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Cardiac CT vs. Stress Testing in Patients with Suspected Coronary Artery Disease: Review and Expert Recommendations

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Abstract

Diagnosis and management of coronary artery disease represent a major challenge to our health care systems affecting millions of patients each year. Until recently, the diagnosis of coronary artery disease could be conclusively determined only by invasive coronary angiography. To avoid risks from cardiac catheterization, many healthcare systems relied on stress testing as gatekeeper for coronary angiography. Advancements in cardiac computed tomography angiography technology now allows to noninvasively visualize coronary artery disease, challenging the role of stress testing as the default noninvasive imaging tool for evaluating patients with chest pain. In this review, we summarize current data on the clinical utility of cardiac computed tomography and stress testing in stable patients with suspected coronary artery disease.

Keywords

Coronary heart disease; cardiac computed tomography angiography; stress imaging; myocardial perfusion imaging; single-photon-emission tomography

Introduction

Cardiovascular diseases, and particular, coronary artery disease (CAD), remain the leading cause of death worldwide with an enormous burden on health care systems [1]. Annually, more than 10 million stress tests and approximately one million diagnostic cardiac catheterizations are being performed in the U.S. alone [1]. Total costs of cardiovascular disease and stroke in the U.S. for 2015 are estimated to exceed 320 billion dollars [1]. Management of CAD requires an accurate diagnosis. For many decades, invasive coronary angiography (ICA) has served as the gold standard for the diagnosis of CAD despite many well recognized limitations of this seasoned technology [2;3]. To avoid risks from cardiac catheterization in low-intermediate risk patients, we have been using myocardial stress testing as gatekeeper for invasive angiography. The emergence of multi-detector computed tomography technology has allowed to noninvasively assess the presence, location, severity, and characteristics of coronary atherosclerotic disease in patients. In recent years, an abundance of clinical studies revealed data on the diagnostic and prognostic performance of

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cardiac computed tomography angiography (CCTA), challenging the role of stress testing as the default noninvasive test for patients presenting with non-acute chest pain. In this paper, we review current data on the clinical utility of CCTA vs. stress testing in stable patients with suspected CAD.

Stress Testing for the Diagnosis of Coronary Artery Disease

Numerous studies and meta-analyses reported accuracy of stress testing for the diagnosis of CAD as defined by the gold standard of cardiac catheterization [4–7]. Without imaging, the sensitivity of an exercise treadmill test for detecting CAD is only modest, i.e. approximately 70%, while specificity is good (75–80%) [6]. Adding myocardial imaging to standard exercise testing increases sensitivity for detecting CAD. Single-photon-emission-computed-tomography (SPECT) is the most commonly used imaging adjunct to exercise testing in the US. In meta-analyses, exercise SPECT yields sensitivity and specificity of 87% and 64% vs. 82% and 75% when combined with pharmacologic 'stress' [4;8]. Stress echocardiography is used less frequently than SPECT in the US. In a meta-analysis, sensitivity and specificity for stress echocardiography was 85% and 77% compared to 80% and 84% with dobutamine [4;8]. Overall, combined stress testing with imaging yields similar diagnostic performance for either SPECT or echocardiography, with sensitivity and specificity of approximately 80–90% and 70–80%, respectively [9]. Remarkably, very few data are available from multi-center analyses using independent core laboratories. In general, multi-center data provide more realistic data on diagnostic test performance and typically reveal lower accuracies compared to the less rigorous analyses by specialized, single centers [10]. Furthermore, multicenter studies commonly require prospective enrollment and reduce inflation of sensitivity through referral or verification bias [11–13]. Recently, SPECT was compared to magnetic resonance imaging (MRI) in three multicenter studies revealing only modest accuracy for detecting CAD, with area under the curve (AUC) between 0.67–0.69 [14–16]. These results from studies with strong methodology suggest that the diagnostic accuracy of stress testing reported by less well conducted single-center studies – and widely disseminated in analyses and practice guidelines – may be overestimated and may therefore not reflect clinical practice.

CCTA for the Diagnosis of Coronary Artery Disease

Diagnostic accuracy of CCTA in stable patients with suspected CAD has been tested in numerous single center studies [17–19]. In meta-analyses, diagnostic accuracy of CCTA for identifying CAD in patients yielded AUC between 0.97–0.99. Pooled sensitivity ranges between 98–99%; specificity between 82–89% [17;18]. There are also several multicenter studies that reported AUCs of 0.93–0.96 for 64-slice detector technology among patients with a different CAD risk characteristics [20–22]. The rigorously performed CORE-64 study [23] revealed an AUC of 0.93 for detecting ≥ 50%, with sensitivity of 85% and specificity of 90%. A recent meta-analysis of 89 studies – including single and multicenter studies – reported a mean sensitivity of 0.97 (95% CI 0.96–0.98) and mean specificity of 0.87 (0.85–0.90) for detecting obstructive CAD [24]. The diagnostic accuracy data for CCTA have been largely consistent among studies when patient characteristics and methodology were considered [20]. In general, single center results yield somewhat greater accuracy compared

to multicenter studies due to the aforementioned reasons. In addition, sensitivity and specificity vary slightly from study to study because of readers specific thresholds, while predictive values may exhibit larger differences owing to their dependence on disease prevalence in the study population [20]. Even an accurate test will see decreasing negative predictive values if disease prevalence is high [20]. Furthermore, severe coronary calcification leads to decreased diagnostic accuracy for CCTA because of lower specificity. Yet, overall diagnostic performance remains excellent even when including patients with high calcium scores [20].

Direct Comparison of Stress Testing to CCTA for the Diagnosis of CAD

Fewer data are available on the diagnostic performance of stress testing and CCTA in direct comparison. In a review of 7 small clinical studies, CCTA yielded a sensitivity of 96% vs. 66% by SPECT [9]. In a meta-analysis evaluating 11 studies with 1,575 patients, which also included data from 16-slice CT technology, the investigators found a pooled sensitivity for CCTA vs. exercise electrocardiography and SPECT of 98% (95% CI: 93% to 99%) vs. 67% (95% CI: 54% to 78%) ($p<0.001$) and 99% (95% CI: 96% to 100%) vs. 73% (95% CI: 59% to 83%), respectively. The pooled specificity of CCTA was 82% (95% CI: 63% to 93%) vs. 46% (95% CI: 30% to 64%, $p<0.001$) for exercise electrocardiography, and 71% (95% CI: 60% to 80%) vs. 48% (95% CI: 31% to 64%, $P=0.14$) for SPECT [25]. However, the retrospective study design and lack of core laboratory analysis in these studies render their results inconclusive. Recently, data were presented from the CORE320 multicenter study on a direct comparison of CCTA and SPECT revealing significantly greater accuracy for CCTA with an AUC of 0.91 vs. 0.69 [26]. Similar to the single center results from direct comparisons, sensitivity was markedly superior for CCTA (92%) compared to SPECT (62%) in this rigorously performed analysis. Furthermore, the diagnostic accuracy for SPECT was in line with data from the multicenter CE-MARC study, i.e., consistent with studies using meticulous methodology, but deviant from results obtained in specialized SPECT centers without core laboratory analysis. In support of the findings from multicenter studies, the CATCH study reported a positive predictive value for CCTA to diagnose CAD of 71% vs. only 36% for standard care using stress testing [27]. In the SCOT-HEART multicenter study [28], 9,849 patients with stable chest pain were randomized to two groups, CCTA plus standard of care and standard of care alone, and were followed for a mean of 1.7 years. At 6 weeks, CCTA resulted in reclassification of CAD diagnosis in 558 (27%) patients vs. 22 (1%) in standard of care group ($p<0.0001$). Furthermore, the greater number of patients identified with CAD led to changes in preventative measures and to a 38% reduction in fatal and non-fatal myocardial infarctions ($p=0.0527$). Table 1 summarizes the diagnostic accuracy of CCTA vs. stress testing.

Prognostic Value of Stress Testing

There is abundant information on patient prognosis associated with stress test results. Most data derive from the nuclear medicine literature. In a meta-analysis with an average follow-up period of 22 and 20 months for pharmacological and exercise stress tests, respectively, the annualized rate of myocardial infarction and cardiac death was 0.65% for patients who had a normal exercise SPECT but 1.78% for a normal pharmacologic SPECT [29].

Conversely, adverse event rates were 4.30% in patients with abnormal exercise SPECT and 9.98% with abnormal pharmacologic SPECT results. In low risk patients, a negative exercise test alone – without imaging -is associated with excellent prognosis as seen in 1,461 patients with a low-risk Duke Treadmill Score [30]. Exercise capacity adds to the imaging information with stress testing [31]. SPECT results were also evaluated for risk assessment in several large clinical studies. However, all these analyses were performed post-hoc and thus, are inflicted with the associated limitations. In a COURAGE substudy, there was greater 5-year survival without myocardial infarction in patients with vs. without myocardial ischemia reduction; however there were no statistically significant differences after risk adjustment [32]. In a second COURAGE imaging substudy, the investigators found similar 7-year event rates regardless of the extent of ischemia by SPECT or treatment assignment (medical therapy alone or PCI) [33]. In the BARI 2D SPECT substudy, the percent ischemic myocardium was not significantly associated with outcome [34]. In the STICH imaging substudy, the presence of ischemia by SPECT or echocardiography did not predict outcome [35]. In the DIAD study of CAD screening using SPECT in 1,123 asymptomatic patients with type II diabetes, abnormal stress testing results were predictive of adverse events but did not improve patient outcome [36].

Prognostic Value of CCTA

Within a few years, a large body of literature has been published on the diagnostic value of CCTA. While most data report intermediate follow up times – similar to the nuclear medicine literature – a few long term studies are also available. In a large meta-analysis, the association of cardiac events with CAD evaluation by 64-slice or greater CCTA was analyzed [37]. The study consisted of more than 82,000 patient-years with over 2,000 ‘hard’ events. The analysis showed a robust association between cardiac death or MI, all-cause mortality and composite MACE, and the presence and severity of CAD by CCTA. Conversely, in 38% of patients with normal CCTA findings, annualized rate of myocardial infarction or cardiac death was only 0.04% [37]. The presence of non-obstructive disease in 1/3 of patients was associated with significantly higher cardiac death or MI, all-cause mortality and composite MACE in this group compared with patients without detected CAD by CCTA (odds ratio of 6.41 [95% CI, 2.44 to 16.84]). In addition, all-cause mortality incrementally increased with CAD severity [37]. In a study with long term follow up (mean of 80 months) in 4,244 symptomatic patients who underwent CCTA, mortality was 4.2% vs. 10.8% in 1706 patients who underwent standard of care [38]. In a study assessing long term follow up after a normal CCTA, the annual rate of major adverse events was 0.9% [39]. The CONFIRM registry followed 24,775 patients who underwent ≥64-detector row CCTA for a median of 2.3 years for the occurrence of death [40]. While a normal CCTA was associated with 0.28% annualized mortality rate, hazard ratios progressively increased for nonobstructive CAD, obstructive 1-vessel, 2-vessel, 3-vessel or left main disease with 1.62 (95% CI: 1.20 to 2.19; p=0.002), 2.00 (95% CI: 1.43 to 2.82; p<0.0001), 2.92 (95% CI: 2.00 to 4.25; p<0.0001), 3.70 (95% CI: 2.58 to 5.29; p<0.0001) respectively.

CCTA versus Stress Testing for the Prognosis of CAD

Only few studies directly compared CCTA vs. stress testing for CAD prognosis. In a study of 541 patients who underwent both CCTA and SPECT and were followed for a median of 672 days, CCTA analysis resulted in incremental prognostic value over SPECT for total mortality. The annualized mortality rate was 1.1 % in patients with normal SPECT results compared to 0.3% in patients with normal CCTA [41]. In another study, outcome of patients after CCTA (n=693) was compared to that after SPECT (n=3,067) using a matched cohort comparison study design, reporting similar annual mortality rates for CCTA (1.16%) and SPECT (1.13%) [42]. In the SPARC study [43], the 2-year-event rate for nonfatal myocardial infarction and death was 0.7% for CCTA, 1.6% for SPECT, and 5.5% for positron emission tomography (PET) in 1,703 patients with suspected CAD. In a study by Shreibati et al. in 8,820 patients undergoing CCTA and 132,343 patients with stress testing, CCTA was associated with a 40% reduction in acute myocardial infarction rates after 6 months follow up [44]. Seven non-randomized studies comprising 216,603 patients with a mean follow-up period of 20 months revealed an odds ratio for myocardial infarction of 0.53 (95% CI, 0.39–0.72, P< 0.001) for CCTA vs. exercise ECG/SPECT testing [45]. Table 2 summarizes the prognostic accuracy of CCTA vs. stress testing in different studies.

Patients Management Based on Stress test and CCTA results

Available data suggest for CCTA to yield greater diagnostic and prognostic information in patients with suspected CAD compared to stress testing but it remains unclear if such information translates into improved patient outcome. Intuitively, detection of non-obstructive CAD by CCTA is an important advantage over stress testing as it may trigger appropriate preventative measures and associated reduced rates of adverse advents [46]. However, because of the relatively low event rates in this population, surveillance of many patient years is required to demonstrate such effect. Indeed, several studies showed trends to lower myocardial infarction rates with CCTA guidance of management compared to the traditional approach with stress testing. In the SPARC study, the use of aspirin and lipid-lowering agents was higher following normal/non-obstructive CCTA findings when compared with SPECT [47]; similar results were found in other studies for use of aspirin and lipid-lowering medication [48–50]. In the SCOT-HEART study, myocardial infarction rates were strongly trending lower with the CCTA guided management compared to the traditional approach using stress testing [28]. The recently completed PROMISE trial [51] randomized 10,003 patients with stable chest pain to either a management strategy using CCTA or functional tests. Patients were of low-intermediate pretest probability for obstructive CAD. The investigators found similar, low event rates after 25 months of follow-up in both groups (3.3% and 3% for CCTA and functional testing group respectively) but significantly lower rates of myocardial infarction and cardiac death in the CCTA group at 12 months (hazard ratio, 0.66; 95% CI, 0.44 to 1.00; p=0.049).

Cost Considerations

Several studies indicated greater downstream utilization of resources after CCTA use compared to traditional approaches. This may not be surprising since CCTA is more

sensitive for detecting CAD than stress testing. A more sensitive test will diagnose a greater number of patients with disease who in turn will require more resources. On the other hand, CCTA also yields lower false positive rates than stress testing which may lower the rate of unnecessary referrals for cardiac catheterization. The relevant questions are if 1) the test utilization is appropriate and 2) if the test utilization is associated with better outcome. The latter typically requires longer follow up which is rarely given in contemporary studies. In an interesting analysis, Neilson et al. investigated the impact of frontline exercise stress testing vs. CCTA on downstream test utilization in low to intermediate risk symptomatic patients [52]. The authors found lower rates of downstream testing in the CCTA group compared with stress testing with fewer uses of cardiac catheterization. In a large retrospective cohort study for the diagnosis of CAD [48], economic outcome of CCTA (1,938 patients) was compared with stress testing (matched 7,752 patients). The results suggested adjusted total healthcare and CAD expenditures to be 27% and 33% lower, respectively, for patients who had CCTA compared with patients who had stress testing. In another retrospective observational study [53], one year costs for CAD management and clinical outcomes in individuals without known CAD who had CCTA (1,647 patients) were compared with matched patients (6,588 patients) who had stress testing. CCTA testing was associated with lower healthcare costs by 25.9% and lower probability of downstream testing and revascularization compared with stress testing. In another study, health care costs were lower in CCTA group (n=1,647) compared to SPECT (n=6,588), with similar rates of myocardial infarction and CAD-related hospitalization [53].

Overall, an approach of initial CCTA testing in patients with suspected CAD appears to be cost effective if it is chosen for the right patients, i.e., of intermediate pretest probability of CAD. Hulten et al. [54] estimated 15–23% cost savings with the use CCTA vs. routine care for the overall population but found that CCTA cost exceeded that of routine care if the prevalence of obstructive CAD is greater than 28%. Shreibati et al. [55] performed a retrospective, observational cohort study using claims data from a 20% random sample of 2005–2008 Medicare fee-for-service beneficiaries aged >65 years with no claims for CAD in the preceding year, who received non-emergent, noninvasive testing for CAD (n=282,830) and compared CCTA with stress testing. CCTA was associated with higher likelihood of cardiac interventions and total healthcare spending. On the other hand, there was a trend towards lower adverse event rates with the CCTA strategy. Another recent study evaluated the two-year costs in patients undergoing CCTA, PET and SPECT reporting lower costs for SPECT imaging than CCTA or PET, primarily because of fewer subsequent invasive procedures [43].

New Technologic Developments

There have been significant advancements in SPECT and CT technology in the last few years. Improvements for SPECT included better software and image reconstruction algorithms, e.g., iterative reconstruction, resolution recovery, and noise compensation algorithms, leading to lower radiation doses and better image quality [56]. Introduction of a new generation of gamma camera systems, which utilizes semiconductor detectors of cadmium zinc telluride (CZT) [57], has led to faster acquisition time, lower radiation dose (about 1 mSv for a single injection) with preserved or higher image quality compared to

conventional myocardial perfusion imaging by SPECT [58;59]. Limited experience exists at this time in regards to the clinical experience with these improvements as these technologies are not widely available. Attenuation correction algorithms, on the other hand, are becoming increasingly prevalent at major medical centers. Several studies demonstrated improved specificity for the diagnosis of CAD in patients using attenuation correction, while sensitivity is similar to uncorrected SPECT [60; 61].

For CCTA, the last few years saw large reductions in radiation dose, particularly, due to prospective scan triggering and iterative reconstruction algorithms, which may lead to submillisievert doses while maintaining acceptable image quality [62]. CT innovations that are at the brink of clinical use include CT myocardial stress perfusion imaging (CTP), CT derived Fractional Flow Reserve (FFR), and transluminal attenuation gradient (TAG) CT analysis. The combination of CCTA and CTP has increased diagnostic accuracy of CCTA for the diagnosis of hemodynamically significant coronary stenosis [63–65]. CT myocardial stress perfusion imaging has recently been shown to be more accurate than SPECT for the diagnosis of CAD [66]. Combining CTA and CTP yielded and AUC of 0.87 for predicting CAD by conventional angiography which was associated with a corresponding myocardial perfusion defect by SPECT [67]. A different approach is the use of computational flow dynamics analysis of conventional CCTA data to predict pressure gradients (FFR) in the coronary arteries [68]. The application of CT-FFR has been evaluated in several studies demonstrating good diagnostic performance compared to invasively derived FFR [69–71]. However, the long and remote analysis required for CT-FFR currently presents an obstacle to clinical use. Another promising concept to derive hemodynamic information using CCTA uses transluminal attenuation gradients (TAG) to estimate blood flow restriction [72]. Preliminary data suggest improvement in diagnostic performance using TAG for detecting hemodynamically significant CAD over standard CCTA [73]. Overall, promising data exist for both stress testing and CCTA to further improved diagnostic performance and to potentially further lower radiation doses.

Discussion and Recommendations

Indirect and direct comparisons between CCTA and stress testing consistently revealed superior diagnostic performance by CCTA for the diagnosis of CAD as defined by standard definitions. The difference in diagnostic performance is particularly apparent for sensitivity while it is less pronounced for specificity. Both negative and positive predictive values are better for CCTA compared to stress testing. The results are not surprising as CCTA – like the reference standard by cardiac catheterization – is a test evaluating the coronary anatomy while stress testing assesses myocardial perfusion. Given the recent emphasis on hemodynamically significant as opposed to merely obstructive CAD, some argue for FFR as the more appropriate reference standard [74]. However, current practice guidelines in Europe and US continue to define CAD according to anatomic criteria [75–77]. This is reasonable because there is a large body of evidence demonstrating high risk of adverse events in patients with obstructive CAD – regardless if the disease is associated with hemodynamic alterations or not [78;79]. Increasing the threshold for the diagnosis of CAD to including hemodynamically significant CAD, e.g., using FFR, would leave many patients with obstructive CAD without a diagnosis of CAD and thus, without current endorsement

for important preventative measures. Recent data from several large clinical series demonstrate substantial adverse event rates in patients with nonobstructive CAD detected by conventional angiography or CCTA [46;80–82]. These studies confirm the importance of detecting coronary atherosclerotic disease even when nonobstructive or hemodynamically insignificant. Therefore, we believe the diagnosis of CAD should remain linked to lumen obstruction and not to its hemodynamic consequence. Confirmation of hemodynamic significance is important, however, when considering PCI in coronary artery lesions for symptom control as no benefit – and possible harm – occurs with coronary intervention in non-flow-limiting lesions [71].

In regards to prognostic information and risk assessment, there is less clarity from head-to-head comparisons for CCTA and stress testing. However, it must be noted that the negative likelihood ratio for cardiac death and myocardial infarction associated with normal CCTA results is remarkably low and likely unmatched by stress testing when reviewing historical data. This again is expected given the inability of stress testing to detect nonobstructive disease which is associated with adverse outcome. Such advantage for risk assessment by CCTA has shown promising trends of improved patient outcome in the SCOT-HEART, PROMISE studies and in the large CONFIRM registry despite the lack of specific treatment prescriptions - a key limitation. We are still learning to optimally use the information by cardiac imaging and we currently likely to over-test and under-treat patients. For example, most patients with evidence of CAD on CCTA have low risk anatomy and require preventative measures along with medical therapy but are unlikely to benefit from cardiac catheterization/coronary artery revascularization. We may reduce risk to patients and lower cost by reserving invasive angiography for high risk patients. Future studies need to more strongly consider specific management algorithms as opposed to randomizing patients to testing without further clinical guidance. Until such data are available, we are left with our best judgment of the available data to make decisions on patient management. As always, patient characteristics and preferences are critically important to individualize decisions. Furthermore, the decision to proceed with stress testing or CCTA in patients with suspected CAD should consider the performance of the available imaging laboratories. In general terms, we believe a patient presenting with stable chest pain to a physician office will be best served with a CCTA if he is of intermediate pretest probability for CAD and if the CT laboratory has a track record of high quality scan acquisitions using low radiation dose protocols along with excellent interpretation skills. Our recommendation is particularly based on the greater sensitivity of CCTA to detect CAD compared to stress testing and based on the opportunity to implement (or withhold) preventative measures depending on the presence and extent of atherosclerotic disease. On the other hand, it appears reasonable to proceed with an exercise stress test with or without echocardiography in low risk patients as they are very unlikely to have CAD and even the risk of low level of radiation by CCTA may not be outweighed by benefit in these patients. Examples of such patients may be women under the age of 40 presenting with atypical chest pain and no risk factors for CAD. In patients with high pretest probability, stress testing with imaging or direct referral to cardiac catheterization remains a reasonable option at this time pending further data.

Abbreviations

ACS	Acute Coronary Syndrome
AUC	Area under the Curve
CAC	coronary artery calcium
CAD	Coronary Artery Disease
CCTA	Cardiac Computed Tomography Angiography
ECG	Electrocardiogram
ICA	Invasive Coronary Angiography
MACE	Major adverse cardiac event
MDCT	Multi-Detector Computed Tomography
MI	Myocardial Infarction
MPI	Myocardial Perfusion Imaging
NPV	Negative predictive value
PCI	Percutaneous intervention
PPV	Positive Predicative value
RCT	Randomized Clinical Trial
SPECT	Single-Photon Emission Computerized Tomography

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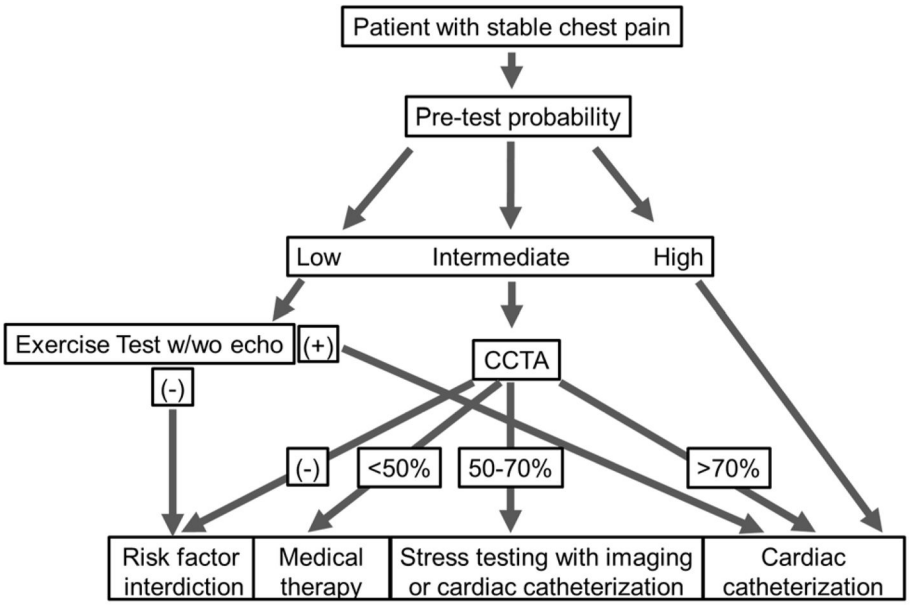

Figure 1.

A proposed algorithm for diagnosis of CAD in patients presenting with stable chest pain. Abbreviations: CAD; coronary artery disease, CCTA; Cardiac Computed Tomography Angiography.

Table 1

Direct Comparison of Diagnostic Accuracy by CCTA and Stress Testing for the Diagnosis of Coronary Artery Disease in Patients

Test	N	Sensitivity	Specificity	Positive predictive value	Negative predictive value
CCTA SPECT, stenosis>50% [26]	381	91% 62%	74% 67%	83% 73%	85% 55%
CCTA SPECT, stenosis>70% [26]	381	94% 71%	60% 67%	55% 73%	82% 73%
CCTA SPECT, stenosis>50% [83]	122	98.9% 56%	74.2% 38.7%	91.8% 72.9%	95.8% 23%
CCTA SPECT, stenosis>70% [83]	122	89.7% 57.7%	86.4% 43.2%	92.1% 64.3%	82.6% 36.5%
CCTA SPECT [84]	58	100% 59%	81% 48%	NA	NA
CCTA SPECT [85]	47	100% 69%	73% 36%	92% 78%	100% 27%
CCTA SPECT [86]	254	97.1% 81.8%	54.2% 32.4%	90.3% 74.2%	81.3% 42.9%
CCTA XECG [87]	62	100% 78%	87% 67%	96% 89%	100% 47%
CCTA XECG [88]	80	91% 73%	83% 31%	98% 67%	91% 65%
CCTA XECG [89]	98	96% 71%	37% 76%	67% 80%	88% 66%
CCTA XECG [90]	100	96% 71%	84% 38%	70% 32%	98% 77%
CCTA XECG [91]	177	100% 46.2%	98.7% 16.6%	92.9% 8.7%	100% 64.1%

CCTA: Cardiac Computed Tomography Angiography; CAD: Coronary Artery Disease; XECG: exercise electrocardiography.

Table 2

Annualized Rates of Myocardial Infarction and Cardiac Death According to CCTA and Stress Testing Imaging Results

Test	CCTA [37]	Exercise treadmill test [92]	Exercise Nuclear MPI [29]	Pharmacologic Nuclear MPI [29]	Exercise Echocardiography [93]	Dobutamine Echocardiography [94]
N	41,960	1,647	9,930	4,988	4,347	1,930
Median Follow-up (months)	23	30	20	22	36	32
MI/Cardiac death with normal test	0.02%	0.80%	0.65%	1.78%	0.5%	1.13%
MI/Cardiac death with abnormal test	3.38%	2.00%	4.30%	9.98%	2.06%	4.33%

CCTA; Cardiac Computed Tomography Angiography, CAD; Coronary Artery Disease, MPI; Myocardial perfusion imaging.