کارکده های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی

کارکده آنلاین
کاربرد نرم افزار SPSS در پژوهش

کارکده آنلاین
اصول تنظیم قراردادها

کارکده آنلاین
پروپوزال نویسی
Impact of Calcification on Diagnostic Accuracy of 64-Slice Spiral Computed Tomography for Detecting Coronary Artery Disease: A Single Center Experience

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Abstract
Background: The main aim of our study was to investigate the influence of calcification on the accuracy of 64-slice computed tomography for identification of significant coronary artery disease.

Methods: A contrast-enhanced 64-slice computed tomography was performed prior to invasive coronary angiography in 168 consecutive patients with suspected coronary artery disease. All coronary segments 1.5 mm or larger in diameter were evaluated for the presence or absence of significant coronary artery stenosis, defined as a diameter reduction of >50%. The patients were also ranked by total calcium score which was expressed in Agatston units and the impacts of calcification on diagnostic accuracy of 64-slice computed tomography were assessed. Results were compared with quantitative coronary angiography as the standard of reference.

Results: The overall sensitivity, specificity, positive predictive value, and negative predictive value of 64-slice computed tomography for detection of significant stenosis were: by segments, 95%, 98%, 91%, and 99%, respectively; by patient, 98%, 97%, 96%, and 99%, respectively; and by artery, 94%, 93%, 91%, and 95%, respectively. In mild and moderate calcium scores (0 – 418 Agatston units), the sensitivity was 100%, specificity was 93%, positive predictive value was 97% and negative predictive value was 100%. Severe calcification (>419 Agatston units) reduced the sensitivity, specificity, positive, and negative predictive values of multi-slice computed tomography to 89%, 60%, 89%, and 60%, respectively.

Conclusion: Our study revealed that the 64-slice computed tomography is a highly accurate diagnostic modality for detecting hemodynamically significant coronary stenosis; however, severe calcification is considered as a shortcoming which limits the routine application of multi-slice computed tomography in daily practice.

Key Words: computed tomography, conventional coronary angiography, coronary calcification, coronary artery stenosis

Impact of Calcification on Diagnostic Accuracy of 64-Slice Spiral Computed Tomography for Detecting Coronary Artery Disease: A Single Center Experience

C. Coronary artery disease (CAD) accounts for nearly 30% of deaths worldwide, consisting of 40% in developed countries and 28% in developing countries. Conventional coronary angiography (CCA) is currently considered the gold standard for the diagnosis of obstructive CAD; however, it is associated with low but real morbidity (1.5%) and mortality (0.11%) rates, as well as inconvenience for patients and considerable cost.

Rapid advances in multi-slice computed tomography (MSCT) technology during the past years have resulted in the introduction of the currently used 64-slice computed tomography (CT) as a non-invasive and reliable method for the assessment of coronary stenosis with optimized image quality. Compared with the older scanner generations (4- and 16-slice CT), the present 64-slice CT scanner...
has superior temporal and spatial resolution, which allows more accurate visualization of the coronary arteries. The MSCT has provided favorable results compared with CCA for the detection of coronary artery stenosis in several previous reports, however, this technology is still affected by a few shortcomings which should be overcome if it is to become a practical alternative to CCA. Motion artifacts caused by cardiac movement, especially in patients with high heart rates, make the evaluation of some coronary segments difficult. Furthermore, although the employment of a smaller voxel size in new generation scanners has substantially reduced the partial volume effect and consequently minimized the degree of calcium blooming and beam hardening artifacts, precise assessment of the coronary artery lumen by the 64-slice scanner in the presence of moderate-to-severe calcification has been challenging.

In this large prospective study, we aimed to evaluate the accuracy of 64-slice CT for the identification of hemodynamically significant coronary lesions and also to investigate the effects of coronary calcification on the diagnostic accuracy of MSCT in patients with suspected CAD. Results were compared with quantitative coronary angiography as the standard.

Patients and Methods

Study population
From September 2006 to May 2007, 168 consecutive patients who were scheduled for CCA because of suspected CAD underwent MSCT within a 3-day interval prior to catheterization. Patient characteristics are summarized in Table 1. Patients were excluded if they had at least one of the following criteria: previous allergic reaction to iodine contrast media, renal insufficiency (serum creatinine level >1.5 mg/dL), inability to comply with breath-hold commands, contraindication to administration of beta-blocker drugs, atrial fibrillation, hemodynamic instability and a history of previous stenting or coronary artery bypass surgery. The study protocol was approved by Institutional Ethics Committee at Day General Hospital, Tehran, Iran; and all participants gave their informed written consent.

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Total number of patients</th>
<th>168</th>
</tr>
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<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>Mean±SD</td>
<td>58±11</td>
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<td>Range</td>
<td>85–32</td>
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<td>Male, n (%)</td>
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<td>Body mass index (kg/m²)</td>
<td>25.7±4.2</td>
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<td>History, n (%)</td>
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<td>Family history of CAD</td>
<td>118 (70)</td>
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<td>Smoker</td>
<td>114 (68)</td>
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<tr>
<td>Hypertension*</td>
<td>98 (58)</td>
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<tr>
<td>Hyperlipidemia†</td>
<td>142 (84.5)</td>
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<tr>
<td>Diabetes mellitus‡</td>
<td>61 (36)</td>
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<tr>
<td>Heart rate during scanning (beats/min)</td>
<td>62±11</td>
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<tr>
<td>CAD severity, n (%)</td>
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<tr>
<td>No significant CAD</td>
<td>46 (27)</td>
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<td>1-vessel disease, n (%)</td>
<td>57 (34)</td>
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<td>2-vessel disease, n (%)</td>
<td>36 (21)</td>
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<td>3-vessel disease, n (%)</td>
<td>29 (17)</td>
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</table>

Patient preparation
To achieve a target heart rate of <65 beats/min, 100 mg metoprolol was administered orally in patients with heart rates over 70 beats/min, 1 hour before the planned multi-slice CT imaging. Additional doses of metoprolol were injected intravenously in patients with heart rates >65 beats/min at the time of the acquisition in order to lower the heart rate to ≤60 beats/min. In addition, all patients received 0.4 mg nitroglycerin sublingually, 2 min prior to the MSCT scanning.

Scan protocol and image reconstruction
All examinations were performed with a 64-slice CT (Somatom Sensation 64, Siemens, Forchheim, Germany). The scanning parameters are summarized in Table 2. To reduce radiation exposure, ECG-gated tube current modulation was applied for all patients. A bolus of 80 mL contrast agent (Vistopaque 320 mg/mL, Amersham Health, Buckinghamshire, UK) was injected intravenously at a rate of 5 mL/s followed by a saline chaser bolus of 50 mL (also at 5 mL/s). As soon as the signal in the ascending aorta reached a predefined threshold of 140 HU (Hounsfield units), the scan started automatically after a 4 second delay from the tracheal bifurcation to the diaphragm during one breath hold in 8 to 9 seconds (s) with simultaneous monitoring of the electrocardiographic tracing. Retrospectively ECG-synchronized image reconstruction was per-
formed using the implemented half-scan algorithm at -300, -350, and -400 ms points of the R-R cycle length (in mid-diastolic phase), with a slice thickness of 0.6 mm, a reconstruction increment of 0.4 mm and a smooth convolution kernel of B30f. In cases of motion artifacts, additional reconstructions were performed, and the dataset with the minimum artifact and the most optimal image quality was selected for further analysis. Using a proposed method by the European Working Group for Guidelines on Quality Criteria in CT,34 the average estimated effective radiation dose was 13 mSv and 18 mSv for men and women, respectively.

A 15-segment model was used for defining the coronary tree, as previously described in the American Heart Association/American College of Cardiology guidelines.35 Accordingly, the following segments were evaluated: left main (LM) coronary artery; proximal, middle and distal right coronary artery (RCA); right and left posterior descending arteries (PDA) and postero-lateral (PL) branch; proximal and distal left circumflex (LCX) artery with obtuse marginal (OM) branch; proximal, middle and distal left anterior descending (LAD) coronary artery and diagonal (DIA) branches. The evaluable segments of the coronary artery system (≥1.5 mm in diameter) were classified as being significantly stenosed or not, defined as a lumen narrowing of >50%.

Patients were ranked by total calcium score which was expressed in Agatston units (AU).36 Segment and artery calcium was rated as follows: none, not calcified; mild, calcium present, no image impairment; moderate, calcium covering <50% of the lumen; and severe, calcium covering >50% of the lumen in all planes including cross section.

Scans were analyzed by two investigators who were blinded to both the clinical data and the angiographic results.

### Comparative analysis

The accuracy of 64-slice CT to detect clinically significant lesions (>50% luminal narrowing) was compared to invasive CA according to the following analyses: 1) per-segment analysis, comparing each segment in every artery; 2) per-patient analysis, evaluating the presence of any significant lesion in a given patient; and 3) per-artery analysis, probing the presence of significant lesions in each of the major coronary arteries (Left main, LAD, RCA, and LCX).

### Statistics

Quantitative variables are described as mean±standard deviation. The diagnostic accuracy of 64-slice CT in the detecting of significant stenosis was expressed as sensitivity, specificity, posi-
tive predictive value (PPV), and negative predictive value (NPV) with their respective 95% confidence interval (CI), using invasive CCA as the “gold standard”. Inter-observer agreements were expressed as Cohen’s kappa statistics.\textsuperscript{37} SPSS 11.5 software (SPSS Incorporation, Chicago, IL, USA) was used.\textsuperscript{37}

**Results**

Out of 186 referred patients, eighteen cases were excluded because of previous coronary stenting (n=8), elevated creatinine levels (n=5) and arrhythmias (atrial fibrillation and extra-systoles) found prior to MSCT (n=5). Accordingly, a contrast-enhanced 64-slice CT was performed successfully and without any complication in 168 patients who were scheduled for CCA. Twenty nine patients (17%) were already under beta-blocker therapy; however, additional administration was needed in 139 (82%) to reduce the heart rate prior to scanning. As a result, the mean heart rate during the scan was 62±11 beats/min (a target heart rate of <65 beats/min was achieved in all patients).

Conventional angiographies revealed a total of 477 hemodynamically significant stenoses, which were identified in 122 patients (72%). Of detected stenoses, 78 lesions (16%) were totally occluded. In addition, while no significant coronary stenosis was detected in 46 patients (27%), one, two- and three-vessel disease were found in 57 patients (34%), 36 patients (21%), and 29 patients (17%), respectively. Using beta blockers, we could successfully overcome motion artifacts in our patient population so that the quality of the images was excellent and good in 73% and 27% of segments, respectively. Thus, no segment was excluded from the analysis due to motion artifact.

**Multi-slice CT compared to coronary angiography**

Concerning MSCT, the kappa values for image quality, stenosis detection, and coronary calcification were 0.92, 0.95, and 0.97, respectively which revealed an excellent inter-observer agreement.

Overall, 2520 coronary segments in 168 patients could be analyzed by both CCA and 64-slice CT. From a total of 477 hemodynamically significant stenoses detected by CCA, 453 (95%) lesions were recognized correctly with MSCT (Figure 1). Twenty four stenoses were missed (n=19) or underestimated (n=5) because of severe coronary wall calcification. No significant stenosis was missed due to motion artifact. Moreover, because of important calcification, 40 lesions diagnosed as significant stenoses by MSCT were false-positives, and 7 lesions were overestimated (Figure 2). Based on segment-by-segment analysis, 64-slice CT had a sensitivity, specificity, PPV, and NPV of 95.0%, 97.7%, 90.6%, and 98.8%, respectively for detecting significant stenosis (Table 3).

Regarding a patient-based analysis, 64-slice CT correctly identified all patients without CAD and 120 of 122 (98%) patients with significant stenoses. Two patients with 1-vessel significant CAD on the distal part of left circumflex (LCX) and right posterior descending artery (PDA) were considered as normal on MSCT. Five patients without important stenosis were classified as positive on MSCT regarding stenoses found on obtuse marginal (n=2), mid-part of right coronary artery (n=1), distal part of right coronary artery (n=1), and mid-part of left anterior descending artery (n=1). The overall sensitivity, specificity, PPV, and NPV of 64-slice CT for identifying patients with and without CAD were 98.4%, 89.1%, 96.0%, and 95.3%, respectively (Table 3).

A total of 672 arteries could be analyzed. On a per-artery basis, 64-slice CT achieved a sensitivity of 93.7%, specificity of 92.7%, PPV of 90.6%, and NPV of 95.2% (Table 3).

**Influence of calcium on 64-slice CT accuracy**

We examined the accuracy of 64-slice CT for detecting significant stenosis in a given patient according to calcium score (AU). We observed that in the presence of low (0 to 100 AU), as well as moderate (101 to 418 AU) calcium scores, MSCT had a high diagnostic accuracy that was shown in a sensitivity of 100%, specificity of 93%, PPV of 97% and NPV of 100%. Nonetheless, severe calcification (419 to 8420 AU) remarkably reduced the specificity and NPV of 64-slice CT (Table 4). In our study, calcium deposit was found to be responsible for 19 false negative and 47 false positive decisions with CT (Figure 2); nevertheless, no patient was excluded because of poor image quality.
The main findings in the current study are two-fold. Our primary finding demonstrates that the 64-slice CT coronary angiography provides an accurate non-invasive method for evaluating coronary arteries. This technique with a high sensitivity and specificity for the detection of hemodynamically relevant coronary artery stenoses can reliably determine the presence or absence of ischemic heart disease in suspected patients.

The current results are consistent with and extend those of previous studies comparing 16- and 64-slice CT scanners with invasive CCA for the evaluation of the native coronary system. To the best of our knowledge, this study represents the largest group of patients with suspected CAD in which the 64-slice CT and invasive CCA are compared.

### Table 3. Diagnostic accuracy of 64-slice CT coronary angiography for detecting significant stenoses in coronary arteries

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<tr>
<th></th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<td><strong>Patients</strong></td>
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<td>120</td>
<td>41</td>
<td>5</td>
<td>98.4</td>
<td>89.1</td>
<td>96.0</td>
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<td>(90.4-98.5)</td>
<td>(82.9-99.2)</td>
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<td>269</td>
<td>357</td>
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<td>(86.5-93.5)</td>
<td>(92.4-97.0)</td>
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<td>453</td>
<td>1996</td>
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<td>(67.9-100)</td>
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<td>(92.0-99.0)</td>
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<td>(84.5-96.3)</td>
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<td>106</td>
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<td>(39.6-100)</td>
<td>(97.1-100)</td>
<td>(39.6-100)</td>
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FN=false negative; FP=false positive; LAD=left anterior descending artery; LCX=left circumflex; LM=left main; NPV=negative predictive value; PLA=postero-lateral artery; PPV=positive predictive value; RCA=right coronary artery; PDA=posterior descending artery; TN=true negative; TP=true positive

**Discussion**

The main findings in the current study are two-fold. Our primary finding demonstrates that the 64-slice CT coronary angiography provides an accurate non-invasive method for evaluating coronary arteries. This technique with a high sensitivity and specificity for the detection of hemodynamically relevant coronary artery stenoses can reliably determine the presence or absence of ischemic heart disease in suspected patients.

The current results are consistent with and extend those of previous studies comparing 16- and 64-slice CT scanners with invasive CCA for the evaluation of the native coronary system. To the best of our knowledge, this study represents the largest group of patients with suspected CAD in which the 64-slice CT and invasive CCA are compared.
Recently, Hamon et al. performed a meta-analysis based on 29 published studies (2024 patients) comparing MSCT (>16-slice scanners) with invasive CCA for the assessment of coronary arteries and reported an overall per-segment sensitivity and specificity of 81% and 93%, respectively. This study also reported an overall per-patient sensitivity of 93%, with a specificity of 74%, across the literature. With the use of 16-slice technology, sensitivities for the identification of significant lesions were between 63 – 96% with specificities between 65 – 99%.

With regard to the assessment of the coronary arteries, 64-slice technology with improved temporal and spatial resolution showed a higher accuracy for the detection of significant stenoses compared with previous scanner generations (sensitivities were between 64 – 99% and specificities were between 94 – 98%). Similar to the results of previous studies employing 64-slice CT, we found a high diagnostic accuracy for MSCT in the assessment of the coronary segments (sensitivity of 95% and specificity of 98%), close to that of angiography. However,
in contrast to some of the prior studies in which motion artifacts were significant sources of false-positive and false-negative interpretations, we successfully eliminated the effect of cardiac motion on image quality by administration of a beta-blocker prior to the CT exam, so that no segment needed to be excluded because of motion artifacts. Furthermore, in view of the fact that small lesions are rarely considered important clinically and as a target for an intervention, we evaluated barely arteries which were >1.5 mm in diameter (as with several previous studies). In fact, we sought to determine the accuracy of 64-slice CT for the detection of clinically significant coronary stenoses.

The second major finding of our study was that despite using smaller voxel size in 64-slice scanners has reduced partial volume effects, image quality is significantly influenced by the presence of severe calcification. This explains the observation that in 100% (71 of 71) of misinterpreted segments by
MSCT, severe calcification was the culprit in poor image quality. In patients with high (>419 U) Agatston scores, diagnostic accuracy was lower (83%) as compared with patients with low and moderate (<419 U) Agatston scores (98%) (Table 4). The present finding is also consistent with previous similar studies.29,39,40 Raff et al.29 found a significant reduction in specificity and PPV in the presence of extreme calcification (401–1804 U). Gao et al.39 showed that severe coronary artery calcification (>100 U) degraded the diagnostic specificity and PPV of 64-slice CT, and Ong et al.40 reported a significant deterioration of accuracy in patients with moderate to heavy calcification (>142 U). Moreover, Weustink et al.41 compared the high-speed dual-source CT scanner (DSCT) with invasive CCA and concluded that in patients with high Agatston scores (927±727), diagnostic accuracy was lower than those of patients with low (17±27) and moderate (198±96) scores. This similarity reveals that severe calcification continues to be a challenging issue with the 64-slice CT scanner despite considerable technological improvements.

Study limitations
Despite several advantages, CT coronary angiography still has shortcomings which make it unqualified to be considered as a practical alternative to invasive CCA in daily practice. First, the technique exposes the patients to a rather high radiation dose. Although the effective dose for 64-slice CT has been reduced significantly by application of tube modulation (17.8 to 12.2 mSv),26,28 compared with the effective dose in invasive CCA (3 to 10 mSv),42 it still remains relatively high. However, most of our patients were older than 55 years, and it has been demonstrated that the risk of developing radiation-induced tumors is less significant in older patients.43 Secondly, MSCT should not be performed in patients with renal failure or those with contraindications to iodinated contrast agents. Thirdly, owing to the degradation of the image quality by cardiac motion, patients in atrial fibrillation and those with contraindications to beta-blockers cannot be accurately studied. Next, severe calcification and metal clip artifacts preclude accurate assessment with MSCT. Finally, as opposed to invasive CCA, MSCT is merely a diagnostic tool and cannot provide an option for immediate intervention.

In addition to the inherent limitations of MSCT, there are drawbacks in this study which should be taken into account. Our study was performed in a selected population consisting of symptomatic patients who were scheduled for catheterization, which translated into a high prevalence of CAD in this population. This was confirmed by the fact that in-

<table>
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<th>Patients’ calcium scores*</th>
<th>Sensitivity</th>
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<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
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<td>0–100 (n= 99)</td>
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<td>13/14 (93%)</td>
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<td>419–8420 (n= 24)</td>
<td>17/19 (89%)</td>
<td>3/5 (60%)</td>
<td>17/19 (89%)</td>
<td>3/5 (60%)</td>
<td>20/24 (83%)</td>
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<th>Calcium rating: Arteries</th>
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<th>Calcium rating: Segments</th>
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<tr>
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<tr>
<td>Moderate</td>
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<td>Severe</td>
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*Calcium score are in Agatston units. PPV=positive predictive value, NPV=negative predictive value.

Table 4. The effect of coronary calcification on diagnostic accuracy of 64-slice CT
vascive CCA could detect at least one stenosis in 71% (120/162) of our patients. This might have resulted in an overestimation of PPV and NPV and these values may differ in asymptomatic subjects with lower occurrences of obstructive coronary disease. Thus, accuracy of the 64-slice CT for the evaluation of asymptomatic patients remains to be demonstrated in further investigations. Furthermore, although it may not be important clinically, we barely evaluated arteries of >1.5 mm in diameter which lead to the exclusion of limited number of segments.

Conclusion

This study reveals that contrast-enhanced 64-slice CT provides a non-invasive and robust tool for the assessment of clinically significant CAD with an excellent diagnostic accuracy. The very high NPV observed in this study suggests that 64-slice CT could be suitably used as a screening test for ruling out hemodynamically significant stenosis. However, this method still has some shortcomings, including reduced accuracy in the presence of heavy coronary calcification, which limit it as a practical alternative to invasive CCA in daily practice. Further studies evaluating the diagnostic importance of the newest generation of MSCT with a larger sample size, including patients with low and moderate pre-test probability of CAD will be critical to provide guidelines for the clinical use of spiral CT coronary imaging.

References

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