCTA by $462 ($1900 vs. $1438)
CAPP[31]	500 patients CCTA vs. functional (EST) 243 CT, 245 EST Median follow-up 12 mo	No difference in MACE Improvement in angina stability and quality of life domains at 3 and 12 mo follow-up with CCTA Lower mean time to management with CCTA Lower number of additional investigations with CCTA Lower ER visits and cardiac admissions with CCTA
Min et al[26]	180 patients CCTA vs. functional (SPECT MPI). Median follow-up 55 d	No MACE in either group Comparable improvement in angina-specific health status with CCTA Increased use of ASA (22% vs. 8%, $P=0.04$) and statins (7% vs. −3.5%, $P=0.03$) with CCTA Similar noninvasive cardiac imaging tests Lower total cost with CCTA ($781.08 vs. 1214.58, $P<0.001$) Lower radiation dose with CCTA (7.4 vs. 13.3 mSv, $P<0.0001$)

CAPP indicates cardiac CT for the assessment of chest pain and plaque; EST, exercise stress test; SCOT-HEART, Scottish Computed Tomography of the Heart; SOC, standard of care.

significant difference in the symptoms between CCTA and functional testing over a 2-year follow-up period.[28] However, the CAPP trial observed a larger improvement in angina using CCTA (vs. exercise stress electrocardiography) at both 3 and 12 months.[33]

No cost advantage from CCTA was observed among the randomized trials. In fact, CCTA was associated with a small increase in costs: in PROMISE, the mean cost difference at 90 days was $254 higher with CCTA, likely driven by the increased use of ICA and revascularization within the CCTA arm.[28] However, after 90 days, the mean cost difference between CCTA and functional testing was small and remained similar through 3 years of follow-up.[36] In SCOT-HEART, the mean cost difference at 6 months was $462, which was attributed directly to the higher costs of CCTA.[27] In an observational cohort study using Medicare claims data of fee-for-service beneficiaries aged 66 years or older, beneficiaries who underwent CCTA were more likely to undergo subsequent invasive cardiac procedures and have higher CAD-related spending than patients who underwent stress testing.[37]

CCTA IS SUPPORTED BY MULTISOCIETY GUIDELINES

Evaluation of stable chest pain with CCTA is now supported by several multisociety guidelines (Table 3). Perhaps the strongest endorsement for CCTA comes with the 2016 National Institute for Health and Care Excellence (NICE) Clinical Guidelines 95, recommendations on the appropriate evaluation of stable chest pain within the National Health Service in the United Kingdom.[38] The 2016 NICE guidelines offer CCTA as a first-line test to all patients with stable chest pain presenting with typical or atypical angina. Functional testing in the form of exercise stress electrocardiography or stress imaging is reserved for patients with positive CCTA findings of uncertain functional significance or nondiagnostic CCTA exams. Unlike other multisociety guidelines and appropriate use criteria, the 2016 NICE guidelines make no attempt to calculate the pretest probability for CAD, endorsing CCTA for everyone with angina. NICE's cost utility analysis showed that CCTA was clearly the most cost-effective first-line strategy for the evaluation of stable chest pain compared with ICA, nuclear MPI, echocardiography,

TABLE 3. Summary of Current Guidelines for Evaluation of Stable Chest Pain[11,39–41]

Guideline	CCTA Recommended for Screening Asymptomatic Patients?	CCTA Recommendation(s) for Stable Chest Pain	Not Recommended	Additional Diagnostic Investigations
National Institute for Health and Care Excellence (NICE), 2016[1]	Not recommended	CCTA is the first-line test for patients with typical or atypical angina	Do not use MR coronary angiography for diagnosing stable angina	Offer noninvasive functional imaging for ischemia if CT has shown CAD of uncertain functional significance or is nondiagnostic Offer invasive coronary angiography as a third-line investigation when noninvasive functional imaging is inconclusive
American College of Cardiology/American Heart Association et al (ACC/AHA) 2012[2]	Class III (no benefit): CCTA is not recommended to assess risk in asymptomatic patients with no evidence of ischemia on noninvasive testing	Class I: Patients who survived sudden death or life-threatening ventricular arrhythmia should undergo CCTA to assess cardiac risk Patients who develop heart failure should be evaluated to determine whether CCTA should be performed for risk CCTA is recommended if clinical characteristics and results of noninvasive testing indicate a high likelihood of severe ischemia Class IIA: CCTA is reasonable in patients who have depressed LV function (EF < 50%) and moderate-risk criteria on noninvasive testing with demonstrable ischemia Coronary angiography is reasonable to further assess risk in patients inconclusive prognostic information after noninvasive testing or in patients for whom noninvasive testing is contraindicated or inadequate Coronary angiography for risk assessment is reasonable for patients who have unsatisfactory quality of life due to angina, have preserved LV function (EF > 50%), and have intermediate-risk criteria on noninvasive testing	Class III (no benefit): CCTA for risk assessment is not recommended in patients who elect not to undergo revascularization or who are not candidates for revascularization CCTA is not recommended to further assess risk in patients who have preserved LV function (EF > 50%) and low-risk criteria on noninvasive testing CCTA is not recommended to assess risk in patients who are at low risk according to clinical criteria and who have not undergone noninvasive risk testing	Complex discussion of other scenario-specific diagnostic methodologies
European Society of Cardiology (ESC) 2013[3]	Class III: CCTA is not recommended as a "screening" test in asymptomatic individuals without a clinical suspicion of coronary artery disease	Class IIa: CCTA should be considered as an alternative to stress imaging techniques for ruling out stable CAD in patients within the lower range of intermediate	Class III: CT coronary calcium scoring is not recommended to identify individuals with coronary artery stenosis CCTA is not recommended in patients with previous	Complex discussion of other scenario-specific diagnostic methodologies

TABLE 3. (*continued*)

Guideline	CCTA Recommended for Screening Asymptomatic Patients?	CCTA Recommendation(s) for Stable Chest Pain	Not Recommended	Additional Diagnostic Investigations
		pretest probability for CAD in whom good image quality can be expected CCTA should be considered in patients with lower to intermediate pretest probability for stable CAD after nonconclusive exercise ECG or stress imaging or who have contraindications to stress testing, if diagnostic image quality can be expected	coronary revascularization	
American College of Cardiology (ACR) Appropriateness Criteria Chronic Chest Pain—Low to intermediate probability of Coronary Artery Disease[4]	Not covered in document	CCTA, SPECT MPI, stress MRI, and Stress Echo are in the "usually appropriate" category (category scores 7, 8, 9)	MRI without stress perfusion, Calcium scoring "usually not appropriate" (category scores 1, 2, 3)	Echocardiography and invasive angiography "may be appropriate" (category scores 4, 5, 6)

MRI indicates magnetic resonance imaging.

and CMR.[39] In fact, economic modeling determined that the cost of CCTA would have to triple to no longer remain the most cost-effective initial investigation. However, critics of NICE question the relevance of CCTA for patients at a higher pretest probability of significant CAD. Within this population, CCTA has a lower negative predictive value and may result in greater downstream testing.[2]

Within the US, the American College of Cardiology (ACC) and American Heart Association (AHA) 2012 multisociety guidelines for the diagnosis and management of patients with SIHD retain exercise stress electrocardiography as a first-line test.[40] As a second-line test, CCTA was given a Class IIA (level of evidence C) rating for the evaluation of patients with intermediate pretest probability of CAD who have continued symptoms with previous normal test findings, inconclusive results from previous exercise or pharmacologic stress testing, or are unable to undergo stress imaging with nuclear MPI or echocardiography.

The 2013 European Society of Cardiology (ESC) guidelines on the management of stable CAD[11] also retain exercise stress electrocardiography as the initial test for establishing a diagnosis of CAD (class I, level of evidence B), with stress imaging recommended as the initial test if supported by local expertise and availability. CCTA is recommended as a second-line test in patients with lower pretest probability or equivocal functional testing in whom good image quality can be expected (class IIA, level of evidence C). Further, CCTA is endorsed for patients within the lower range of intermediate pretest probability after a nonconclusive exercise stress electrocardiogram or stress imaging, or contraindications to stress imaging to avoid ICA, assuming that fully diagnostic image quality can be expected (class IIA, level of evidence C). The 2013 ESC guidelines, 2016 NICE CG95, and 2012 ACC/AHA guidelines all do not recommend CCTA as a screening test in asymptomatic patients without a clinical suspicion of CAD.

CONCLUSIONS

In summary, mounting evidence from large-scale registries and randomized trials support CCTA as a first-line test for the evaluation of stable chest pain in appropriately selected patients. CCTA has proven value as an effective gatekeeper to cardiac catheterization, a guide for revascularization and tailored therapeutic decision-making, a valuable risk stratification tool, and a strategy for improving outcomes. Multisociety guidelines have endorsed CCTA for the evaluation of stable ischemic heart disease, including the updated 2016 NICE guidelines, which now advocate for CCTA as a first-line test in all patients with angina and suspected CAD. As advances in CT technology continue to expand, including functional strategies such as CTP and CT-FFR, CCTA may soon become a "one-stop" comprehensive examination for CAD.

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