Diagnostic Accuracy of Noninvasive 64-row Computed Tomographic Coronary Angiography (CCTA) Compared with Myocardial Perfusion Imaging (MPI):

The PICTURE Study, A Prospective Multicenter Trial

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Rationale and Objectives: Although multiple studies have shown excellent accuracy statistics for noninvasive angiography by coronary computed tomographic angiography (CCTA), most studies comparing nuclear imaging to CCTA were performed on patients already referred for cardiac catheterization, introducing referral and selection bias. This prospective trial evaluated the diagnostic accuracy of 64-row CCTA to detect obstructive coronary stenosis compared to myocardial perfusion imaging (MPI), using quantitative coronary angiography (QCA) as a reference standard.

Materials and Methods: Twelve sites prospectively enrolled 230 patients (49% male, 57.8 years) with chest pain. All patients underwent MPI and CCTA (Lightspeed VCT/Visipaque 320, GE Healthcare, Milwaukee, WI, USA) prior to invasive coronary angiography (ICA). All patients were evaluated, and those found to have either an abnormal MPI or CCTA were clinically referred for ICA. CCTAs were graded on a 15-segment American Heart Association model by three blinded readers for presence of obstructive stenosis (>50% or >70%); MPI was graded by two blinded readers using a 17-segment model for estimation of the % myocardium ischemic or with stress defects. ICAs were independently graded for % stenosis by QCA. The efficacies of MPI and CCTA were assessed including all vessel segments for per-patient and per-vessel analyses.

Results: The prevalence of stenosis ≥50% by ICA was 52.1% (25 of 48). The sensitivity of CCTA was significantly higher than nuclear imaging (92.0% vs 54.5%, $P < 0.001$), with similar specificity (87.0% vs 78.3%) when obstructive disease was defined as ≥50%. CCTA provided superior sensitivity (92.6% vs 59.3%, $P < 0.001$) and similar specificity (88.9% vs 81.5%) using QCA stenosis ≥70%. For ≥50% stenosis, the computed tomographic angiography odds ratio for ICA disease was 51.75 (95% CI = 8.50–314.94, $P < 0.001$). For summed stress score ≥5%, the odds ratio for ICA CAD was 12.73 (95% CI = 2.43–66.55, $P < 0.001$). Using receiver operating characteristic curve analysis, CCTA was better at classifying obstructive coronary artery disease when compared to MPI (area = 0.85 vs 0.71, $P < 0.0001$).

Conclusions: This study represents one of the first prospective multicenter, controlled clinical trials comparing 64-row CCTA to MPI in the same patients, demonstrating superior diagnostic accuracy of CCTA over myocardial perfusion single photon emission computed tomography (MPS) to reliably detect >50% and >70% stenosis in stable chest pain patients.

Key Words: Coronary CT Angiography; myocardial perfusion imaging; diagnostic accuracy; comparative studies.

Acad Radiol 2017; 24:22–29

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http://dx.doi.org/10.1016/j.acra.2016.09.008

INTRODUCTION

Although multiple studies have shown excellent accuracy for coronary computed tomographic angiography (CCTA), most studies comparing nuclear imaging with CCTA were performed on patients already referred for cardiac catheterization, introducing selection and referral bias (1–5). Stress testing is the most common current noninvasive approach to detecting obstructive coronary artery disease (CAD). Current guidelines recommend functional imaging to risk-stratify and identify patients with higher likelihood of CAD prior to elective coronary angiography. However, a high percentage of patients are found to have nonobstructive CAD (6). Functional imaging provides physiologic evidence of clinically significant coronary artery stenosis by demonstrating the effects of diminished coronary flow reserve on symptoms leading to myocardial perfusion defects on scintigraphy. Unfortunately, in the United States, a majority of patients who have undergone invasive coronary angiography (ICA) after nuclear testing are found to have nonobstructive or normal coronary arteries, suggesting low diagnostic accuracy of myocardial perfusion imaging (MPI) in current clinical practice (6). In the National Cath Data Registry (NCDR), stress testing with MPI led to 302,651 patients undergoing ICA, with only 134,670 (44%) demonstrating obstructive disease at ICA. Invasive cardiac catheterization is costly and associated with a small but measurable risk of serious complication due to its invasive nature. In comparison, in the aforementioned NCDR, cardiac computed tomographic angiography (CTA) was performed in 8323 patients and 5791 (70%) were found to have obstructive disease at the time of ICA, representing a 50% improvement in specificity as compared to single photon emission computed tomography (SPECT) MPI. The purpose of this prospective clinical trial is to evaluate the diagnostic accuracy of CCTA to detect obstructive coronary stenosis compared to MPI, using quantitative coronary angiography (QCA) as a reference standard.

METHODS

Patient Population

The Perfusion Imaging and CT—Understanding Relative Efficacy (PICTURE) study was a prospective trial with a primary end point to evaluate the diagnostic accuracy of both nuclear imaging and CTA to ICA. Individuals were eligible for participation in the PICTURE trial if they were ≥18 years of age, experienced typical or atypical chest pain, and were being referred for nuclear testing for evaluation of their chest pain. Individuals were excluded from participation in the PICTURE trial for the following reasons: known allergy to iodinated contrast; baseline renal insufficiency (creatinine ≥1.7 mg/dL); irregular cardiac rhythm; resting heart rate >100 beats per minute; resting systolic blood pressure <100 mmHg; contraindication to beta blocker, calcium channel blocker, or nitroglycerin; pregnancy; or known history of CAD (prior myocardial infarction, percutaneous transluminal coronary angioplasty or intracoronary stent, or coronary artery bypass surgery). All patients had to undergo both MPI and CCTA prior to ICA to be enrolled. Importantly, patients were not excluded for elevated coronary artery calcium score or body mass index.

The study was performed at 12 centers in the United States (Appendix A). Before the study commenced, each Institutional Review Board had reviewed and approved the study protocol and patient safety monitoring plan. Protocols associated with patient enrollment, safety analysis, image acquisition, image interpretation, and statistical analysis were developed by a steering committee independent of the sponsor (GE Healthcare, Milwaukee, WI, USA). GE Healthcare performed study monitoring, data management, and quality control. Adverse events and serious adverse events were determined for follow-up by a data and safety monitoring board.

Twelve sites prospectively enrolled 230 patients (49% male, 57.8 years) with chest pain who were referred for stress MPI to assess CAD. Baseline demographics are reported in Table 1. A total of 48 patients were clinically referred for ICA for either positive MPI or abnormal CCTA, and used as our reference

TABLE 1. Clinical and Demographic Characteristics of Study Subjects

	Total Enrolled	Patients Undergoing QCA		
	(n = 230)	Yes (n = 48)	No (n = 182)	P Value
Age (years)	57.8 ± 11.4	59.7 ± 12.2	57.2 ± 11.2	0.185
Female, n (%)	113 (51.4)	18 (37.5)	95 (55.2)	0.03
Race/Ethnicity, n (%)				0.305
Caucasian	132 (60.0)	34 (70.8)	98 (57.0)	
African American	13 (5.9)	2 (4.2)	11 (6.4)	
Hispanic/Latino	27 (12.3)	2 (4.2)	25 (14.5)	
Oriental/Asian	34 (15.5)	7 (14.6)	27 (15.7)	
Others	14 (6.4)	3 (6.3)	11 (6.4)	
BMI (kg/m^2)	30.1 ± 6.9	29.7 ± 6.8	30.2 ± 7.0	0.683
Diabetes, n (%)	38 (17.6)	9 (18.8)	29 (17.3)	0.528
Family history of CAD, n (%)	129 (59.7)	31 (64.6)	98 (58.3)	0.136
Hypertension, n (%)	130 (60.2)	27 (56.3)	103 (61.3)	0.98
Hyperlipidemia, n (%)	126 (54.8)	28 (58.3)	98 (53.8)	0.97
Smoking status, n (%)				0.03
Current smoker	43 (19.5)	14 (29.2)	29 (16.9)	
Prior smoker	122 (55.5)	25 (52.1)	97 (56.4)	
Nonsmoker	55 (25.0)	9 (18.8)	46 (26.7)	

BMI, body mass index; CAD, coronary artery disease; QCA, quantitative coronary angiography.

group to establish diagnostic accuracy. All patients underwent both stress MPI and CCTA (Lightspeed VCT/Visipaque 320, GE Healthcare) prior to ICA as per protocol, without referral or selection bias. CCTAs were graded on a 15-segment American Heart Association (AHA) model by 3 blinded readers for presence of obstructive stenosis (≥50% or ≥70%); MPI was graded by 2 blinded readers using a 17-segment model for estimation of the % myocardium ischemic or with stress defects. ICAs were independently graded for % stenosis by QCA by a core QCA laboratory. The efficacies of MPI and CCTA were assessed including all vessel segments for per-patient and per-vessel analyses.

Rest and Stress MPI Protocol

MPI using SPECT at rest was obtained following the intravenous (IV) injection of 3.4 mCi thallium-201 using a multihead detector. Image data were reconstructed in the short-axis, vertical long-axis, and horizontal long-axis planes. The patients were then exercised on the treadmill for stress or provided with pharmacologic stress using adenosine and 26.2 mCi Tc99m Sestamibi, injected 1 minute prior to terminating the exercise or at the end of IV adenosine infusion. The patients were imaged again using a gated SPECT format. All injections were made in the left antecubital fossa. The rest and stress MPI images were scored using the 17-segment myocardial model, with each segment being coded from 0 (normal) to 4 (absent radiotracer uptake). The scores from each segment were summed at rest and stress to calculate a summed rest and stress score (and the difference, the sum difference score). The gated images were used to assess regional wall motion to improve differentiation between perfusion abnormalities and attenuation artifacts. MPI studies were interpreted and quantified blinded to clinical, CCTA, and invasive angiography results. Doses were not directly measured in this study; however, the approximate doses for the two modalities were 9 mSev for CCTA and 26 mSev for functional imaging based on the protocols used in this study (7).

CCTA Image Acquisition

Study subjects underwent CCTA prior to conventional ICA. All CCTA scans were performed with a 64-detector row Lightspeed VCT scanner (GE Healthcare). All patients were in normal sinus rhythm at the time of the CCTA scan. Individuals presenting with baseline heart rates >65 beats per minute (bpm) were administered oral beta-blocker therapy. IV administration was allowed in the protocol, using IV metoprolol at 5 mg increments to a total possible dose of 25 mg to achieve a resting heart rate <65 bpm. All patients eligible for CCTA were scanned, irrespective of whether the goal of <65 bpm heart rate was achieved.

Following a scout radiograph of the chest (anteroposterior and lateral), a timing bolus (using 10–20 cc of contrast) was performed to detect time to optimal contrast opacification in the axial image at a level immediately superior to the ostium of the left main artery. Nitroglycerine 0.4 mg sublingual was administered immediately prior to contrast injection. During CCTA acquisition, 80 cc iodinated contrast (Visipaque, GE Healthcare, Amersham, UK) was injected utilizing a triple-phase contrast protocol: 60 cc iodixanol, followed by 40 cc of a 50:50 mixture of iodixanol and saline, followed by a 50 cc saline flush. Retrospectively, electrocardiography-gated contrast-enhanced CCTA was performed, with scan initiation 20 mm above the level of the left main artery to 20 mm below the inferior myocardial apex. The scan parameters were 64 mm × 0.625 mm collimation, tube voltage of 120 mV, and effective mA of 350–780 mA. Radiation reduction algorithms using electrocardiography based tube current modulation were employed, which reduces tube current (mA) during systole and end diastole. After scan completion, multiphasic reconstruction of CCTA scans was performed, with reconstructed images from 70% to 80% by 5% increments and 5% to 95% by 10% increments.

CCTA Interpretation

CCTA images were interpreted separately by three readers blinded to all patient characteristics and ICA results. All CCTA images were evaluated on three-dimensional image analysis workstation (GE Advantage Workstation, GE Healthcare). CCTA readers were permitted to utilize any or all of available postprocessing image reconstruction algorithms, including two-dimensional axial, or three-dimensional maximal intensity projection, multiplanar reformat, cross-sectional analysis, or volume-rendered technique.

Coronary arteries were scored using a 15-segment AHA coronary artery classification (7). An overall assessment of image quality and coronary supply dominance was performed on the subject level. For each coronary segment, readers assessed whether coronary segments were evaluable. For any coronary artery segments considered nonevaluable, stenosis severity was assigned based on the outcome of the most adjacent proximal and identifiable segment as previously described (7). A semi-quantitative scale was employed by CCTA readers to grade the extent of luminal stenosis as a percentage of the vessel diameter using visual estimations. Stenosis severity was recorded in the following manner: no stenosis; 1% to 29% stenosis; 30% to 49% stenosis; 50% to 69% stenosis; 70% to 99% stenosis; 100% stenosis. For coronary artery segments considered to have 100% stenosis by CCTA, all segments distal to the occlusion were excluded from analysis. The degree of coronary artery stenosis identified by CCTA was assigned based on a consensus of ≥2 of 3 blinded CCTA readers who identified narrowing of the coronary artery lumen at a threshold of ≥50% or ≥70%. Consensus was achieved on a per-patient and per-vessel level.

ICA Image Acquisition and Interpretation

If ≥1 noninvasive test was abnormal, patients underwent ICA. Selective ICA was performed by standard transfemoral arterial catheterization. A minimum of eight projects were obtained (minimum of 5 views for the left coronary artery system, and minimum of 3 views for the right coronary artery system). Owing to differences in cardiac position, angles of projection for ICA differed slightly among study subjects.

All ICA images were interpreted by an independent ICA reader (J.J.) blinded to all patient characteristics and CCTA results. ICAs were quantitatively evaluated for coronary artery stenosis with QCA software (CAAS, Pie Medical Imaging, Maastricht, the Netherlands). Any segment deemed visually to have greater than 15% stenosis was quantified. Coronary artery segments by QCA were also evaluated using a 15-segment AHA coronary tree model, and were judged as having significant stenosis at two levels, that is, if ≥50% or ≥70% luminal narrowing of the coronary artery diameter was present.

Data Analysis

In all analyses, all patients and all vessels were included. Analyses were performed separately for two distinct thresholds—≥50% and ≥70% luminal diameter narrowing—that defined obstructive coronary artery stenosis. For the patient-based analysis, a true positive was defined as the presence of ≥1 coronary artery segment considered to have an obstructive stenosis by both CCTA and ICA, irrespective of location. For the vessel-based analysis, a true positive was defined as the presence of ≥1 coronary artery segment considered to have an obstructive stenosis by both CCTA and ICA in a single arterial system. Four arterial systems were predefined, and consisted of the (1) left main artery, (2) left anterior descending artery inclusive of diagonal branches, (3) left circumflex artery inclusive of obtuse marginal and left-sided posterolateral branches, and (4) right coronary artery inclusive of posterior descending artery and right-sided posterolateral branches. Ramus intermediate arteries were considered as the first obtuse marginal branch for per-vessel analyses.

Statistical Analysis

Categorical variables are presented as frequencies and percentages, and continuous variables as mean ± standard deviations. Categorical variables were compared using a chi-square statistic. Continuous variables, such as age, were compared to the presence or absence of CAD using *t* tests. The area under the receiver operating characteristic curve was calculated for CCTA to identify obstructive coronary artery stenosis at the 50% or 70% threshold. All statistical analyses were performed using SAS Proprietary Software, Release 9.1 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Clinical Characteristics

Among the total population enrolled ($n = 230$), there were differences in characteristics between those who did not undergo invasive angiography ($n = 182$) and those that did ($n = 48$). The 48 (21%) patients who underwent invasive angiography were older (60 years vs 57 years), more likely to be male (62% vs 45%, $P = 0.03$), and more likely to be active smokers (29% vs 17%, $P = 0.03$). Other demographics did not differ significantly between groups (Table 1).

Prevalence of MPI and CCTA Findings

The distribution of abnormalities of CTA and stress MPI by number of vessels is demonstrated in Figure 1. The prevalence of a ≥50% stenosis by cath was 52% (25/48), and mean calcium score among those going for ICA was 434 ± 926.

Diagnostic Accuracy

The primary efficacy end point in this study was the sensitivity of CCTA vs myocardial perfusion stress (MPS) for the diagnosis of CAD at the subject level when compared to CATH (catheterization) as the standard of reference. When the CCTA and CATH results were interpreted using a ≥50% and ≥70% stenosis criterion by QCA, the sensitivities of CCTA were 92.0% and 92.6% among subjects having 50% and 70% stenosis, respectively, whereas the sensitivities of MPS were 56% and 59.3%, respectively. For 50% stenosis, the difference in sensitivity between CCTA and MPS was 36% and the one-sided 95% lower confidence limit for the difference was 19.7% ($P < 0.0001$) and for 70% stenosis, the difference in sensitivity was 33.3% and the one-sided 95% lower confidence limit was 13.6% ($P = 0.0009$). The specificity of CCTA was similar to nuclear imaging (78.3% vs 87.0%) when obstructive disease was defined as ≥50% and ≥70% (88.9% vs 81.5%). Accuracy compared to quantitative angiography was significantly higher using CCTA than MPS for both cutpoints of disease.

CCTA and CATH results were in concordance with the majority of subjects and vessels (left main [LM], left anterior descending [LAD], left circumflex [LCX], and right coronary artery [RCA]). At 50% stenosis, the sensitivities of CCTA for subject diagnosis of CAD, in the LM, LAD, LCX, and in the RCA were 93.9%, 100.0%, 81.8%, and 76.5%, respectively. At 70% stenosis, the sensitivities of CCTA for subject diagnosis of CAD, in the LM, LAD, LCX, and in the RCA were 92.6%, 90.0%, 80.0%, and 70.0%, respectively.

The concordance of MPS and CATH results were lower than the concordance of CCTA and CATH results for the majority of subjects and vessels (LAD, LCX, and RCA). At 50% stenosis, the sensitivities of MPS for subject diagnosis of CAD, in the LM, LAD, LCX, and in the RCA, were 54.5%, 44.0%, 36.4%, and 35.3%, respectively. At 70% stenosis, the sensitivities of MPS for subject diagnosis of CAD, in the LM, LAD, LCX, and in the RCA, were 59.3%, 55.0%, 60.0%, and 40.0%, respectively.

The diagnostic accuracy (per-patient analysis) of CCTA and stress MPI compared to ICA is reported in Table 2 including negative predictive values. For ≥50% stenosis, the CTA odds ratio for ICA disease was 51.75 (95% CI = 8.50–314.94, $P < 0.001$). For summed stress score ≥5%, the odds

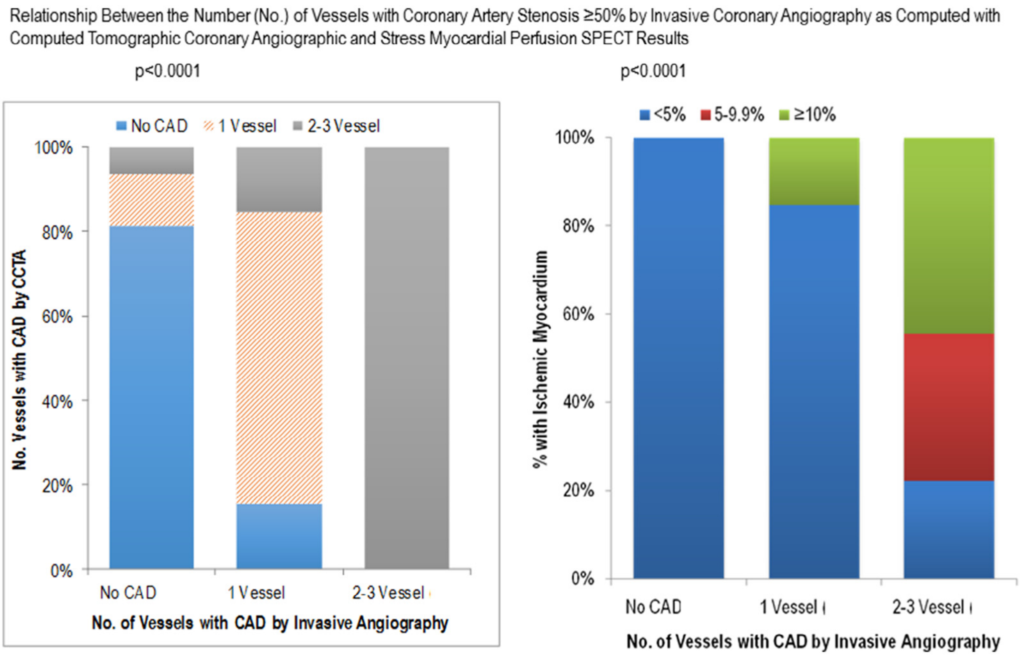

Figure 1. The study demonstrates the results of both computed tomographic coronary angiography (CCTA) (*left*) and stress myocardial perfusion SPECT results (*right*) based on number of vessels with coronary artery stenosis ≥50% by invasive coronary angiography (both $P < 0.0001$). CAD, coronary artery disease; SPECT, single photon emission computed tomography.

TABLE 2. Diagnostic Accuracy Statistics for Coronary Computed Tomographic Angiography and Stress Myocardial Perfusion Imaging (MPI) SPECT in Patients Prospectively Enrolled in the PICTURE Trial Undergoing ICA

	% (95% CI) Sensitivity	% (95% CI) Specificity	% (95% CI) Positive Predictive Value	% (95% CI) Negative Predictive Value
CT angiography				
≥50%	92.0 (74.0, 99.0)	78.3 (56.3, 92.5)	82.1 (63.1, 93.9)	90.0 (68.3, 98.8)
≥70%	92.6 (73.8, 99.0)	88.9 (70.8, 97.7)	84.2 (60.4, 96.6)	82.8 (64.2, 94.2)
MPI				
≥50%	54.5 (34.9, 75.6)	87.0 (66.4, 97.2)	82.4 (56.6, 96.2)	64.5 (45.4, 80.8)
≥70%	59.3 (34.0, 78.2)	81.5 (61.9, 93.7)	70.6 (44.0, 89.7)	71.0 (52.0, 85.8)

CI, confidence interval; ICA, invasive coronary angiography; PICTURE, Perfusion Imaging and CT–Understanding Relative Efficacy; SPECT, single photon emission computed tomography.

ratio for ICA CAD was 12.73 (95% CI = 2.43–66.55, $P < 0.001$). Using receiver operating characteristic curve analysis, CCTA was better at classifying obstructive CAD when compared to MPI (area = 0.85 vs 0.71, $P < 0.0001$) (Fig 2).

The concordance of CCTA and MPS was lower than the concordance of CCTA and CATH results for the majority of subjects and vessels (LAD, LCX, and RCA). At 50% stenosis, the sensitivities of CCTA for subject diagnosis of CAD, in the LAD, in the LCX, and in the RCA were 51.3%, 43.8%, 27.8%, and 27.8%, respectively. At 70% stenosis, the sensitivities of CCTA for subject diagnosis of CAD, in the LAD, in the LCX, and in the RCA were 54.5%, 46.2%, 41.7%, and 45.5%, respectively.

DISCUSSION

The present results of the PICTURE trial represent a prospective blinded multicenter study evaluating the diagnostic performance of CCTA compared to MPI in chest pain subjects without known CAD. The novelty of the present study is the fact that patients exclusively underwent ICA only after noninvasive imaging, thus eliminating some reference bias compared to other studies. The current data demonstrate higher diagnostic performance of 64-detector row CCTA for detection of obstructive coronary artery stenosis at both ≥50% and ≥70% stenosis thresholds as compared to MPI. Of equal importance and of clinical relevance is the higher negative predictive values of CCTA compared to MPI at the subject

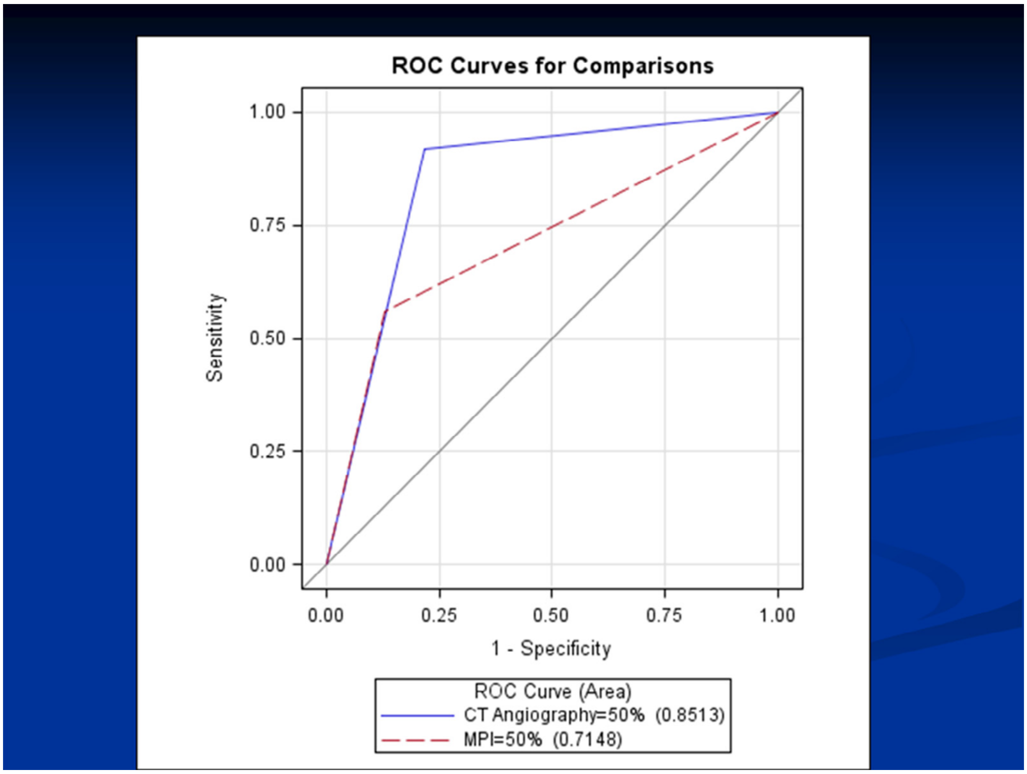

Figure 2. Receiver operator characteristic (ROC) curves showing area under the curve for stenosis >50% by invasive angiography for cardiac computed tomographic angiography and stress myocardial perfusion imaging (MPI).

and vessel levels. This improved accuracy establishes CCTA as a highly effective method to assess CAD that outperforms MPI for the exclusion of obstructive coronary artery stenosis. While most prior studies evaluated lower probabilities of disease, this population undergoing ICA had over 50% prevalence of obstructive disease, and CCTA performed well despite this high pretest probability and high coronary artery calcification (CAC) score (mean >400). While several studies have demonstrated very high accuracies for CCTA to diagnose obstructive CAD (8), this study is concordant with the recently published ENVINCI Study (9), which, in a lower probability population, demonstrated that CCTA had the highest diagnostic accuracy, and with sensitivity of 91% and specificity of 92%. MPI had significantly lower performance in that study ($P < 0.001$), with sensitivity of 74% and specificity of 73%. The current study and ENVINCI both demonstrated similar overall accuracies for MPI (71% and 73%, respectively). However, the methodologies in the two studies were different (ENVINCI used an FFR standard in those with moderate disease), so the present study's sensitivity of MPI was substantially lower but the specificity was higher than in ENVINCI.

It is not surprising that when using anatomy as the diagnostic standard of reference, CCTA performs better than SPECT because not all significant lesions are hemodynamically relevant and, thus, cause ischemia detectable by SPECT. However, the goal of referring a patient to the invasive angiography laboratory is to be able to find a significant stenosis and perform appropriate revascularization. The number of false positives can be markedly diminished by using CCTA, leading to a more appropriate utilization of expensive and invasive ICA. This finding confirms the American College of Cardiology Foundation/AHA expert consensus document (10) that states: "Coronary CTA may reduce both the time spent in the diagnostic process and the overall costs of clinical evaluation in selected populations, who otherwise would have been subjected to more expensive and possibly less accurate testing strategies."

One could argue that patient outcome, rather than diagnostic measures, should be used as the preferred standard of reference for cardiac imaging. Recent meta-analyses and multiple outcome studies demonstrate superior outcomes in those persons undergoing CCTA as compared to functional testing (with the exception of the PROspective Multicenter Imaging Study for Evaluation of chest pain [PROMISE] Trial) (11–13), the presumption being that CCTA is more diagnostically accurate and allows evaluation of subclinical atherosclerosis. A diminished sensitivity, as seen here, using nuclear imaging, may lead to diminished administration of preventive and interventional strategies (as demonstrated in both the Scottish COmputed Tomography of the HEART [SCOT-HEART] and PROMISE Trials) (14,15). The SPARC (Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in Coronary Artery Disease) Study demonstrated that the 2-year event rates for nonfatal myocardial infarction and death were 1% (6 of 590) for CCTA, 2.8% (16 of 565) for SPECT, and 6.6% (36 of 548) for positron emission tomography ($P < 0.001$), favoring CCTA (11). This may explain the better performance of CCTA over functional testing in SCOT-HEART (14,16), SPARC (11), and other studies directly comparing outcomes between the testing strategies.

The use of an anatomic gold standard clearly favors anatomic testing (CCTA), and may misrepresent the true prognostic implications of the two tests. However, the current study supports the current guidelines, which state, “In low-risk patients with chest pain, coronary CT angiography can result in a more rapid, more cost-effective diagnosis than stress myocardial perfusion imaging” (17). In PROMISE, in a prespecified end point, CCTA led to a significantly lower rate of invasive catheterization without obstructive disease (28% vs 52%, $P = 0.022$) (15). Very similar to the NCDR, just over 70% of catheterizations done after CCTA were found to have obstructive CAD, whereas only 47.5% after functional testing had disease. Almost identically, NCDR found 44%–45% positive rate with functional tests (nuclear, echocardiography, exercise treadmill, or magnetic resonance imaging).

The major limitation of the current study is the final number of patients who underwent invasive angiography. When the study was conceived, it was anticipated that 50% of participants would ultimately require invasive angiography, but only 21% required the said procedure, limiting the sample size to compare diagnostic accuracy, and introducing verification bias. Due to the ethical nature of not subjecting participants with both normal CCTA and MPI to invasive angiography, there remains a verification bias, as only those participants with either obstructive disease by CCTA and/or perfusion defect by MPI were subsequently referred for ICA. However, given the very high negative predictive value of normal CCTA (99% in most studies, including those studies by the same core CCTA laboratory) (1–5,7), it would be unlikely that subjecting the large number of patients with normal nuclear and CCTA to invasive angiography would have identified any significant number of cases of obstructive CAD. Furthermore, they would have to also have a normal nuclear stress test, further making obstructive disease unlikely. The anatomical end point of this study is suboptimal, but remains the clinical standard by which most patients undergo ICA in the United States today (6), and future designs with direct comparisons of the modalities to fractional flow reserve are planned. Also, no attenuation correction or prone imaging was performed for SPECT-MPI. This may have substantially influenced the accuracy of SPECT due to artifacts. A further limitation is the use of thallium/technetium increase the radiation dose and may affect diagnostic accuracy.

CONCLUSION

For the clinician faced with diagnostic evaluation of a patient with cardiac symptoms, choosing an imaging modality to accurately assess the presence of obstructive disease, and decide on a treatment strategy is dependent on the extent of atherosclerosis and stenosis. In a US population of patients with stable chest pain, CCTA is more accurate than nuclear testing for detecting significant CAD, despite high pretest probability and high calcium scores. The results of the PICTURE trial support the clinical role of CCTA in the accurate identification of the burden of coronary atherosclerosis and the presence of obstructive disease for consideration of revascularization.

ACKNOWLEDGMENT

This study is funded by General Electric (GE-189-003). The authors are solely responsible for the design, all study analyses, and the drafting and editing of the paper and its final contents.

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