Incremental value of combining 64-slice computed tomography angiography with stress nuclear myocardial perfusion imaging to improve noninvasive detection of coronary artery disease

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Background. **To compare the accuracy of combined 64-slice computed tomography angiography (CTA) and stress nuclear myocardial perfusion imaging (MPI) in the noninvasive detection of coronary artery disease (CAD) with that of 64-slice CTA alone.**

Methods and results. **One hundred thirty symptomatic patients with suspected CAD underwent both 64-slice CTA and stress thallium-201 MPI before invasive coronary angiography (ICA). Coronary lesions with ≥50% luminal narrowing were considered as significant stenoses on CTA and ICA. Of 390 arteries in 130 patients, 54 (14%) were nonevaluable by CTA due to severe calcifications, motion artifacts, and/or poor opacification. All nonevaluable arteries were considered positive. The sensitivity, specificity, PPV and NPV were 95%, 80%, 69%, and 97%, respectively, for CTA alone and 94%, 92%, 85%, and 97%, respectively, for CTA with stress nuclear MPI for all nonevaluable arteries on CTA. Per-patient analysis showed significant increase in specificity and PPV. The majority (75%, 9/12) of nonevaluable severely calcified vessels in the left anterior descending artery were positive on stress nuclear MPI, whereas the majority (89%, 8/9) of nonevaluable vessels with motion artifacts in the right coronary artery were negative.**

Conclusions. **Combined CTA and stress nuclear MPI provide improved diagnostic accuracy for the noninvasive detection of CAD. (J Nucl Cardiol 2010;17:19–26.)**

Key Words: Computed tomography angiography • imaging • coronary stenosis • perfusion

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INTRODUCTION

Since the recent advent of multidetector computed tomography angiography (CTA), image quality has greatly improved with the progression from 8- to 16- and now 64-slice capability, thus allowing for more precise evaluation of coronary artery stenosis.[1] However, CTA is technically limited by suboptimal image quality when severe calcifications or motion artifacts are present. Even with the use of 64-slice CT scanners, the positive predictive value (PPV) of CTA is relatively low when evaluating patients with chest pain.[2] This limited PPV is clinically important because it could result in the performance of unnecessary invasive coronary angiography (ICA). The latest multicenter 64-slice CT trial (CORE 64) indicated that multidetector CTA cannot be used as a replacement for ICA at present, given its negative predictive value (NPV) of 83% and PPV of 91% in symptomatic patients.[3]

Stress nuclear myocardial perfusion imaging (MPI) using single-photon emission tomography (SPECT) is an established method for assessment of the functional significance of coronary stenosis and delivers valuable information for risk stratification.[4] Recently, the results of hybrid SPECT/CTA imaging have provided a marked increase in specificity and PPV to detect hemodynamically significant coronary lesions compared to those of 16-slice CTA alone.[5] However, diagnostic performance of the 16-slice CT device used in that study was only moderate for detection of significant coronary artery stenosis, with 23% of coronary segments not evaluable.

We previously indicated that 64-slice CTA alone is not always sufficient to assess the functional significance of anatomic stenoses, especially stenoses of intermediate grade.[6] When stenosis severity by CTA was <60%, ischemia was seldom observed, and when stenosis severity was ≥80%, ischemia was common. For intermediate stenosis severity values of 60-80%, the prevalence of reversible defects was difficult to determine, given CTA's current spatial resolution.[6] The aim of the present study was to compare the accuracy of combined use of 64-slice CTA and stress nuclear MPI for the noninvasive detection of coronary artery disease (CAD) with that of 64-slice CTA alone.

MATERIALS AND METHODS

Study Population

Initially, 142 symptomatic patients with suspected CAD who underwent both 64-slice CTA and stress nuclear MPI from January 2006 to August 2006 were enrolled in this study. Inclusion criteria included sinus heart rhythm; no previous myocardial infarction; no previous percutaneous coronary intervention or coronary bypass surgery; and no unstable angina. The subjects included in this study underwent ICA as the standard of reference within 1 month after the CTA and stress nuclear MPI tests. Of the 142 patients, 12 patients were excluded for the following reasons: Scheduled ICA was canceled on patients on the basis of normal 64-slice CTA and stress nuclear MPI studies (n = 10), patient noncompliance (n = 1) and poor intravenous access (n = 1). The remaining 130 patients represent the subjects of this study. Typical angina was defined as having three characteristics: substernal discomfort; precipitation by physical exertion or emotion; and relief with rest or nitroglycerin within 10 minutes. Atypical angina pectoris was defined as having two of the three defined characteristics. Nonanginal chest pain was characterized as having only one or none of the defined chest pain features.[7] Pre-test likelihood of CAD was determined according to the Diamond and Forrester method using percent cutoffs of <13.4%, >87.2%, and in between for low, high, and intermediate pre-test likelihood, respectively.[8] The study protocol was approved by our institutional review board and written informed consent was obtained from all the patients after explaining the study details including the risk of radiation exposure.

64-Slice CTA Scanning, Reconstruction and Image Analysis

Scanning was performed with a 64-slice CT scanner (Aquilion 64; Toshiba Medical Systems Corporation, Otawara, Japan). The Aquilion 64 is a 64 × 0.5 mm collimation scanner with 400-ms gantry rotation speed. Scanning was performed at 120 kV and 400 mAs. Table feed was 6.4 mm/gantry rotation with a beam pitch of 0.2. The CT dose index volume and dose-length product of this scan protocol were 75.2 mGy and 1.10 Gy·cm corresponding to an approximate mean radiation dose of 15 mSv.[3] Sixty milliliters of contrast agent (Iopamidol 370 mgI/mL; Schering AG, Berlin, Germany) was injected intravenously at a rate of 4 mL/s. When the signal density level in the ascending aorta reached a predefined threshold of 100 Hounsfield units (HU), acquisition of CT data and an electrocardiogram (ECG) trace were automatically started during a 7-9 second breath-hold. Patients were given oral metoprolol 20 mg 1 hour before the scheduled scan if their heart rate was >65 beats/minute. All patients were given sublingual nitroglycerin 0.3 mg 5 minutes before the scan.

Analysis of the scans was performed with a ZIOSTATION workstation (ZIOSOFT Inc., Tokyo, Japan). Images were initially reconstructed at 75% of the cardiac cycle with a slice thickness of 0.5 mm at an increment of 0.3 mm. In case of motion artifacts, additional reconstructions were made at different time points of the R-R interval. Each scan was analyzed independently by two experienced readers who were blinded to the results of stress nuclear MPI and ICA. Any disagreement between the readers was resolved by a third reader. If coronary plaques were present, the CTA studies were classified as obstructive CAD (≥50% luminal narrowing) by visual assessment. If severe motion artifacts or severe calcifications were present, the scan was classified as nonevaluable. Patients with at least one identified significant stenosis were classified as having obstructive CAD.

Stress Nuclear MPI

One-day stress-redistribution nuclear MPI with thallium-201 (Tl-201) was performed within 1 week of CTA. Beta-blockers, calcium channel blockers and nitrates were discontinued for 24-48 hours before the test. Eighty-seven of the 130 patients underwent symptom-limited exercise on a bicycle ergometer in the sitting position with 12-lead ECG and blood pressure measurements taken at baseline and every minute during the exercise. The test was terminated with achievement of 100% of maximal predicted heart rate, ischemic ST-segment depression of >2 mm, severe cardiac arrhythmia, severe chest pain or significant hypotension. At the peak of the exercise, a dose of 111 MBq of Tl-201 was injected intravenously. For the 43 patients unable to exercise, adenosine was administered intravenously at 0.14 mg/kg/minute for 5 minutes, and Tl-201 was injected intravenously. ECG and blood pressure were monitored before, throughout, and following the infusion. The initial image was obtained in the supine position at 5 minutes after Tl-201 injection and a delayed image was obtained 4 hours later.

SPECT was performed using a double-detector system (PICKER PRISM 2000XP; Shimadzu Corporation, Kyoto, Japan) equipped with a low-energy high-resolution collimator. Seventy-two projection data were obtained with a 64 × 64 matrix over 360°. Data were acquired for 25 seconds for each projection. The energy window was set at the 67 keV photo peak of Tl-201 with a 15% window. Reconstruction was performed using a Butterworth filter at a cutoff frequency of 0.24 cycles/pixel and an order of 8. No attenuation or scatter correction was used. SPECT images were assessed using a 17-segment model and data were presented in polar map format (normalized to 100%).[9] Perfusion defects were identified on the stress images (segmental tracer activity <75% of maximum) and classified as ischemia or scar tissue. Stress and delayed images were independently analyzed by two nuclear physicians who were blinded to the CTA and ICA data. Disagreement between readers was resolved by a third reader. Visual grading was defined as normal (no perfusion defects) or abnormal (stress perfusion defects with redistribution or fixed defects).

Invasive Coronary Angiography

The patients were scheduled for ICA within 1 month after CTA and nuclear MPI study. Experienced interventional cardiologists performed ICA through the brachial approach with 5F catheters and analyzed all angiographic data quantitatively with validated automated edge-detection software (CAAS II; Pie Medical, Maastricht, The Netherlands). The outer diameter of the catheter tip, unfilled with contrast agent, was used as the calibration standard. Minimal lumen diameter, reference diameter, and percentage diameter stenosis of the lesion were measured from multiple projections in diastole. Coronary lesions with ≥50% luminal narrowing were considered as significant stenoses on ICA.

Statistical Analysis

All data are expressed as the mean ± SD or median and interquartile range. The diagnostic performance of CTA, stress nuclear MPI, and the two in combination were compared on a per-vessel and per-patient basis to determine sensitivity and specificity as well as PPV and NPV for the detection of coronary artery stenoses as defined by ICA. The performance indexes of CTA alone and in combination with stress nuclear MPI results were compared by the McNemar test. Differences between the number of positive vessels among the nonevaluable calcified vessels versus those with motion artifacts and the number of left anterior descending artery (LAD) versus right coronary artery (RCA) vessels with motion artifacts were analyzed by chi-square test. *P* values of <.05 were considered significant.

RESULTS

Patient Characteristics

Baseline clinical characteristics of the 130 patients enrolled in the study are summarized in Table 1. Before-test likelihood of CAD determined by the methods of Diamond and Forrester was low in 8 (6%), intermediate in 109 (84%), and high in 13 (10%) patients.

Table 1. Characteristics of the patients (n = 130)

Age (years)	67 ± 11
Male/female	91/39
Hypertension (%)	66 (51%)
Hyperlipidemia (%)	69 (53%)
Diabetes (%)	46 (35%)
Smoking (%)	53 (41%)
BMI (kg/m^2), median (IQR)	24.6 (22.3-26.6)
Symptoms	
Typical angina	85 (65%)
Atypical angina	33 (25%)
Nonanginal chest pain	12 (10%)
Pre-test likelihood of CAD	
Low	8 (6%)
Intermediate	109 (84%)
High	13 (10%)

BMI, Body mass index; *IQR*, interquartile range; *CAD*, coronary artery disease.

Invasive Coronary Angiography

Among the 130 patients, 124 (32%) of 390 arteries had a stenosis of more than 50% by ICA (single-vessel disease: 40 patients; 2-vessel disease: 26 patients; 3-vessel disease: 11 patients).

Stress Nuclear MPI Finding

Normal myocardial perfusion was observed in 49 (38%) of the 130 patients. In the remaining 81 (62%) patients, reversible and fixed defects were observed in 73 and 12 patients, respectively, with 4 patients showing both reversible and fixed defects. Normal myocardial perfusion was present in 256 vascular territories (66%), whereas reversible and fixed defects were observed in 122 (31%) and 12 (3%) vascular territories, respectively. For the detection of significant stenosis, stress nuclear MPI had a sensitivity of 81% (101 of 124), specificity of 87% (233 of 266), PPV of 75% (101 of 134), and NPV of 90% (233 of 256).

Comparison of 64-Slice CTA and CTA + Stress Nuclear MPI Results to ICA for Detection of Coronary Stenoses

The performance indexes of CTA as a stand-alone diagnostic procedure were recorded in the evaluable vessels. When vessels were not evaluable on CTA, stress nuclear MPI results were incorporated in the territories supplied by nonevaluable arteries (Figures 1 and 2).

Vessel-based analysis. Of the 390 arteries in 130 patients, 54 (14%) were deemed nonevaluable by 64-slice CTA due to severe calcifications (n = 32; LAD: n = 12, LCx: n = 12, RCA: n = 8), motion

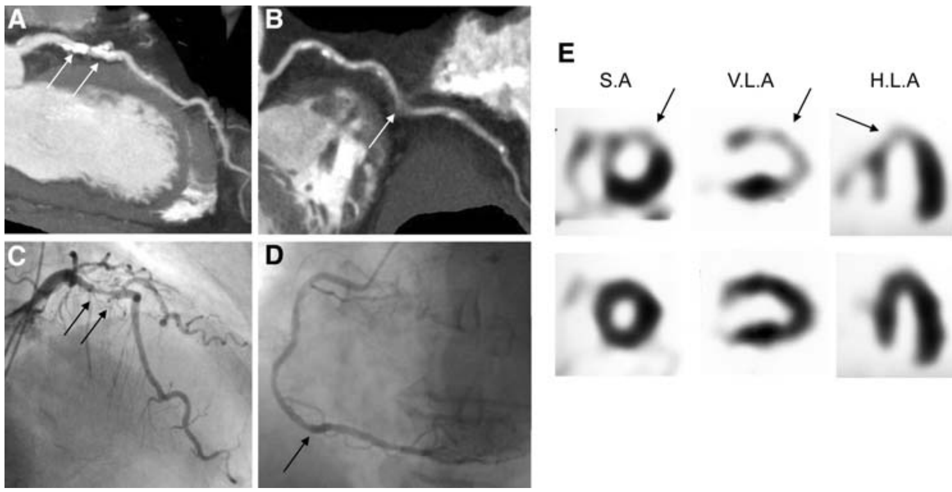

Figure 1. Results of a 68-year-old man with chest pain. **A**, Computed tomography angiography (CTA) reveals a severely calcified lesion (*arrows*) in the proximal LAD. **B**, CTA shows a poor image with motion artifact (*arrow*) in the mid RCA. **C**, Invasive coronary angiography (ICA) shows the presence of a significant stenosis in the proximal LAD. **D**, ICA shows no significant stenosis in the mid RCA. **E**, Corresponding nuclear myocardial perfusion imaging during stress (*top row*) and rest (*bottom row*) shows a reversible perfusion abnormality in the anterior, septal and apical walls (*arrows*). *SA*, Short axis; *VLA*, vertical long axis; *HLA*, horizontal long axis.

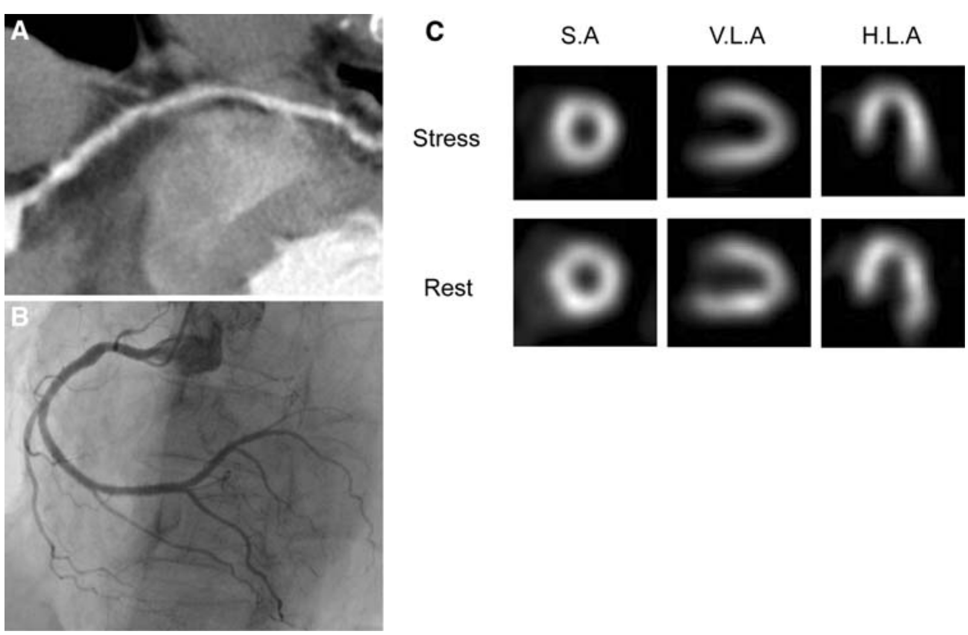

Figure 2. Results of a 60-year-old woman with chest pain. **A**, CTA shows a poor image with motion artifact in the RCA. **B**, Invasive coronary angiography shows no significant stenosis in the RCA. **C**, Corresponding nuclear myocardial perfusion imaging shows normal perfusion at peak exercise and at rest. Abbreviations as in Figure 1.

artifacts (n = 16; LAD: n = 2, LCx: n = 5, RCA: n = 9), and poor opacification (n = 6; LAD: n = 2, LCx: n = 2, RCA: n = 2). Motion artifacts were observed significantly more frequently in the RCA than in the LAD ($P < .05$). After excluding all nonevaluable arteries, 64-slice CTA had a sensitivity of 94%, specificity of 91%, PPV of 82%, and NPV of 97% for the detection of significant stenosis. Table 2 shows vessel-based analysis after censoring all nonevaluable arteries as positive, and after adding stress MPI results for all nonevaluable arteries evaluated by CTA. There was a statistically significant increase in the specificity and PPV for all three vessels when applying stress nuclear MPI results to all nonevaluable vessels as compared with all vessels for analysis with nonevaluable vessels considered positive ($P < .001$ for both).

The proportion of nonevaluable severely calcified vessels (59%, 19/32) positive on stress nuclear MPI was larger than that of nonevaluable vessels (25%, 4/16) with motion artifact ($P < .001$). There was no statistical difference in the proportion of nonevaluable severely calcified vessels positive on stress nuclear MPI between the vascular territories of the LAD (75%, 9/12), RCA (50%, 4/8), and LCx (50%, 6/12). The majority (89%, 8/9) of nonevaluable vessels with motion artifacts in the RCA were negative on stress MPI compared to those in LAD (50%, 1/2) and LCx (60%, 3/5).

Patient-based analysis. Of the 130 patients, 107 were classified as evaluable. For the detection of patients with at least one significant stenosis, the sensitivity, specificity, PPV and NPV of 64-slice CTA were 98%, 82%, 88%, and 97%, respectively. Table 3 shows patient-based analysis after censoring all nonevaluable patients as positive and after adding stress MPI results for all nonevaluable patients evaluated by CTA. There was a statistically significant increase in specificity and PPV when applying stress nuclear MPI results to all nonevaluable patients as compared with all patients for analysis with nonevaluable patients considered positive ($P < .001$ for both).

Table 3. Per-patients analysis of 64-slice CTA and combined stress nuclear MPI for the detection of coronary stenoses

	All patients for analysis with nonevaluable patients considered positive (n = 130)	Combined stress MPI results to all nonevaluable patients (n = 130)
Sensitivity	99% (76/77)	99% (76/77)
Specificity	70% (37/53)	87% (46/53)*
PPV	82% (76/92)	91% (76/83)*
NPV	97% (37/38)	98% (46/47)
Accuracy	87% (113/130)	94% (122/130)*

*$P < 0.001$ vs all patients for analysis with nonevaluable patients considered positive. Abbreviation as in Table 2.

DISCUSSION

The major findings in the present study are as follows. First, our analysis was performed once for CTA alone after censoring nonevaluable arteries as positive and was then repeated with the stress nuclear MPI

Table 2. Per-vessel analysis of 64-slice CTA and combined CTA and stress nuclear MPI for the detection of coronary stenoses

	n	Sensitivity	Specificity	PPV	NPV
All vessels for analysis with nonevaluable vessels considered positive					
All vessels	390	95% (118/124)	80% (214/266)	69% (118/170)	97% (214/220)
LAD	130	100% (56/56)	74% (55/74)	75% (56/75)	100% (55/55)
LCx	130	94% (34/36)	85% (80/94)	71% (34/48)	97% (80/82)
RCA	130	87% (28/32)	81% (79/98)	60% (28/47)	95% (79/83)
Combined stress nuclear MPI results to all nonevaluable vessels					
All vessels	390	94% (116/124)	92% (245/266)*	85% (116/137)*	97% (245/253)
LAD	130	100% (56/56)	85% (62/73)*	84% (56/67)*	100% (62/62)
LCx	130	89% (32/36)	94% (92/97)*	86% (32/37)*	96% (92/96)
RCA	130	88% (28/32)	94% (91/96)*	85% (28/33)*	96% (91/95)

CTA, Computed tomography angiography; *MPI*, myocardial perfusion image; *LAD*, left anterior descending artery; *LCx*, circumflex coronary artery; *RCA*, right coronary artery; *PPV*, positive predictive value; *NPV*, negative predictive value.
*$P < .001$ vs all vessels for analysis with nonevaluable vessels considered positive.

results substituted for nonevaluable CTA results. Stress nuclear MPI studies improved the specificity and PPV of CTA for the detection of coronary artery stenosis in all three vessels and could be used to complement the finding from coronary CTA. Second, the majority of nonevaluable severely calcified LAD vessels on CTA were positive on stress nuclear MPI, whereas the majority of nonevaluable RCA vessels with motion artifacts were negative on stress nuclear MPI. Combining 64-slice CTA with selective stress nuclear MPI in nonevaluable coronary vessels provides improved diagnostic accuracy for the noninvasive detection of CAD.

Combined 64-Slice CTA and Stress Nuclear MPI for Detection of Coronary Artery Disease

Pooled data from six 64-slice CTA studies showed a sensitivity of 96% and specificity of 92% to detect or exclude significant CAD.[1,10,11] However, the PPV of CTA is suboptimal when severe calcifications, stents, or motion artifacts are present.[12] Currently, the main clinical advantage of CTA appears to be related to its high NPV.[13] In the present study, the addition of stress nuclear MPI data to all nonevaluable CTA cases significantly increased the specificity and PPV of CTA for the detection of coronary artery stenosis in all three vessels. Because of its excellent NPV, 64-slice CTA can be used as the first-line test for noninvasive evaluation of CAD. When CTA results are abnormal or nonevaluable, additional information may be provided noninvasively by the addition of stress nuclear MPI. In patients with normal perfusion or small reversible defects, primary prevention will be gained by medical therapy because of the favorable long-term prognosis.[14] However, patients with large reversible defects should undergo ICA with appropriate revascularization of the culprit lesion. To complement the suboptimal results of CTA, integration of CTA with stress nuclear MPI seems to be a more accurate method for evaluation of these specific subgroups. Recently, cardiac 3D SPECT/CT fusion imaging has been shown to provide additional information about hemodynamic relevance and facilitates lesion interpretation by allowing exact allocation of perfusion the defects to the subtending coronary artery.[15]

Assessment of both coronary stenosis and perfusion has great potential application to further advance the evaluation of patients with CAD. However, the choice of the optimal first line-test remains a question that is not answered by the present study. In fact, the high diagnostic accuracy of stress nuclear MPI in this study may argue in favor of stress nuclear MPI as the initial test. Available clinical experience points toward tailoring the initial diagnostic approach according to the pretest probability of the patient.[7] In low-to-intermediate likelihood patients, CTA may well be the best initial test due to its high NPV however, in intermediate-to-high probability patients CTA's low PPV may result in unnecessary radiation exposure, which in this study was considerable, and stress nuclear MPI might be a better first-line test. From the present study, we cannot definitely conclude which is the better first-line test, and we acknowledge that further head-to-head comparisons between the two modalities are required.

Added Value of Stress Nuclear MPI for Nonevaluable Vessels on CTA

We showed that the majority of the nonevaluable severely calcified vessels in the LAD were positive on stress nuclear MPI, whereas the majority of nonevaluable vessels with motion artifacts in the RCA were negative. Berman et al reported that the frequency of myocardial ischemia on nuclear MPI increased progressively as the coronary artery calcification (CAC) score increased in magnitude above 100, and 20% of patients with CAC scores exceeding 1000 manifested ischemia.[16] The sensitivity of stress nuclear MPI to recognize disease in the LAD is higher than that for disease in the LCx or RCA.[17] To improve cost-effectiveness and avoid the additional radiation exposure of stress nuclear MPI, one potential approach would be to perform ICA to evaluate severely calcified LAD vessels not evaluable on CTA. In contrast, to avoid unnecessary invasive procedures, stress nuclear MPI could be performed to evaluate RCA vessels with motion artifacts not evaluable on CTA.

Discrepancy Between 64-Slice CTA and Nuclear MPI Results

Disagreement between CTA $\geq$ 50% stenosis and reversible MPI defects is common.[12] CTA and MPI are measuring two different things, vessel patency and perfusion, respectively. Only 50% of obstructed vessels with $\geq$50% luminal narrowing by CTA show abnormal MPI.[18] In our study, discrepancy between CTA and nuclear MPI was observed in 65 (19%) of 336 evaluable vessels, suggesting that coronary anatomy and function cannot always be expected to correlate well. An important limitation of this kind of study is the use of QCA as the gold standard. In a study by Risper and colleagues, a combination of SPECT and coronary angiography was used as the standard of reference for 'hemodynamically significant CAD'.[5] However, the simple QCA stenosis is probably a poor gold standard for reflect the pathophysiologic and prognostic severity of CAD. Therefore, combined assessment of coronary anatomy and myocardial perfusion is generally recommended in patients with stable CAD. The comprehensive information obtained from SPECT may in fact exceed the pure diagnostic value for detecting a stenosis of more than 50%. For all these reasons, an imperfect match between SPECT/CT and coronary angiography is unavoidable by nature of the tests used.

The effect of the presence of microvascular endothelial dysfunction such as that of diabetes or known microvascular disease was not addressed.[19] Even if the CTA is normal, patients with such disease may well have perfusion abnormalities, and we suggest that nuclear MPI be done first in these cases. Although CTA would likely not detect microvascular endothelial dysfunction, such patients are less likely to benefit from ICA and coronary intervention.

Clinical Limitations

The current study is limited by the relatively small number of subjects involved, the use of thallium without attenuation and scatter correction, and the lack of ECG-gated nuclear MPI. Also technetium-99m sestamibi or tetorofosmin are associated with lower radiation exposure than that with thallium. Secondly, a calcium score was not performed before starting with CTA. Radiation dose levels are high when a study algorithm combining CTA, stress nuclear MPI and ICA is used, with levels estimated at 15 mSv for CTA, 16.9 mSv for thallium and 5 mSv for ICA. ECG modulation of tube current was not performed to reduce radiation exposure in this study. Recently, prospective ECG-gating protocols have been used to reduce radiation exposure from CTA by 60-80%. In addition, we did not analyze the cost-effectiveness of combined CTA and stress nuclear MPI against that of ICA.

CONCLUSIONS

Combining 64-slice CTA and stress nuclear MPI provides improved diagnostic accuracy for the noninvasive detection of CAD and is especially useful in nonevaluable coronary vessels on CTA. This study underlies the value of a combined assessment of coronary anatomy and myocardial perfusion in patients with CAD and adds to an increasing body of evidence suggesting an added diagnostic value when combining both modalities.

Acknowledgment

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References

1. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. J Am Coll Cardiol 2005;46:552-7.
2. Mollet NR, Cademartiri F, van Miegheim CA, Runza G, McFadden EP, Baks T, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005;112:2318-23.
3. 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;359:2324-36.
4. Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, et al. Incremental prognostic value of myocardial perfusion SPECT for the prediction of cardiac death: Differential stratification for risk of cardiac death and MI. Circulation 1998;97:535-43.
5. Rispler S, Keidar Z, Ghersin E, Roguin A, Soil A, Dragu R, et al. Integrated single-photon emission computed tomography and computed tomography coronary anigography for the assessment of hemodynamically significant coronary artery lesions. J Am Coll Cardiol 2007;49:1059-67.
6. Sato A, Hiroe M, Tamura M, Ohigashi H, Nozato T, Hikita H, et al. Quantitative measures of coronary stenosis severity by 64-slice computed tomography angiography and relation to physiologic significance of perfusion in non-obese patients: Comparison with stress myocardial perfusion imaging. J Nucl Med 2008;49:564-72.
7. Meijboom WB, van Mieghem CA, Mollet NR, Pugliese F, Weustink AC, van Pelt N, et al. 64-Slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. J Am Coll Cardiol 2007;50:1469-75.
8. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary artery disease. N Engl J Med 1979;300:1350-8.
9. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the cardiac imaging committee of the council on clinical cardiology of the American Heart Association. Circulation 2002;105:539-42.
10. Leschka S, Alkadhi H, Plass A, Desbiolles L, Grunenfelder J, Marincek B, et al. Accuracy of MSCT coronary angiography with 64-slice technology: First experience. Eur Heart J 2005;26:1482-7.
11. Ropers D, Rixe J, Anders K, Kuttner A, Baum U, Bautz W, et al. Usefulness of multidetector row spiral computed tomography with 64 × 0.6 mm collimation and 330-ms rotation for noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343-8.
12. Hacker M, Jakobs T, Matthiesen F, Vollmar C, Nikolaou K, Becker C, et al. Comparison of spiral multidetector CT angiography and myocardial perfusion imaging in the noninvasive detection of functionally relevant coronary artery lesions: First clinical experiences. J Nucl Med 2005;46:1294-300.
13. Schuijf JD, Bax JJ, Shaw LJ, de Roos A, Lamb HJ, van der Wall EE, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. Am Heart J 2006;94:427-30.
14. Iskander S, Iskandrain AE. Risk assessment using single-photon emission computed tomographic technetium-99m sestamibi imaging. J Am Coll Cardiol 1998;32:57-62.

15. Gaemperli O, Schepis T, Valenta I, Husmann L, Scheffel H, Duerst V, et al. Cardiac image fusion from stand-alone SPECT and CT: Clinical experience. J Nucl Med 2007;48:696-703.
16. Berman DS, Wong ND, Gransar H, Miranda-Peats R, Dahlbeck J, Hayes SW, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol 2004;44:923-30.
17. Elhendy A, Sozzi FB, van Domburgh RT, Miranda-Peats R, Dahlbeck J, Hayes SW, et al. Accuracy of exercise stress technetium 99m sestamibi SPECT imaging in the evaluation of the extent and location of coronary artery disease in patients with an earlier myocardial infarction. J Nucl Cardiol 2000;7:432-8.
18. Schuijf JD, Wijns W, Jukema JW, Atsma DE, de Roos A, Lamb HJ, et al. Relationship between noninvasive coronary angiography with multi-slice computed tomography and myocardial perfusion imaging. J Am Coll Cardiol 2006;48:2508-14.
19. Hasdai D, Gibbons RJ, Holmes DR, Higano ST, Lerman A. Coronary endothelial dysfunction in humans is associated with myocardial perfusion defects. Circulation 1997;96:3390-5.