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Diagnostic accuracy of Visipaque enhanced coronary computed tomographic angiography: a prospective multicenter trial

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Background Although several studies have shown promise for noninvasive angiography by coronary computed tomographic angiography (CCTA), few prospective multicenter trials have been conducted. This study evaluated the diagnostic accuracy of Visipaque enhanced CCTA to detect obstructive coronary stenosis compared with quantitative coronary angiography (QCA).

Patients and methods Three sites prospectively enrolled 77 patients (58.1% men, 54 years) with chest pain referred for invasive coronary angiography (ICA). Patients underwent CCTA (Lightspeed VCT/Visipaque 320) before ICA. CCTAs were graded on a 15-segment American Heart Association model by a CCTA core lab with blinded readers for the presence of obstructive stenosis (>50% or >70%); ICAs were independently graded for %stenosis by QCA, considered the reference standard. The efficacy of CCTA was assessed including all vessel segments for per-patient and per-vessel analyses.

Results A total of 46 >50% stenoses in 27 (35%) patients, and 31 >70% stenoses in 20 (26%) patients, were identified by QCA. Per-patient and per-vessel efficacy of CCTA

compared with QCA yielded sensitivities of 85% and specificities of 90 and 95%, respectively.

Conclusion This study shows the high accuracy of CCTA to reliably detect >50% and >70% stenoses in low-probability to intermediate-probability chest pain patients being referred for ICA. The high negative predictive values observed (92–100%) indicate that CCTA is also an effective noninvasive alternative to exclude obstructive coronary stenosis. *Coron Artery Dis* 00:000–000 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

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Keywords: coronary artery disease, computed tomography angiography, diagnostic accuracy, quantitative cardiac catheterization

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Introduction

Although multiple studies of diagnostic accuracy have been carried out to validate cardiac computed tomographic angiography (CCTA), most have been small studies and many are retrospective [1–4]. Systematic analysis of published studies to date has shown marked variation in results, which can partially be explained by the limitations of the selection and the single-center study design [5]. There are only a few multicenter prospective studies evaluating the diagnostic accuracy of this technique compared with quantitative coronary angiography (QCA) [6–8]. Several expert consensus documents, guidelines, and appropriate use criteria support the use of CCTA in the diagnosis of obstructive coronary artery disease (CAD). However, limited prospective studies exist to establish the diagnostic accuracy in the stable outpatient with suspected CAD. This study was carried out as a prospective, multicenter study to evaluate the diagnostic accuracy of Visipaque enhanced CCTA to detect obstructive coronary stenosis compared with QCA.

Patients and methods

We carried out a multicenter study to examine the accuracy of 64-row, 0.625-mm multidetector computed tomography (CT) angiography compared with invasive coronary angiography (ICA) in patients with suspected CAD. This multicenter study used centralized, blinded analysis to determine the diagnostic accuracy of multi-detector CT angiography for the purpose of identifying stable, outpatient symptomatic patients with suspected CAD who should be referred for conventional coronary angiography.

Patient population

Individuals were eligible for participation in the study if they were 18 years of age or older, experienced typical or atypical chest pain, and were being referred for ICA for evaluation of their chest pain. Individuals were excluded from participation in the trial for the following reasons: known allergy to iodinated contrast; baseline renal insufficiency (creatinine \geq 1.7 mg/dl); irregular cardiac rhythm; resting heart rate more than 100 beats/min

(bpm); resting systolic blood pressure less than 100 mmHg; contraindication to β -blocker, calcium-channel blocker, or nitroglycerin; pregnancy; known history of CAD [previous myocardial infarction (MI), percutaneous transluminal coronary angioplasty or intra-coronary stent, or coronary artery bypass surgery]. All patients had to undergo CCTA before ICA to be enrolled. Importantly, patients were not excluded for elevated coronary artery calcium score or BMI.

Before the study commenced, each IRB 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, Wisconsin, 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.

Three sites (Medical College of Wisconsin, Milwaukee, Wisconsin; Cardiovascular Associates, Mobile, Alabama; Harbor-UCLA, Torrance, California) prospectively enrolled 77 patients (58.1% men, 54 years) with chest pain referred for ICA. patients underwent CCTA (Lightspeed VCT/Visipaque 320; GE Healthcare, London, UK) before ICA. CCTAs were graded on a 15-segment American Heart Association (AHA) model by a CCTA core lab with blinded readers for the presence of obstructive stenosis (>50% or >70%); ICAs were independently graded for %stenosis by QCA, considered the reference standard. The efficacy of CCTA was assessed including all vessel segments for per-patient and per-vessel analyses.

Baseline demographics are reported in Table 1. ICAs were independently graded for %stenosis by QCA by a

Table 1 Patient demographics

	Mean \pm SD
Age (years)	54.0 \pm 10.5
Sex (%)	
Female	41.9
Male	58.1
Race/ethnicity (%)	
White	70.9
African-American	21.4
Hispanic/Latino	5.9
Oriental/Asian	0.9
Others	0.9
BMI (kg/m ²)	32.8 \pm 7.1
SBP (mmHg)	127.5 \pm 18.0
DBP (mmHg)	74.7 \pm 9.8
HDL (mg/dl)	46.3 \pm 14.9
LDL (mg/dl)	110.0 \pm 34.9
Triglycerides (mg/dl)	162.5 \pm 103.6
Fasting glucose (mg/dl)	116.9 \pm 44.1
Nonfasting glucose (mg/dl)	101.2 \pm 20.3
Creatinine (mg/dl)	1.0 \pm 0.2

DBP, diastolic blood pressure; SBP, systolic blood pressure.

reader blinded to both CCTA results and clinical information. The efficacy of CCTA was assessed including all vessel segments for per-patient and per-vessel analyses.

Coronary computed tomographic angiography image acquisition

All CCTA scans were performed with a 64-detector row MDCT scanner. All patients were in normal sinus rhythm at the time of the CCTA scan. Individuals presenting with baseline heart rates more than 65 bpm were administered oral β -blocker therapy. Intravenous administration was allowed in the protocol, using intravenous metoprolol at 5 mg increments to a total possible dose of 25 mg to achieve a resting heart rate less than 65 bpm. All patients eligible for CCTA were scanned, irrespective of whether the goal less than 65 bpm heart rate was achieved. Following a scout radiograph of the chest (anteroposterior and lateral), a timing bolus (using 10–20 ml 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 before contrast injection. During CCTA acquisition, 80 ml iodinated contrast (Visipaque; GE Healthcare, London, UK) was injected utilizing a triple-phase contrast protocol: 60 ml iodixanol, followed by 40 ml of a 50:50 mixture of iodixanol and saline, followed by a 50 ml saline flush. Retrospectively ECG-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 \times 0.625 mm collimation, tube voltage (120 mV), and effective milliampere (350–780 mA). Radiation reduction algorithms using ECG-based tube current modulation were used, 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.

Coronary computed tomographic angiography interpretation

CCTA images were interpreted separately by two expert CCTA readers blinded to all patient characteristics and ICA results, a third reader was employed when there was divergence between the readers, and final interpretation was determined by consensus. All CCTA images were evaluated on a 3D image analysis workstation (GE Advantage Workstation; GE Healthcare, Milwaukee, Wisconsin, USA). 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, multi-planar 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 patient level. For each coronary segment, readers assessed whether coronary segments were evaluable. For any coronary artery segments considered nonevaluable, stenosis severity was assigned on the basis of the outcome of the most adjacent proximal and identifiable segment as described previously [6]. A semi-quantitative scale was used 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; 1–29% stenosis; 30–49% stenosis; 50–69% stenosis; 70–99% stenosis; and 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 on the basis of a consensus of at least two of three blinded CCTA readers who identified narrowing of the coronary artery lumen at a threshold of $\geq 50\%$ or $\geq 70\%$. Consensus was achieved on a per-patient and per-vessel level.

Invasive coronary angiography image acquisition and interpretation

All patients enrolled underwent ICA. Selective ICA was performed by standard transfemoral arterial catheterization. A minimum of eight projects were obtained (a minimum of five views for the left coronary artery system and a minimum of three views for the right coronary artery system). Owing to differences in cardiac position, angles of projection for ICA differed slightly among the study participants.

All ICA images were interpreted by an independent ICA reader blinded to all patient characteristics and CCTA results. ICAs were evaluated quantitatively for coronary artery stenosis using 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 $\geq 50\%$ or $\geq 70\%$ luminal narrowing of the coronary artery diameter was present.

Data analysis

In all analyses, all patients and all vessels were included. Analyses were carried out separately for two distinct thresholds – $\geq 50\%$ and $\geq 70\%$ luminal diameter narrowing – that defined obstructive coronary artery stenosis. For the patient-based analysis, a true positive was defined as the presence of at least one 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 one or more 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 (a) left main artery, (b) left anterior descending artery inclusive of diagonal branches, (c) left circumflex artery inclusive of obtuse marginal and left-sided posterolateral branches, and (d) right coronary artery inclusive of posterior descending artery and right-sided posterolateral branches. Ramus intermediate arteries were considered the first obtuse marginal branch for per-vessel analyses.

Statistical analysis

Categorical variables are presented as frequencies and percentages, and continuous variables as mean \pm SD. Categorical variables were compared using a χ^2 -statistic. Continuous variables, such as age, were compared with the presence or absence of CAD using *t*-tests. The area under the receiver operator characteristics curve was calculated for CCTA to identify obstructive coronary artery stenosis at the 50% or 70% threshold. All statistical analyses were carried out using SAS Proprietary Software, Release 9.1 (SAS Institute Inc., Cary, North Carolina, USA).

Results

A total of 46 $> 50\%$ stenoses in 27 (35%) patients and 31 $> 70\%$ stenoses in 20 (26%) patients were identified by QCA. Per-patient and per-vessel efficacy of CCTA compared with QCA is reported in Table 2.

Patient-based evaluation

CCTA test characteristics and performance for patient-based evaluation are listed in Table 2. Discordance – that is, one reader scoring a patient's examination nonevaluable, a second reader scoring an examination without obstructive stenosis, – occurred for two (2.5%) patients, and was resolved with consensus and included in the patient-level efficacy analysis. Among the 27 patients with $\geq 50\%$ stenosis by QCA, 23 were correctly identified as having $\geq 50\%$ stenosis by CCTA. Among the 20 patients with $\geq 70\%$ stenosis by QCA, 20 were correctly identified as having $\geq 70\%$ stenosis by CCTA. The area

Table 2 Efficacy of coronary computed tomography compared with quantitative computed tomography

	Efficacy of CCTA vs. QCA (%)			
	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Per patient				
> 50%	85	90	81	92
> 70%	100	92	75	100
Per vessel				
> 50%	85	95	74	97
> 70%	97	96	65	97

CCTA, coronary computed tomographic angiography; QCA, quantitative coronary angiography.

under the curve for the identification of patients with $\geq 50\%$ coronary artery stenosis by QCA was 0.88 [95% confidence interval (CI): 0.84–0.92]. Applying CCTA stenosis thresholds to identify $\geq 70\%$ stenosis by QCA resulted in improved area under the curve of 0.95 (95% CI: 0.92–0.97). Sensitivity at both the $\geq 50\%$ and $\geq 70\%$ thresholds of disease was 85 and 100%; specificity was 90 and 92%, respectively (Table 2). The negative predictive values were consistently high (92–100%) and positive predictive values were moderate (75–81%).

Vessel-based evaluation

CCTA test performance for vessel-based evaluation is listed in Table 2. In total, 46 (14.9%) and 31 (10.0%) vessels reached the $\geq 50\%$ or $\geq 70\%$ stenosis threshold by QCA. Among the 46 vessels with $\geq 50\%$ stenosis by QCA, 39 vessels were correctly identified as having $\geq 50\%$ stenosis by CCTA. Among the 31 vessels with $\geq 70\%$ stenosis by QCA, 30 were correctly identified as having $\geq 70\%$ stenosis by CCTA. For $\geq 50\%$ and $\geq 70\%$ stenosis thresholds, sensitivity was 85 and 97% respectively, specificity was 95 and 96% respectively, and negative predictive power was 97% (Table 2).

Discussion

In this multicenter study of symptomatic patients with suspected CAD comparing 64-row multidetector CT angiography with conventional coronary angiography, we found that MDCT has a reliable accuracy for the diagnosis of obstructive coronary disease.

This study aimed to determine the presence or absence of obstructive disease in patients already at considerable risk for CAD who may require coronary revascularization.

Previous studies in different populations comparing CCTA and ICA have yielded variable results [5,9]. Underlying these differing findings are limitations inherent to single-center designs and the degree of rigor used in controlling for bias. Several multicenter studies have been reported. The first such study, ACCURACY, showed very high sensitivity (95%) and moderate specificity (83%) [6]. The limitation of ACCURACY was a low prevalence of disease, resulting in a very high negative predictive value (99%); however, the positive predictive value was low (64 and 48% for $\geq 50\%$ and $\geq 70\%$ thresholds of disease, respectively). The next, CORE-64, had multiple intrinsic limitations, including a mix of patients with and without revascularization, excluded calcium scores more than 600, and an excessively high pretest probability of disease on the basis of the probable target of use of CCTA (56% for $\geq 50\%$ stenosis on conventional coronary angiography), making translation into current clinical practice impossible [7]. The use of CCTA in postrevascularization patients is still considered of uncertain appropriateness, and exclusion of coronary artery calcium more than 600 is neither practical nor necessary to perform or interpret CCTA.

Our results for the diagnostic performance of CCTA should be considered in the context of recommended use of the test [10]. We show that CCTA yields robust diagnostic performance among symptomatic patients with suspected CAD and does better with more severe stenosis. This finding is not surprising as the limitations of attempting to categorize stenosis to a range (i.e. 50–69%) may lead to some level of discordance with QCA. However, severe stenosis ($\geq 70\%$) is easier to interpret on CCTA [including total occlusions and very severe (i.e. $> 90\%$) stenosis all lumped into one category]. This is highly relevant as stenosis more than 70% is most frequently found to have abnormal fractional flow reserve and may thus be good clinical candidates for revascularization [11,12].

Recent comparative effectiveness studies evaluating functional testing and CCTA show significantly higher accuracy of the anatomic test, further supported by the current study [13–17].

The recent Scottish COmputed Tomography of the HEART Trial (SCOT-HEART) study reported a 50% reduction in fatal and nonfatal MI in the CCTA group compared with the functional testing group (hazard ratio: 0.50; 95% CI: 0.28–0.88; $P=0.020$) at 3 years of follow-up [18], supporting the meta-analysis that also showed a 47% reduction in nonfatal MI with CCTA testing over both nuclear and exercise testing groups (odds ratio 0.53; 95% CI: 0.39–0.72; $P<0.001$) [9]. Multiple studies have now validated the significant prognostic potential of atherosclerosis imaging with CCTA [19–21].

Conclusion

This study shows high accuracy of CCTA to reliably detect $> 50\%$ and $> 70\%$ stenoses in low-probability to intermediate-probability chest pain patients being referred for ICA. The high negative predictive value observed (92–100%) indicates that CCTA is also an effective noninvasive alternative to exclude obstructive coronary stenosis.

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Conflicts of interest

Dr Matthew J. Budoff is a consultant for GE Healthcare. For the remaining authors there are no conflicts of interest.

References

- 1 Chow BJ, Abraham A, Wells GA, Chen L, Ruddy TD, Yam Y, *et al.* Diagnostic accuracy and impact of computed tomographic coronary angiography on utilization of invasive coronary angiography. *Circ Cardiovasc Imaging* 2009; **2**:16–23.
- 2 Van Velzen JE, Schuijf JD, de Graaf FR, Boersma E, Pundziute G, Spanó F, *et al.* Diagnostic performance of non-invasive multidetector computed tomography coronary angiography to detect coronary artery disease using different endpoints: detection of significant stenosis vs. detection of atherosclerosis. *Eur Heart J* 2011; **32**:637–645.

- 3 Hamirani YS, Isma'eel H, Larijani V, Drury P, Lim W, Bevilal M, *et al.* The diagnostic accuracy of 64-detector cardiac computed tomography compared with stress nuclear imaging in patients undergoing invasive cardiac catheterization. *J Comput Assist Tomogr* 2010; **34**:645–651.
- 4 Jug B, Gupta M, Papazian J, Li D, Tsang J, Bhatia H, *et al.* Diagnostic performance of 64-slice multidetector coronary computed tomographic angiography in women. *J Nucl Cardiol* 2012; **19**:1154–1161.
- 5 Hamon M, Biondi-Zoccai GG, Malagutti P, Agostoni P, Morello R, Valgimigli M, Hamon M. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a meta-analysis. *J Am Coll Cardiol* 2006; **48**:1896–1910.
- 6 Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, *et al.* Diagnostic performance of 64-detector row coronary computed tomographic angiography of individuals undergoing invasive coronary prospective multicenter ACCURACY (Assessment by Coronary Computed Individuals Without Known Coronary Artery Disease: Results From the Tomographic Angiography for Evaluation of Coronary Artery Stenosis in Angiography) Trial. *J Am Coll Cardiol* 2008; **52**:1724–1732.
- 7 Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, *et al.* Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008; **359**:2324–2336.
- 8 Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, *et al.* Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol* 2008; **52**:2135–2144.
- 9 Nielsen LH, Ortner N, Norgaard BL, Achenbach S, Leipsic J, Abdulla J. The diagnostic accuracy and outcomes after coronary computed tomography angiography vs. conventional functional testing in patients with stable angina pectoris: a systematic review and meta-analysis. *Eur Heart J* 2014; **15**:961–971.
- 10 Taylor AJ, Cerqueira M, Hodgson JM, Mark D, Min J, O'Gara P, Rubin GD. ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. *J Cardiovasc Comput Tomogr* 2010; **4**:407.e1–407.e33.
- 11 Leipsic J, Yang TH, Thompson A, Koo BK, Mancini GB, Taylor C, *et al.* CT angiography (CTA) and diagnostic performance of noninvasive fractional flow reserve: Results from the Determination of Fractional Flow Reserve by Anatomic CTA (DeFACTO) Study. *Am J Roentgenol* 2014; **202**:989–994.
- 12 Nakanishi R, Matsumoto S, Alani A, Li D, Kitslaar PH, Broersen A, *et al.* Diagnostic performance of transluminal attenuation gradient and fractional flow reserve by coronary computed tomographic angiography (FFR_{CT}) compared to invasive FFR: a sub-group analysis from the DISCOVER-FLOW and DeFACTO studies. *Int J Cardiovasc Imaging* 2015; **31**:1251–1259.
- 13 Budoff MJ, Liu S, Chow D, Flores F, Hsieh B, Gebow D, *et al.* Coronary CT angiography versus standard of care strategies to evaluate patients with potential coronary artery disease; effect on long term clinical outcomes. *Atherosclerosis* 2014; **237**:494–498.
- 14 Budoff MJ, Li D. Coronary CT angiography again results in better patient outcomes. *J Am Coll Cardiol* 2014; **64**:741–742.
- 15 SCOT-HEART Investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet* 2015; **385**:2383–2391.
- 16 Neglia D, Rovai D, Caselli C, Pietila M, Teresinska A, Aguadé-Bruix S, *et al.* Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. *Circ Cardiovasc Imaging* 2015; **8**:e002179.
- 17 Budoff MJ, Kazerooni EA, Thomas GS, Mieres JH, Shaw LJ. Diagnostic accuracy of noninvasive 64-row computed tomographic coronary angiography (CCTA) compared with myocardial perfusion imaging (MPI): the PICTURE Study, a prospective multicenter trial. *Int J Cardiovasc Imaging* 2016; **31**:1–11, in press.
- 18 Williams MC, Hunter A, Shah ASV, Assi V, Lewis S, Smith J, *et al.* Use of coronary computed tomographic angiography to guide management of patients with coronary disease. *J Am Coll Cardiol* 2016; **67**:1759–1768.
- 19 Chow BJ, Wells GA, Chen L, Yam Y, Galiwango P, Abraham A, *et al.* Prognostic value of 64-slice cardiac computed tomography severity of coronary artery disease, coronary atherosclerosis, and left ventricular ejection fraction. *J Am Coll Cardiol* 2010; **55**:1017–1028.
- 20 Ostrom MP, Gopal A, Ahmadi N, Nasir K, Yang E, Kakadiaris I, *et al.* Mortality incidence and the severity of coronary atherosclerosis assessed by CT angiography. *J Am Coll Cardiol* 2008; **52**:1335–1343.
- 21 Ahmadi N, Nabavi V, Hajsadeghi F, Flores F, French WJ, Mao SS, *et al.* Mortality incidence of patients with non-obstructive coronary artery disease diagnosed by computed tomography angiography. *Am J Cardiol* 2011; **107**:10–16.

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