64-slice CT angiography for the detection of functionally significant coronary stenoses: comparison with stress myocardial perfusion imaging

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Objective: To evaluate the accuracy of 64-slice CT angiography (CTA) compared with single photon emission CT (SPECT) myocardial perfusion imaging (MPI), which served as the reference standard, for the detection of functionally significant coronary artery disease (CAD).

Methods: 141 consecutive patients (60 ± 10 years, 101 men) were investigated with 64-slice CTA and SPECT MPI; a subset of 35 patients had additional invasive coronary angiography (ICA). The data from CTA and ICA were compared with those from MPI for both cut-offs of ≥50% and ≥70% stenosis, respectively.

Results: The sensitivity, specificity, positive and negative predictive values, and accuracy of CTA, using a cut-off of ≥50% for significant stenosis, in detecting inducible perfusion defects on MPI were 96% [95% confidence interval (CI) 88–100%], 61% (95% CI 52–70%), 37% (95% CI 23–49%), 99% (95% CI 97–100%) and 68%, respectively, in patient-based analysis and 97% (95% CI 91–100%), 86% (95% CI 83–89%), 33% (95% CI 24–42%), 100% (95% CI 99–100%) and 87%, respectively, in vessel-based analysis. Applying a cut-off of ≥70% for significant stenosis, CTA yielded the following sensitivity, specificity, positive and negative predictive values, and accuracy for the detection of inducible MPI defects: by patient, 65% (95% CI 46–84%), 95% (95% CI 91–99%), 74% (95% CI 50–92%), 92% (95% CI 87–97%) and 89%, respectively; by vessel, 58% (95% CI 42–74%), 97% (95% CI 95–99%), 62% (95% CI 45–79%), 97% (95% CI 95–99%) and 95%, respectively.

Conclusion: 64-slice CTA is a reliable tool to exclude functionally significant CAD when using a cut-off of ≥50% diameter stenosis. By contrast, a cut-off of ≥70% diameter narrowing is a strong predictor of ischaemia.

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In recent years, multislice coronary CT angiography (CTA), with improved spatial and temporal resolution, has been consistently shown to have a very high negative predictive value (NPV) for the diagnosis of coronary artery disease (CAD) [1–4]. With NPVs approaching nearly 100%, the technique has also been promoted as a particularly effective tool for excluding the presence of significant CAD. Therefore, patients with normal coronary arteries on multislice CTA may be reassured and generally do not require further testing. Nevertheless, in many instances multislice CTA will unexpectedly reveal the presence of atherosclerotic lesions, as the technique identifies both early subclinical and more advanced CAD. Intuitively, this non-invasive identification of atherosclerosis may have advantages for patient management, as it provides

an opportunity for targeted and more individualised antiatherosclerotic treatment. However, management decisions such as referral for revascularisation remain largely dependent on the severity of symptoms in combination with the extent of ischaemia demonstrated during functional testing. Unfortunately, this important information is currently not obtained from multislice CTA, and the diagnostic value of CTA in the detection of functionally significant coronary artery lesions as defined by reversible or fixed perfusion defects on myocardial perfusion imaging (MPI) remains uncertain as only limited data are available on this specific issue [5–11].

Stress MPI using single photon emission CT (SPECT) is a well-established method for the non-invasive detection of CAD [12]. Besides its diagnostic accuracy, SPECT MPI allows evaluation of the functional severity of coronary stenoses and provides valuable information for cardiac risk assessment, which will facilitate clinical decision-making and may help avoid unnecessary invasive coronary angiography or intervention [13–16]. By contrast, the purely anatomical delineation depicted by

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invasive and non-invasive angiography offers limited functional and prognostic information [17–19]. In fact, SPECT MPI now forms a strong symbiotic relationship with coronary angiography, which can guide therapy.

With increasing use of multislice CTA, clinicians will be more frequently confronted with patients having confirmed atherosclerotic coronary lesions but yet of uncertain haemodynamic relevance. Therefore, the aim of this retrospective study was to evaluate the accuracy of 64-slice CTA compared with SPECT MPI, which served as the reference standard, for the detection of functionally significant coronary lesions. In addition, the non-invasive imaging findings were compared with invasive coronary angiography (ICA) in a subset of patients.

Methods and patients

Patient selection

141 consecutive patients who had undergone MPI within 60 days of 64-slice CTA were included in this study. The patients underwent both studies for clinical reasons. Exclusion criteria were: (1) previous myocardial infarction; (2) acute coronary syndrome between the two examinations; (3) previous percutaneous coronary intervention or coronary artery bypass surgery; and (4) cardiac interventions between the two studies. For each patient, baseline clinical characteristics were recorded. In a subset of 35 patients, ICA was performed. The examinations were performed between January 2008 and October 2009 according to the following protocols. This study was approved by our institutional review board, which waived the need for informed patient consent in a retrospective analysis.

Coronary calcium scoring

An initial unenhanced electrocardiogram (ECG)-gated scan was performed for calcium scoring in all patients before CTA [20]; 3 mm contiguous slices were reconstructed. The presence of calcification was determined using the Agatston method with a 130 Hounsfield unit threshold. All calcified lesions with an area $>1\text{ mm}^2$ were scored. Both total and vessel-based coronary calcium scores were recorded.

64-slice CT angiography

The CTA images were acquired with a 64-detector CT scanner (Brilliance; Philips Medical Systems, Best, Netherlands). Patients with initial heart rates greater than 65 beats per minute (b.p.m.) were administered 20–100 mg of propranolol orally 1 h before the scan. The usual scanning parameters were: detector configuration $64 \times 0.625\text{ mm}$ collimation, 120–140 kV and 800–1000 mA with variations according to patient body habitus, 0.42 s rotation time, a pitch value of 0.2, 0.8 mm slice thickness and 0.6 mm reconstruction interval. A bolus of 60–90 ml of non-ionic contrast agent (Ultravist 370 mg ml^{-1} ; Schering AG, Berlin, Germany) followed by 50 ml of normal saline was injected intravenously using a two-phase injection

protocol at a rate of 5 mls^{-1} . A semiautomated bolus-tracking program was utilised. Using retrospective ECG gating, routine reconstructions at several time points of the cardiac cycle were performed.

The CT scans were analysed, in consensus, by two experienced radiologists blinded to the results of MPI and ICA using a dedicated workstation (Philips Extended Brilliance Workspace v3.5; Philips Medical Systems). The CTA images were assessed from axial source images, supplemented by three-dimensional volume-rendered images, maximum intensity projections and multiplanar reformations. Image quality was graded as excellent (no motion artefacts present), good (minor motion artefacts present), moderate (substantial motion artefacts present, but luminal assessment of significant stenoses still possible), heavily calcified (vessel lumen obscured by calcification) or blurred (only contrast visualisation inside the vessel possible; no luminal assessment of significant stenosis possible) [5]. Only excellent, good or moderate quality was considered acceptable for reliable image interpretation. Coronary arteries were assessed using a 17-segment modified American Heart Association classification [21] that included an extra segment to allow classification of the intermediate artery when present (right coronary artery: 1, proximal; 2, mid; 3, distal; 4, posterior descending; 16, posterolateral; left main coronary artery: 5; left anterior descending coronary artery: 6, proximal; 7, mid; 8, distal; 9, first diagonal; 10, second diagonal; left circumflex coronary artery: 11, proximal; 12, first marginal; 13, mid; 14, second marginal; 15, distal; and 17, intermediate branch). Both blurred and heavily calcified segments were excluded from further analysis. In the remaining coronary segments, lesions with clear, well-defined borders were measured quantitatively. Quantitative CT angiographic analysis was performed on the most severe well-defined lesion in each segment using a digital electronic caliper, and luminal diameter stenoses were recorded in percentages and reported as mild ($<50\%$), moderate (50–69%) or severe ($\geq 70\%$) narrowing.

Myocardial perfusion imaging

A dipyridamole stress SPECT MPI protocol, with adjunctive handgrip exercise, was performed on all patients by intravenous administration of 0.56 mg of dipyridamole per kilogram of body weight over 4 min and 2–2.5 mCi of ^{201}Tl 3 min after the end of the dipyridamole infusion. Patients were told to refrain from caffeine-containing beverages and food for 24 h and stop taking nitrates, calcium channel blockers and β -blockers for at least 12 h before the cardiac SPECT study.

All SPECT studies were acquired using a dual-head camera (Forte; Philips Medical Systems, Cleveland, OH), with a low-energy all-purpose collimator using standard settings and parameters [22]. SPECT images were processed by filtered back-projection using a Butterworth filter at a cut-off frequency of 0.41 of the Nyquist frequency, order 5, and transaxial slices were reoriented to obtain short axis, horizontal long axis and vertical long axis slices encompassing the entire left ventricle. No attenuation correction was used.

SPECT image interpretation was visually performed, in consensus, using a dedicated workstation by two

experienced nuclear cardiologists who were blinded to the results of CTA and ICA but were aware of the sex, height and weight of the patients (Philips JETStream Workspace v3.0; Philips Medical Systems). Stress and redistribution images were scored semiquantitatively using the standard left ventricle 17-segment model [22] and a five-point scale: 0, normal tracer uptake; 1, mild reduction of tracer uptake; 2, moderate reduction; 3, severe reduction; and 4, absent uptake. A segment was considered abnormal if its score was 1 or more. Each segment was classified further as showing a reversible, partially reversible or fixed perfusion defect, or as normal. Perfusion defects in the anterior wall and septum were allocated to the left anterior descending coronary artery (LAD); defects in the lateral wall, to the left circumflex coronary artery (LCx); and inferior defects, to the right coronary artery (RCA). Apical defects were considered to be in the LAD region, unless the defect extended to the lateral (LCx) or inferior (RCA) wall. In the watershed regions, allocation was determined according to the main extension of the defects to the anterior, lateral or inferior wall. Furthermore, distinct defects affecting both the LAD region and the LCx region were rated as left main (LM) artery disease. Coronary dominance, as assessed on CTA, was provided without details of calcification or stenoses, to ensure correct assignment of the appropriate defects.

Invasive coronary angiography

A total of 35 patients were referred for ICA on the basis of clinical manifestations and/or non-invasive imaging findings at the discretion of the referring cardiologists. ICA was performed according to standard clinical protocols. Quantitative coronary angiography (QCA) was performed on the most severe well-defined lesion in each diseased segment with a digital electronic caliper using image analysis software (Sigmascan Pro, trial version) by an experienced cardiologist blinded to the CTA and MPI results using the same 17-segment model employed for CTA analysis, with luminal diameter stenoses also recorded in percentages and reported as mild (<50%), moderate (50–69%) or severe ($\geq 70\%$) narrowing.

Radiation dose

The effective radiation dose for CTA was calculated by multiplying the dose-length product (DLP) provided by the scan console by a constant ($k=0.014 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$) [23]. In order to estimate the radiation dose for SPECT MPI, the total megabecquerel was converted to millisievert (mSv) [24].

Data analysis

The data from CTA and QCA were compared with those from SPECT MPI, which served as the standard of reference. Since assignment of single coronary segments on CTA or ICA images to myocardial territories on MPI is not feasible, data analyses were performed on a per patient basis and a per artery basis (LAD, LCx, RCA and

LM artery), as previously reported [5]. Both analyses were performed separately for luminal diameter narrowing $\geq 50\%$ and $\geq 70\%$. Furthermore, quantitative per lesion analysis compared the maximal percentage diameter stenosis of the most severe lesion in each segment as assessed with CTA and QCA, and the diagnostic accuracy of CTA to detect coronary lesions with various degrees of luminal obstruction was evaluated using QCA as the standard of reference.

Statistics

Continuous variables were expressed as the mean $\pm$ SD and compared with the *t*-tests. Categorical variables were described as percentages and compared with the χ^2 test, when appropriate, or Fisher's exact test. A *p*-value <0.05 was considered statistically significant. Sensitivity, specificity, PPV, NPV and accuracy were calculated for both lesion degrees ($\geq 50\%$ and $\geq 70\%$). Accuracy was determined as the percentage of correct diagnoses in the entire sample. Quantitative lesion severity was compared between CTA and QCA using Pearson's correlation analysis.

Results

Patient characteristics

In total, 141 patients (101 men, 40 women, mean age 60 ± 10 years) were included and underwent both 64-slice CTA and MPI within 60 days of each other (mean 29 ± 22 days). The clinical characteristics of the study population are summarised in Table 1. On the basis of clinical presentation and/or imaging results, 35 patients (25 men, 10 women, mean age 61 ± 11 years) were referred for ICA. The clinical characteristics of these patients are described in Table 2.

Coronary calcium scoring

The mean coronary calcium score, calculated as the Agatston score equivalent (ASE), in the entire group of patients was 168 ± 359 (range, 0–2516). 43 patients had an

Table 1. Patient characteristics (*n*=141)

Sex (male/female)	101/40
Age (years)	60 ± 10
BMI (kg m^{-2})	25.1 ± 2.8
BMI $\geq 30 \text{ kg m}^{-2}$	7 (5%)
Risk factors for CAD	
Diabetes mellitus	25 (18%)
Hypertension	80 (57%)
Dyslipidaemia	91 (65%)
Positive family history	21 (15%)
Current smoker	57 (40%)
Symptoms	
Asymptomatic	56 (40%)
Atypical chest pain	56 (40%)
Typical angina	19 (13%)
Dyspnoea	10 (7%)

BMI, body mass index; CAD, coronary artery disease.

Table 2. Characteristics of patients referred for invasive angiography (*n*=35)

Characteristics	Results
Sex (male/female)	25/10
Age (years)	61 ± 11
BMI (kg m ⁻²)	25.4 ± 3.8
BMI ≥ 30 kg m ⁻²	4 (11%)
Risk factors for CAD	
Diabetes mellitus	5 (14%)
Hypertension	20 (57%)
Dyslipidaemia	25 (71%)
Positive family history	4 (11%)
Current smoker	16 (45%)
Symptoms	
Asymptomatic	6 (17%)
Atypical chest pain	12 (34%)
Typical angina	14 (40%)
Dyspnoea	3 (9%)

BMI, body mass index; CAD, coronary artery disease.

ASE of 0, 52 patients had an ASE of 1–100, 34 patients had an ASE of 101–400, 6 patients had an ASE of 401–1000, and 6 patients had an ASE of ≥1000. Coronary artery calcification was greatest in the LAD (mean 78 ± 147), and then in the RCA (mean, 52 ± 132), LCx (mean, 26 ± 83) and LM artery (mean, 12 ± 38).

64-slice CT angiography

All patients were in sinus rhythm at the time of their studies with a mean heart rate of 62 ± 7 b.p.m. during image acquisition (range, 45–84 b.p.m.). 49 patients required β -blockade before CTA. In 141 patients analysed, image quality was excellent in 44 patients, good in 87, moderate in 6 and poor in 4. In total, 137 patients were considered acceptable for reliable image interpretation. In these 137 patients, a total of 2237 coronary segments in 547 main coronary arteries were assessed (1 patient had no LM artery because of separate origin of the LAD and the LCx and 46 patients had intermediate arteries). The number of segments classified as excellent, good or moderate was 2013 (90%). 68 segments (3.0%) were rated as heavily calcified and 156 (7.0%) as blurred or non-visualised. Thus, vessel diameter could not be evaluated in 224 (10%) of 2237 segments. The coronary calcium score was significantly higher in patients with calcified segments who had to be excluded from analysis than in the rest of the patients (1242 ± 502 *vs* 74 ± 97 ASE, *p* < 0.001). Overall, 10 patients had normal coronary arteries, 59 had coronary stenoses of less than 50%, 68 were shown to have at least 1 coronary stenotic lesion of ≥50%, and 23 were identified as having at least 1 coronary narrowing of ≥70%. In the evaluable 2013 segments, quantitative CTA revealed stenoses of ≥50% in 171 segments (8.5%), corresponding to 106 of 547 main coronary arteries (19.4%) in 68 out of 137 patients (49.6%). 91 of these stenotic segments were located in the LAD, 38 in the RCA, 40 in the LCx and 2 in the LM artery. Stenoses of ≥70% were identified by quantitative CTA in 65 segments (3.2%), corresponding to 34 main coronary arteries (6.2%) in 23 patients (16.8%). 31 stenotic segments were located in the LAD, 16 in the RCA and 18

in the LCx. One patient had an occluded lesion in the proximal RCA.

In the subset of 35 patients undergoing ICA, quantitative CTA revealed stenoses of ≥50% in 72 of 512 evaluable segments (14%), corresponding to 43 of 140 main coronary arteries (30.7%) in 21 patients, with 35 segments in the LAD, 20 in the RCA, 15 in the LCx, 1 in the intermediate branch and 1 in the LM. Stenoses of ≥70% were identified by quantitative CTA in 24 segments (4.7%), corresponding to 19 of 140 main coronary arteries (13.6%) in 15 patients, with 10 segments in the LAD, 8 in the RCA and 6 in the LCx.

Myocardial perfusion imaging

MPI was performed successfully on all patients, and all studies were amenable to interpretation. Visual image analysis revealed 35 reversible and 1 fixed perfusion defect in 26 of 137 patients with interpretable CTA. Of the 35 reversible perfusion defects, 15 were located in the LAD territory, 13 in the RCA territory and 7 in the LCx territory. The only fixed perfusion defect was located in the RCA territory, of which the supplying artery was occluded. 111 patients showed no perfusion abnormalities on MPI.

Invasive coronary angiography

Of the 35 patients undergoing ICA, evidence of atherosclerosis was demonstrated in each case, with 15 patients showing coronary stenosis of less than 50%. In the remaining 20 patients, at least 1 coronary narrowing of ≥50% was detected in each case, and 16 patients were shown to have at least 1 coronary stenosis of ≥70%. QCA revealed stenoses of ≥50% in 53 segments of 39 main coronary arteries, with 25 segments in the LAD, 15 in the RCA and 13 in the LCx. Stenoses of ≥70% were identified by QCA in 22 segments of 17 main coronary arteries, with 9 segments in the LAD, 7 in the RCA and 6 in the LCx.

Comparison of 64-slice CT angiography and myocardial perfusion imaging

Patient-based analysis

4 of 141 patients were excluded from the per patient analysis because of poor image quality on CTA. Patients who had coronary stenoses which could not be reliably evaluated but had assessable stenoses in another segment of the same coronary artery were not excluded from the per patient analysis as they were correctly diagnosed as having CAD. For CTA lesions of ≥50% stenosis, 25 (37%) of 68 patients with stenotic main coronary arteries were shown to have inducible perfusion defects on MPI. Of the 69 patients with less than 50% stenoses on CTA, only 1 had a reversible perfusion defect in the inferior wall. This patient had a 40% stenotic lesion in the RCA. For CTA lesions of ≥70% stenosis, 17 (74%) of 23 patients with stenotic main coronary arteries were demonstrated to have inducible perfusion defects on MPI. Of the remaining 114 patients with stenoses less

Table 3. Diagnostic results of 64-slice CTA in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

64-slice CTA	≥50% stenosis, %	≥70% stenosis, %
Sensitivity	96 (25/26, 88~100)	65 (17/26, 46~84)
Specificity	61 (68/111, 52~70)	95 (105/111, 91~99)
PPV	37 (25/68, 23~49)	74 (17/23, 50~92)
NPV	99 (68/69, 97~100)	92 (105/114, 87~97)
Accuracy ^b	68 (93/137)	89 (122/137)

CM, CT angiography; NPV, negative predictive value; PPV, positive predictive value.

^aPer patient analysis ($n=137$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.01$ for comparison between stenoses ≥50% and ≥70%.

than 70%, 9 had a perfusion defect on MPI. The sensitivity, specificity, PPV, NPV and accuracy of CTA for the detection of inducible perfusion defects on MPI are shown in Table 3, for coronary stenoses ≥50% and ≥70%. Of the 45 patients with the most severe lesions of 50–69% stenosis on CTA, only 8 (18%) were associated with an inducible perfusion defect in the corresponding territory on MPI.

Vessel-based analysis

Comparing CTA lesions of ≥50% stenosis with MPI, only 35 (33%) of 106 stenotic main coronary arteries were associated with an inducible perfusion defect in the corresponding territory on MPI. 71 (67%) of 106 stenotic main coronary arteries were not associated with any perfusion defect on MPI. Only 1 of 36 MPI perfusion defects was identified in the inferior wall subtended by a RCA with a <50% stenotic lesion on CTA. For CTA lesions of ≥70% stenosis, 21 (62%) of 34 stenotic main coronary arteries were demonstrated to be associated with an inducible perfusion defect in the corresponding territory on MPI. 14 of 36 (39%) MPI perfusion defects were identified in areas subtended by arteries with lesions of 50–69% stenosis on CTA. The sensitivity, specificity, PPV, NPV and accuracy of CTA for the detection of inducible perfusion defects on MPI are shown in Table 4, for coronary stenoses ≥50% and ≥70%. Of the 72 stenotic main coronary arteries with the most severe lesions of 50–69% narrowing on CTA, only 14 (19%) were associated with an inducible perfusion defect in the corresponding territory on MPI.

Table 4. Diagnostic results of 64-slice CTA in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

64-slice CTA	≥50% stenosis, %	≥70% stenosis, %
Sensitivity	97 (35/36, 91~100)	58 (21/36, 42~74)
Specificity	86 (440/511, 83~89)	97 (498/511, 95~99)
PPV	33 (35/106, 24~42)	62 (21/34, 45~79)
NPV	100 (440/441, 100~100)	97 (498/513, 95~99)
Accuracy ^b	87 (475/547)	95 (519/547)

CM, CT angiography; NPV, negative predictive value; PPV, positive predictive value.

^aPer artery analysis ($n=547$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.01$ for comparison between stenoses ≥50% and ≥70%.

Table 5. Consensus table of stenosis severity determined by 64-slice CTA versus QCA

QCA	64-slice CTA			
	No stenosis	1–49%	50–69%	≥70%
No stenosis	311	46	8	2
1–49%	11	62	16	0
50–69%	3	3	19	9
≥70%	1	1	6	14

CTA, CT angiography; QCA, quantitative coronary angiography.

Comparison of 64-slice CT angiography, quantitative coronary angiography and myocardial perfusion imaging in 35 patients

A comparison between 64-slice CTA and QCA was available in 512 segments (91%) from the 35 patients. Table 5 compares the classification of lesions derived from CTA and QCA. Consensus in classifying the degree of coronary stenosis with both imaging modalities was achieved in 95 of 145 stenotic segments and in 311 of 367 disease-free segments on QCA. Overall, 15 lesions could not be visualised and 10 lesions were underestimated by CTA, 56 segments were incorrectly graded as stenotic (most are 1–49%), and in 25 segments a present lesion was overestimated. Of 8 stenoses ≥70% on QCA that were incorrectly classified by CTA, 7 were underestimated and 1 could not be visualised as a result of its location in a side branch. 8 of 11 lesions that were incorrectly classified as ≥70% stenosis by CTA were located in the distal segments. Comparing the degree of stenosis measured by CTA with that measured by QCA, the Pearson correlation coefficient between the 2 modalities was 0.766 ($p<0.01$, $n=512$) (Figure 1).

The diagnostic results of CTA and QCA for the detection of inducible perfusion defects in corresponding territories on MPI are shown in Tables 6–9. As depicted in Tables 6–9, there was no statistical difference (χ^2 test, $p=NS$) in diagnostic accuracy between the two imaging modalities for both cut-offs of ≥50% and ≥70% diameter stenosis and for patient-based or vessel-based analysis. One example of a patient with stable angina undergoing CTA, ICA and MPI is shown in Figure 2.

Radiation dose

The average radiation exposure for the complete CTA protocol was 14.9 ± 2.6 mSv. The estimated radiation dose for the SPECT MPI was 16.3–20.4 mSv.

Discussion

Our study demonstrates an excellent ability of 64-slice CTA to exclude functionally significant coronary artery stenoses as indicated by the extremely high NPV when using a cut-off of 50% diameter stenosis. The low PPV (37%, 25/68) for diameter stenosis of ≥50% to predict ischaemia in the present study is in line with previous studies which reported ischaemia in approximately 30–60% for patients with ≥50% stenosis on 64-slice CTA [6, 8, 9], and suggests that this level of stenosis should not be used to stratify patients for invasive

Figure 1. Overall correlation of 64-slice CT angiography (CTA) and quantitative coronary angiography (QCA) measurements of diameter stenosis in comparable coronary segments. Pearson's correlation coefficient $r=0.766$, $p<0.01$, $n=512$.

Table 6. Diagnostic results of 64-slice CTA and QCA using a cut-off of $\geq 50\%$ diameter stenosis in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

Index	64-slice CTA, %	QCA, %
Sensitivity	100 (14/14, 100~100)	100 (14/14, 100~100)
Specificity	67 (14/21, 46~88)	71 (15/21, 51~91)
PPV	67 (14/21, 46~88)	70 (14/20, 50~90)
NPV	100 (14/14, 100~100)	100 (15/15, 100~100)
Accuracy ^b	80 (28/35)	83 (29/35)

CTA, CT angiography; QCA, quantitative coronary angiography; PPV, positive predictive value; NPV, negative predictive value.

^aPer patient analysis ($n=35$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.76$ for comparison between 64-slice CTA and QCA.

coronary angiography. In the current study, only 1 of 59 patients with $<50\%$ stenosis had a reversible perfusion defect in the inferior wall, demonstrating that lesions under 50% stenosis are highly unlikely to cause perfusion abnormalities on SPECT MPI and patients who have stenosis of $<50\%$ may be reassured or even safely deferred for further functional testing.

Fewer studies, however, are available comparing the presence of $\geq 70\%$ diameter stenosis on 64-slice CTA

Table 7. Diagnostic results of 64-slice CTA and QCA using a cut-off of $\geq 70\%$ diameter stenosis in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

Index	64-slice CTA, %	QCA, %
Sensitivity	86 (12/14, 67~100)	86 (12/14, 67~100)
Specificity	86 (18/21, 71~100)	81 (17/21, 64~98)
PPV	80 (12/15, 59~100)	75 (12/16, 53~97)
NPV	90 (18/20, 77~100)	89 (17/19, 75~100)
Accuracy ^b	86 (30/35)	83 (29/35)

CTA, CT angiography; QCA, quantitative coronary angiography; PPV, positive predictive value; NPV, negative predictive value.

^aPer patient analysis ($n=35$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.56$ for comparison between 64-slice CTA and QCA.

Table 8. Diagnostic results of 64-slice CTA and QCA using a cut-off of $\geq 50\%$ diameter stenosis in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

Index	64-slice CTA, %	QCA, %
Sensitivity	94 (16/17, 82~100)	100 (17/17, 100~100)
Specificity	78 (96/123, 71~85)	82 (101/123, 75~89)
PPV	37 (16/43, 22~52)	44 (17/39, 28~60)
NPV	99 (96/97, 97~100)	100 (101/101, 100~100)
Accuracy ^b	80 (112/140)	84 (118/140)

CTA, CT angiography; QCA, quantitative coronary angiography; PPV, positive predictive value; NPV, negative predictive value.

^aPer artery analysis ($n=140$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.35$ for comparison between 64-slice CTA and QCA.

with evidence of ischaemia on SPECT MPI. Our data reveal that the yield of abnormal SPECT MPI studies (a PPV of 74%) and the diagnostic accuracy (89%) increased substantially when a cut-off of 70% diameter stenosis on 64-slice CTA was used for the detection of ischaemia rather than a 50% cut-off. Interestingly, somewhat higher agreement (86%, 6/7) for $\geq 70\%$ diameter narrowing on CTA and ischaemia on functional testing has been reported by Nicol et al [9], who compared 64-slice CTA

Table 9. Diagnostic results of 64-slice CTA and QCA using a cut-off of $\geq 70\%$ diameter stenosis in detecting inducible perfusion defects in corresponding areas on myocardial perfusion imaging^a

Index	64-slice CTA, %	QCA, %
Sensitivity	71 (12/17, 49~93)	53 (9/17, 29~77)
Specificity	94 (116/123, 90~98)	94 (115/123, 90~98)
PPV	63 (12/19, 41~85)	53 (9/17, 29~77)
NPV	96 (116/121, 92~99)	94 (115/123, 90~98)
Accuracy ^b	91 (128/140)	89 (124/140)

CTA, CT angiography; QCA, quantitative coronary angiography; PPV, positive predictive value; NPV, negative predictive value.

^aPer artery analysis ($n=140$). Values in parentheses represent ratios and 95% confidence intervals.

^b $p=0.43$ for comparison between 64-slice CTA and QCA.

Figure 2. 64-slice coronary CT angiogram, corresponding invasive angiogram and single photon emission CT (SPECT) myocardial perfusion scan in a patient presenting with stable angina and a calcium score (Agatston) of 461. (a, b) Maximum intensity projection technique demonstrates severe narrowing of the left anterior descending (LAD) coronary artery below the first diagonal branch (a), moderate stenosis of the proximal right coronary artery (RCA) (b), and coronary calcifications of both LAD and RCA. (c, d) Invasive coronary angiography of the same arteries. (e) SPECT stress-redistribution myocardial perfusion imaging shows a large reversible perfusion defect involving the anterior wall, apex and septum.

and gated SPECT MPI with ^{99m}Tc tetrofosmin in 52 consecutive patients, of whom a smaller proportion (13%, 7/52) had abnormal MPI studies. Conversely, a lower PPV (55%, 11/20) for diameter stenosis of $\geq 70\%$ to detect ischaemia was recently reported by Haramati et al [11], who compared 64-slice CTA and SPECT MPI using treadmill exercise or adenosine and $^{201}\text{Tl}/^{99m}\text{Tc}$ sestamibi in 61 consecutive patients. In contrast to these two studies, our larger study population allowed the

clinically more relevant per patient analysis to be conducted. Notably, each study had a different study population and design, used different stress techniques and radiopharmaceuticals for MPI, dealt with non-evaluable segments on CTA in various ways, and applied qualitative or quantitative assessment of coronary lesions, making direct comparisons between studies difficult. Indeed, the accuracy of estimating percentage stenosis with CTA is highly dependent on

image quality and frequently suffers from image degradation due to blooming and motion artefacts [25]. In addition, spatial resolution of 64-slice CTA is still limited compared with that of ICA, which was demonstrated in our subset of patients undergoing ICA and might have influenced the precision of stenosis evaluation in these examinations and led to the discrepancies between the studies. Nonetheless, regardless of the accuracy of stenosis assessment, one should realise that, although high percentage narrowing ($\geq 70\%$) is a strong indicator of coronary resistance, other CTA characteristics, including lesion length, morphology and location as well as non-calcified plaque burden, are also important determinants [26, 27]. Notably, in our patients with lesions of $\geq 70\%$ stenosis on CTA, still approximately 1 of 4 (26%, 6/23) showed normal perfusion on SPECT MPI. This result is in agreement with a meta-analysis of 31 studies comparing QCA and fractional flow reserve (FFR) and showing that only about 70% of lesions with $\geq 70\%$ diameter stenosis on QCA were associated with abnormal FFR values [28]. Thus, even in the presence of high-grade lesions of $\geq 70\%$ stenosis on 64-slice CTA, a further functional test, such as stress echocardiography or MPI, may still be required before the decision for revascularisation, especially in asymptomatic patients.

Moreover, the poor PPV (18%, 8/45) for diameter stenosis of 50–69% on 64-slice CTA to predict ischaemia in our study has been previously reported in direct comparison between ICA and MPI by Chamuleau et al [29], who performed SPECT and ICA in 19 patients with at least 1 severe lesion ($\geq 70\%$ diameter narrowing) and 1 intermediate lesion (defined as between 40% and 70% diameter narrowing) on invasive angiography. In this study, 153 (80%) patients showed ischaemia on SPECT in the vascular territory corresponding to the severe lesion, but only 30 (16%) patients exhibited ischaemia in the territory of the intermediate lesion. These observations highlight that neither invasive nor non-invasive angiography provides information on the haemodynamic relevance of the intermediate lesions, and functional testing is still required to avoid unnecessary invasive angiography in those patients whose stenotic lesions are not flow limiting.

Finally, as shown in the subset of 35 patients undergoing invasive angiography, quantitative 64-slice CTA and QCA exhibited a comparable diagnostic ability in detecting ischaemia. Remarkably, compared with the overall study population analysis, a much higher PPV (67% *vs* 37%) for diameter stenosis of $\geq 50\%$ on 64-slice CTA to predict ischaemia was found in the patient-based analysis in this subset of patients. The discrepancy between the two analyses was caused by catheterisation referral bias. Of the 45 patients (8 ischaemic and 37 non-ischaemic) with 50–69% stenotic lesions on CTA, only 6 were referred for invasive angiography, of whom 2 were ischaemic. By contrast, of the 23 patients (17 ischaemic and 6 non-ischaemic) with $\geq 70\%$ stenotic lesions on CTA, 15 underwent invasive angiography, of whom 12 were ischaemic.

Study limitations

There are shortcomings when applying SPECT MPI as the reference standard for functionally significant

coronary stenoses. SPECT MPI has a high sensitivity for detecting significant coronary stenoses, but its specificity is somewhat lower [12]. Additionally, SPECT MPI is a technically demanding procedure which is subjected to a variety of artefacts, particularly breast or diaphragmatic attenuation artefacts. However, there is no perfect gold standard test for myocardial ischaemia, and, considering the extensive experience accumulated over past 20 years, this technique can be regarded as being the best evaluated and most widely used non-invasive imaging tool for the functional assessment of CAD. Moreover, on the basis of our own data, both diaphragmatic and breast attenuation artefacts are not frequent occurrences in Eastern people with smaller body sizes. Thus, attenuation correction is not used in our daily routine practice. Furthermore, to maximise the reliability of this diagnostic modality, we excluded patients with prior myocardial infarction to allow the relationship between CTA and MPI to be assessed in the absence of the confounding variable of viability.

Conclusions

64-slice CTA is a reliable tool to exclude functionally significant CAD when using a cut-off of $\geq 50\%$ diameter stenosis. Patients who have stenoses of less than 50% may be reassured or even safely deferred for functional study. By contrast, a cut-off of $\geq 70\%$ diameter narrowing is a strong predictor of ischaemia. However, even in the presence of high-grade lesions of $\geq 70\%$ stenosis on 64-slice CTA, a further functional test, such as stress echocardiography or MPI, may still be required before the decision for revascularisation, especially in asymptomatic patients. In addition, in patients whose lesions are 50–69% narrowing, functional testing remains mandatory to avoid unnecessary invasive angiography.

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