Chapter 4

Impact of Coronary Calcium Score on Diagnostic Accuracy of Multislice Computed Tomography Coronary Angiography for Detection of Coronary Artery Disease

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Abstract

Background: The impact of coronary calcium score on diagnostic accuracy of multi-slice computed tomography (MSCT) to detect obstructive coronary stenoses remains controversial.

Methods: Forty-one patients (Agatston score 340±530 (range 0–2546)) with coronary artery disease were examined with 16-slice MSCT and 60 patients (Agatston score 446±877 (range 0–6264)) with 64-slice MSCT. CT scans were analyzed with invasive coronary angiography (CA) as standard of reference. Lesions with ≥50% luminal narrowing were considered obstructive.

Results: In total, 9% and 2% of uninterpretable segments were excluded from analysis in patients examined with 16- and 64-slice MSCT, respectively. On segment-basis, the percentage of false negative segments in the groups with Agatston scores 0-100, 101-400 and >400 with 16-slice MSCT were 0%, 5.3%, 2.9% (p=0.0005), other comparisons of false positive and negative segments were not significant. The sensitivity and specificity on vessel- and patient-basis with 16- and 64-slice MSCT were not significantly different in different calcium score groups.

Conclusions: A slight impact of coronary calcium was observed on the diagnostic accuracy of 16-slice MSCT CA on a segment-basis with no significant impact on a vessel- and patient-basis. No significant impact of coronary calcium was observed on the diagnostic accuracy of 64-slice MSCT CA on a segment-, vessel- and patient-basis.

Introduction

Over the past years, multi-slice computed tomography (MSCT) has been demonstrated as a feasible alternative to invasive coronary angiography, allowing noninvasive evaluation of the coronary arteries.[1-4] Rapid development of the technique resulted in superior visualization of the coronary arteries and the initial reports published with 64-slice MSCT show extremely promising results, with sensitivities and specificities ranging from 94% to 99% and 95% to 97%, respectively.[3-4] With the first generations of MSCT scanners, severe coronary calcifications have been recognized as an important factor hampering precise evaluation of coronary artery stenoses thereby limiting diagnostic accuracy.[5] Accordingly, coronary calcifications may represent an important limitation of the technique. Nonetheless, accurate assessment in the presence of elevated coronary artery calcium scores is important as increased prevalence and extent of coronary artery calcifications have been observed in certain populations including the elderly and diabetic patients.[6,7] With the introduction of 16-slice MSCT, image quality has improved significantly due to superior spatial and temporal resolution. However, contradictory results of the effect of coronary artery calcium score on diagnostic accuracy of 16-slice MSCT CA have been reported, with some studies showing no influence[8] and others reporting high numbers of uninterpretable or incorrectly diagnosed coronary lesions due to severe coronary calcifications.[9,10] Moreover, data on the influence of coronary calcium score on diagnostic accuracy of 64-slice MSCT are limited. The purpose of the present study was to evaluate the impact of coronary artery calcium score on the diagnostic accuracy of 16- and 64-slice MSCT.

Methods

Patients and study protocol

A total of 101 patients who were already scheduled for conventional CA having presented with known or suspected coronary artery disease were included in the study. All patients underwent MSCT followed by conventional CA for the evaluation of the coronary arteries; 41 patients (30 men, mean age 58±13 years) were examined with 16-slice MSCT and 60 consecutive patients (47 men, mean age 60±11 years) have undergone examination with 64-slice MSCT. The median interval between conventional CA and MSCT was 4 weeks (range 0-27 weeks). No intervening changes in clinical conditions in patients have occurred between the 2 examinations. Only patients with regular heart rate in sinus rhythm and without contraindications to iodinated contrast medium have been included. All patients gave written informed consent to the study protocol, which was approved by the local ethics committee.

MSCT data acquisition

The MSCT examinations were performed with a 16- and 64-slice Toshiba Multi-slice Aquilion systems (Toshiba Medical Systems, Tokyo, Japan). No additional beta blockers were administered before the examinations. A prospective coronary calcium scan was performed prior to MSCT angiography with the same parameters for 16- and 64-slice MSCT scanner: collimation 4x3.0 mm, gantry rotation time 500 ms, the tube voltage and tube current 120 kV and 200 mA, respectively. The temporal window was set at 75% after the R-wave for electrocardiographically triggered prospective reconstruction.

The 16-slice MSCT CA scan was performed after the intravenous administration of 120 to 150 ml iodinated contrast medium depending on the total scan time, with an injection rate of 4 ml/s through the antecubital vein (Xenetix 300, Guerbet, Aulnay S. Bois, France). The scan parameters were as follows: collimation 16 x 0.5 mm, tube rotation time 400, 500 or 600 ms, depending on the heart rate, the tube current 250 mA and tube voltage 120 mV. The 64-slice MSCT CA scan was performed with a collimation of 64x0.5 mm and a tube rotation time of 400, 450 or 500 ms, depending on the heart rate. The tube current was 300 mA, at 120 kV. Non-ionic contrast material was administered in the antecubital vein with an amount of 80 to 110 ml, depending on the total scan time, and a flow rate of 5 ml/sec (Iomeron 400, Bracco Altana Pharma, Konstanz, Germany). Automated detection of peak enhancement in the aortic root was used for timing of the scan. All images were acquired during an inspiratory breath hold of approximately 20 s and 10 s with 16- and 64-slice MSCT respectively, with simultaneous registration of the patient's electrocardiogram. With the aid of a segmental reconstruction algorithm, data of one, 2 or three consecutive heartbeats were used to generate a single image.

To evaluate the presence of coronary artery stenoses, separate reconstructions in diastole (typically 75% of the cardiac cycle) were generated with a reconstructed section thickness of either 0.3 mm or 0.4 mm. If motion artefacts were present, additional reconstructions were made in different time points of the R-R interval. Axial data sets were transferred to a remote workstation (Vitrea2, Vital Images, Plymouth, Minn, USA) for post-processing and subsequent evaluation.

MSCT data analysis

Coronary calcium score

Coronary calcium score was assessed with the application of dedicated software (Vitrea2, Vital Images, Plymouth, Minn, USA). Coronary calcium was identified as a dense area in the coronary artery exceeding the threshold of 130 HU. In addition to per vessel measurements, an overall Agatston score was recorded for each patient. For precise evaluation of calcium score, all coronary segments were visually inspected and care was taken to avoid inclusion of coronary stents.

Coronary angiography

MSCT angiograms performed with 16- and 64-slice scanners were retrospectively evaluated by the same 2 experienced observers (within a limited period of time), who were unaware of the results of the conventional angiogram. The following protocol was applied in the evaluation of the MSCT coronary angiograms: the 3D volume rendered images were evaluated first to get a general impression of the course and status of left and right coronary arteries. Coronary arteries were divided into 17 segments according to the modified American Heart Association classification and regarded as interpretable or not by visual inspection. Subsequently, the interpretable segments were evaluated for the presence of obstructive stenoses (≥50% reduction of lumen diameter) both scrolling through the axial images and inspecting curved multiplanar reconstructions.

Conventional coronary angiography

Conventional coronary angiography was performed according to standard protocols. For vascular access, the femoral approach with the Seldinger technique was applied. Coronary angiograms were visually evaluated by consensus of 2 experienced observers blinded to the MSCT data.

Statistical analysis

Continuous data are expressed as mean±standard deviation. The differences in descriptives between the 2 patient cohorts examined with 16- and 64-slice MSCT were tested with T-test. Coronary segments and patients were divided into 3 groups according to overall Agatston score (0-100, 101-400 and >400). The differences of continuous variables between the 3 groups were tested with one way Anova test. In case of significant differences, the differences were further assessed with Post Hoc (Bonferroni) test. Analysis of impact of calcium score on diagnostic accuracy of MSCT CA was performed on 3 levels: segment by segment, vessel by vessel and patient by patient. The percentages of false positive and false negative segments were compared using Fisher's exact test and the number of interpretable segments was compared with Chi-square test. Sensitivity, specificity, positive and negative predictive values for the detection of ≥50% luminal narrowing in coronary arteries is expressed as percentages with 95% confidence intervals. The p value of 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS software (version 12.0, SPSS Inc, Chicago, Il, USA).

Results

In total, 102 patients were enrolled in the study. MSCT was successfully performed in 101 patients. One patient has been excluded from the analysis because of insufficient image quality due to elevated heart rate during the scan. Main characteristics of the study population are listed in Table 1.

Table 1. Descriptives of the study population

Variable	Agatston score 0-100	Agatston score 101-400	Agatston score >400
16-slice Multi-slice Computed Tomography Coronary Angiography			
Coronary segments in men/women	125/94	128/41	105/0
Mean age (yrs) *	51±15	62±11	66±7
Mean heart rate (beats/min)	72±13	65±16	70±18
Mean Agatston score	18±21 (0-81)	281±100 (102–397)	1077±731 (428–2546)
Mean BMI (kg/m²)	27±5	26±4	27±5
64-slice Multi-slice Computed Tomography Coronary Angiography			
Coronary segments in men/women	188/65	183/83	239/42
Mean age (yrs) *	57±9	57±10	66±9
Mean heart rate (beats/min)	59±11	57±14	61±11
Mean Agatston score	14±21 (0-70)	213±74 (111–336)	1088±1306 (410–6264)
Mean BMI (kg/m²)	27±3	29±4	27±3

* $p<0.05$

BMI, body mass index; values in parentheses represent range.

Fifty-seven (57%) patients had known CAD: 53 (53%) patients had a history of myocardial infarction and 56 (56%) had previous percutaneous coronary intervention. Known CAD was present in 23 (56%) patients examined with 16-slice MSCT and 34 (57%) who underwent 64-slice MSCT CA. The prevalence of CAD risk factors was as follows: 21 (21%) patients had diabetes mellitus, 57 (57%) hypercholesterolemia, 51 (51%) hypertension, 38 (38%) had a family history of CAD, and 49 (49%) had a history of current or previous smoking. There were no significant differences in the prevalence of risk factors between the two patient populations. Thirty-two (78%) patients examined with 16-slice MSCT and 43 (72%) examined with 64-slice MSCT ($p=0.47$) used beta-blocking agents as part of their baseline treatment. No significant differences were observed between the 2 patient cohorts examined with 16- and 64-slice MSCT in age and body mass index. However, a significant difference in mean heart rate during data acquisition was noted between the 2 groups of patients with low overall Agatston scores examined with different MSCT scanners. The mean Agatston score in the overall population was 340±530 (range 0–2546) and 446±877 (range 0–6264) for the patients examined with 16- and 64-slice MSCT, respectively. Examples of heavily calcified and noncalcified coronary lesions are provided in Figure 1 and Figure 2.

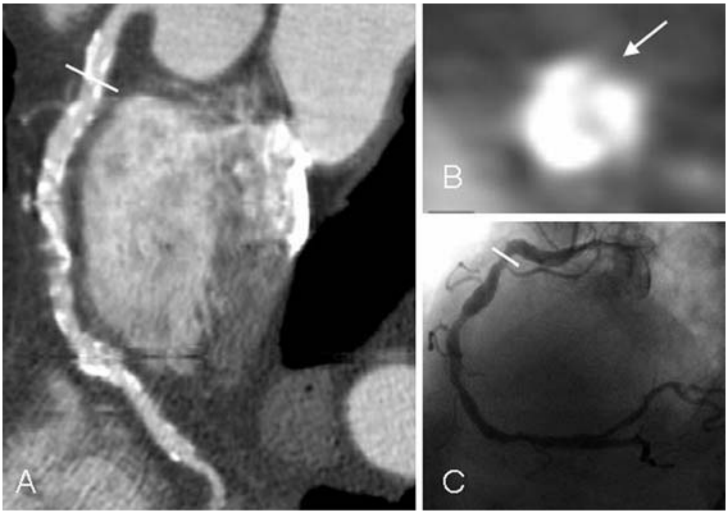

Figure 1. Example of evaluation of stenoses in highly calcified right coronary artery (RCA). (A) Curved multiplanar reconstruction of the RCA is shown, demonstrating multiple obstructive stenoses. Cross sectional reconstruction perpendicular to centerline of the RCA (B) demonstrates highly calcified coronary plaque in the proximal segment of the RCA (corresponding sites in the longitudinal view of the RCA are depicted in (A) and (C)). Invasive coronary angiography confirmed multiple obstructive stenoses in the RCA (C).

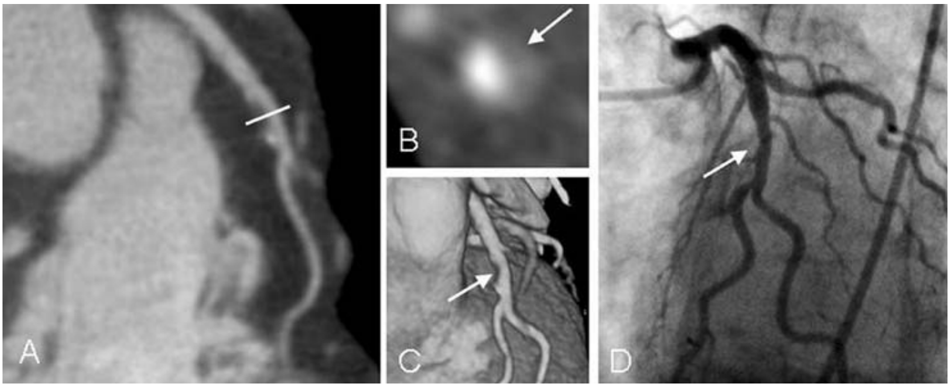

Figure 2. Example of evaluation of stenosis due to a coronary plaque with minimal calcification in the left anterior descending (LAD) coronary artery. (A) Curved multiplanar reconstruction demonstrates a non-obstructive stenosis in the middle part of the vessel. (B) The corresponding cross sectional reconstruction. The same lesion was observed on the three dimensional volume rendered reconstruction (C). Findings were confirmed by conventional coronary angiography (D).

Evaluation of impact of calcium on diagnostic accuracy of MSCT CA: segment by segment analysis

Out of 570 coronary segments of 41 patients examined with 16-slice MSCT, 30 stented segments and 47 uninterpretable coronary segments due to calcium unrelated reasons were excluded, resulting in 493 segments included in the analysis. Reasons for uninterpretability were small vessel size (n=16), motion artefacts (n=13), insufficient contrast enhancement (n=10), missing slice or trigger artefact (n=2), and 6 segments were excluded because of lack of information on conventional CA. After exclusion of stented segments, 9% of coronary artery segments were regarded as uninterpretable. Twenty-eight (11%) segments were excluded in the group with Agatston score 0-100, 16 (9%) in the group with Agatston score 101-400 and 3 (3%) in the group with Agatston score >400 (p=0.03). After exclusion of 43 stented segments and 13 coronary segments having insufficient image quality due to motion artefacts (n=3) or too small vessel size (n=10), 800 segments of 60 patients examined by 64-slice MSCT were included in the analysis. Having excluded stented segments, 2% of coronary artery segments were regarded as uninterpretable. No coronary segments were excluded in the group with Agatston score 0-100, while 8 (3%) were excluded in the group with Agatston score 101-400 and 5 (2%) in the group with Agatston score >400 (p=0.03).

The percentages of false positive and false negative segments in the groups with overall Agatston score 0-100, 101-400 and >400 in patients examined with 16- and 64-slice MSCT are given in Table 2. Only the difference between false negative segments in patients examined with 16-slice MSCT was found to be significant (0%, 5.3%, 2.9%, p=0.0005).

Table 2. Percentages of interpretable, false positive and false negative segments in the groups with different calcium scores

	Agatston score 0-100	Agatston score 101-400	Agatston score >400	p value
16 -slice Multi-slice Computed Tomography Coronary Angiography				
Interpretable, nr (%)	219/247 (89)	169/185 (91)	105/108 (97)	p=0.03
False positive, nr (%)	1/219 (0.5)	2/169 (1.2)	3/105 (2.9)	*p=0.1
False negative, nr (%)	0/219 (0)	9/169 (5.3)	3/105 (2.9)	*p=0.0005
64-slice Multi-slice Computed Tomography Coronary Angiography				
Interpretable, nr (%)	253/253 (100)	266/274 (97)	281/286 (98)	p=0.03
False positive, nr (%)	1/253 (0.4)	7/266 (2.6)	5/281 (1.8)	*p=0.07
False negative, nr (%)	4/253 (1.6)	5/266 (1.9)	7/281 (2.5)	*p=0.55

* the lowest p values of the comparisons between the groups.

Evaluation of impact of calcium on diagnostic accuracy of MSCT CA: vessel by vessel analysis

The results of per vessel analysis are provided in Table 3 and Figure 3. In the patient population examined with 16-slice MSCT, 5 vessels were regarded as uninterpretable due to >1 uninterpretable segment present in the coronary artery, resulting in 159 vessels included in the analysis. Conventional CA detected 33 (21%) coronary vessels with obstructive coronary lesions in the patient group examined with 16-slice MSCT CA, resulting in overall sensitivity of 76% and specificity of 97%. All 240 vessels were regarded as interpretable in patients examined with 64-slice MSCT. Fifty-seven (24%) vessels examined with 64-slice MSCT CA showed obstructive coronary stenoses and the calculated sensitivity and specificity were 79% and 96%, respectively. No significant differences of diagnostic accuracies of 16-, 64-slice and combined evaluation of 16- and 64-slice MSCT CA were noted between the groups of patients with Agatston scores in the range of 0-100, and >100 (Table 3 and Figure 3).

Table 3. Diagnostic accuracy of Multi-slice Computed Tomography Coronary Angiography in vessels with different calcium scores

	All vessels (n=159)	Agatston score 0-100 (n=120)	Agatston score >100 (n=39)
16-slice Multi-slice Computed Tomography Coronary Angiography			
Sensitivity, %	76 (61-91)	67 (43-91)	83 (66-100)
Specificity, %	97 (94-100)	99 (97-100)	86 (71-100)
Positive predictive value, %	86 (73-98)	91 (74-100)	83 (66-100)
Negative predictive value, %	94 (90-98)	95 (91-99)	86 (71-100)
	All vessels (n=240)	Agatston score 0 -100 (n=175)	Agatston score >100 (n=65)
64-slice Multi-slice Computed Tomography Coronary Angiography			
Sensitivity, %	79 (68-89)	77 (61-93)	81 (67-95)
Specificity, %	96 (93-99)	97 (94-100)	92 (85-98)
Positive predictive value, %	87 (78-96)	83 (68-98)	89 (77-100)
Negative predictive value, %	94 (91-97)	96 (93-99)	84 (72-96)

Values in parentheses represent 95% confidence intervals.

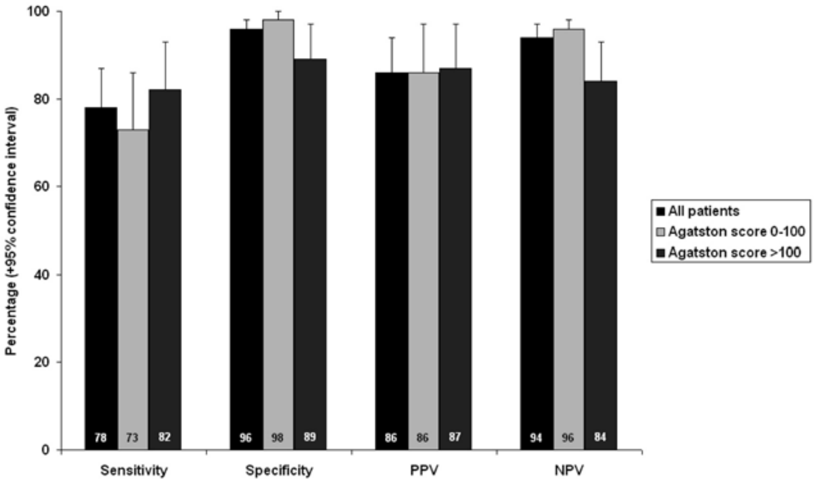

Figure 3. Diagnostic accuracies (per vessel analysis) and confidence intervals of 16- and 64-slice multi-slice computed tomography coronary angiography.
PPV, positive predictive value; NPV, negative predictive value.

Evaluation of impact of calcium on diagnostic accuracy of MSCT CA: patient by patient analysis

The diagnostic performance of MSCT CA for detecting obstructive lesions in patient groups with different overall Agatston scores on a patient-based analysis is detailed in Table 4 and Figure 4. In the patient group examined with 16-slice MSCT CA, obstructive coronary lesions were detected by conventional CA in 18 patients (44%), resulting in overall sensitivity of 89%, the specificity being 87%. Thirty-two patients (53%) examined with 64-slice MSCT CA had obstructive coronary stenoses, the calculated sensitivity was 91% and the specificity was 96%. As can be derived from Table 4 and Figure 4, no significant differences of diagnostic accuracies of 16-, 64-slice and combined evaluation of 16- and 64-slice MSCT CA were noted between the groups of patients having the Agatston scores in the range of 0-100, 101-400, >400 and >100.

Table 4. Diagnostic accuracy of Multi-slice Computed Tomography Coronary Angiography in patient groups with different calcium scores

	All patients (n=41)	Agatston score 0-100 (n=18)	Agatston score 101-400 (n=14)	Agatston score >400 (n=9)	Agatston score >100 (n=23)
16-slice Multi-slice Computed Tomography Coronary Angiography					
Sensitivity, %	89 (75-100)	100	75 (45-100)	100	86 (68-100)
Specificity, %	87 (73-100)	93 (80-100)	83 (53-100)	67 (29-100)	78 (51-100)
Positive predictive value, %	84 (68-100)	80 (45-100)	86 (60-100)	86 (60-100)	86 (68-100)
Negative predictive value, %	91 (79-100)	100	71 (37-100)	100	78 (51-100)
	All patients (n=60)	Agatston score 0-100 (n=19)	Agatston score 101-400 (n=20)	Agatston score >400 (n=21)	Agatston score >100 (n=41)
64-slice Multi-slice Computed Tomography Coronary Angiography					
Sensitivity, %	91 (81-100)	83 (53-100)	83 (62-100)	100	92 (82-100)
Specificity, %	96 (89-100)	100	88 (65-100)	100	93 (80-100)
Positive predictive value, %	97 (91-100)	100	91 (74-100)	100	96 (88-100)
Negative predictive value, %	90 (79-100)	93 (80-100)	78 (51-100)	100	88 (72-100)

Values in parentheses represent 95% confidence intervals.

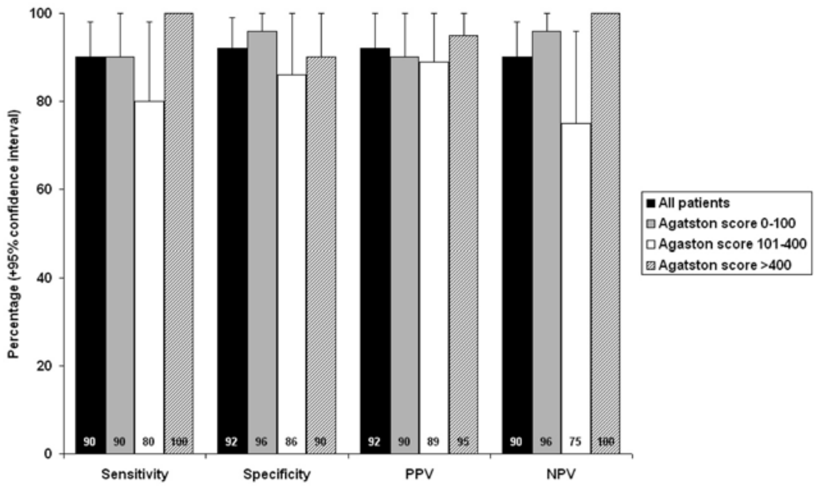

Figure 4. Diagnostic accuracies (per patient analysis) and confidence intervals of 16- and 64-slice multi-slice computed tomography coronary angiography.
PPV, positive predictive value; NPV, negative predictive value.

Discussion

The most important findings of the present study can be summarized as follows: (1) a negative impact of elevated coronary artery calcium score on diagnostic accuracy of MSCT CA was observed in the segment based analysis using 16-slice MSCT; this effect was not observed with 64-slice MSCT. Moreover, (2) elevated coronary artery calcium scores did not have a negative impact on the diagnostic accuracy of 16- and 64-slice MSCT CA when data were analyzed on vessel and patient basis.

In the current analysis, the accuracies of both the 16- and 64-slice MSCT to detect obstructive coronary artery disease were high, in line with previous publications.[3-5,10,11] In particular, the sensitivity and specificity of 16-slice MSCT were 89% and 87% for the detection of obstructive coronary artery stenoses, and pooled data from 11 studies with 681 patients using 16-slice MSCT revealed a sensitivity and specificity of 88% and 96% respectively.[2] The sensitivity and specificity of the 64-slice MSCT were higher being 91% and 96%. These values are in line with recently published data. For example, Mollet et al.[4] evaluated 52 patients with 64-slice MSCT and reported a sensitivity of 99% with a specificity of 95%. Of interest, the results of the current study confirm the high accuracies in populations with much higher prevalence of coronary artery disease as compared to the previous studies (being 44% for the patients undergoing 16-slice MSCT and 53% for the patients undergoing 64-slice MSCT).

In general, the sensitivity and specificity of 64-slice MSCT appear higher than of 16-slice MSCT. This may be related to improved image quality with 64-MSCT, which is reflected by the reduction in non-interpretable segments. Increased temporal and spatial resolution with 64-slice MSCT have led to a decrease in number of segments with impaired image quality, being 9% and 2% for 16- and 64-slice MSCT in the current study. These observations are in line with the literature; pooled analysis of 11 studies with 16-slice MSCT revealed that 4% (ranging between 0% to 17%) of segments were of uninterpretable image quality[2] as compared with all coronary segments included in the analysis in most 64-slice MSCT studies,[3,4] although one study reported exclusion of as high as 12% of segments.[11]

In addition, the reduced voxel size with 64-slice MSCT also positively influences partial volume effects of coronary calcifications. Coronary calcifications have high density and dominate the density of adjacent tissues in the same voxel. With reduction of voxel size, the blooming of calcium thus decreases. Indeed, the findings in the current study demonstrate the absence of influence of calcium score on the percentage of falsely diagnosed segments with 64-slice MSCT. A significant influence of the calcium score on the percentage of false negative segments was however observed with 16-slice MSCT. These results are in line with previous observations, with 16-slice MSCT, that a significant number of coronary segments had to excluded from analysis due to severe calcifications.[9] Coronary calcifications were also demonstrated to be the major cause of false positive findings with 16-slice MSCT.[10]

Another important finding in the present study is that calcium score did not significantly impair the diagnostic accuracy of a vessel and a patient based analysis, both for 16- and 64-slice MSCT examinations. Although more false negative segments were observed in patients with higher calcium scores, indicating decreased sensitivity on a segmental basis, sensitivity increased when shifting to a patient level, most likely due to the higher prevalence of CAD in patients with higher calcium scores. These findings are particularly important in clinical practice as further diagnostic and therapeutic decisions are based on a patient based (rather than segment or vessel based) analysis in daily practice.

Limitations

Several limitations of the current study need to be acknowledged. The protocols used for 16- and 64-slice MSCT were not precisely identical; therefore it remains unknown to what extent small differences may have influenced our results in addition to the difference in collimation of the two scanner generations. Also, inclusion of patients examined with 16-slice MSCT scanner was limited, and may have influenced results. Finally, the effect of the presence of dense calcifications restricted to a small area (resulting in low overall calcium score), was not explored in the present study, while these calcifications may potentially also negatively influence diagnostic accuracy despite a low overall calcium score. Limitations of MSCT in general are that only qualitative analysis of severity of coronary stenoses with MSCT is feasible and more quantitative analysis techniques should be developed. Also, coronary MSCT remains limited by the high radiation exposure and the use of iodinated contrast.

Conclusions

In conclusion, the findings of the present study demonstrate that coronary calcium score only slightly affected the diagnostic accuracy of 16-slice MSCT on a segment based analysis and showed no statistically significant impact on vessel and patient basis. No significant impact of coronary calcium score was observed on the diagnostic accuracy of 64-slice MSCT CA on segment, vessel and patient basis.

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