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【 ORIGINAL ARTICLE 】

An Increased Diagnostic Accuracy of Significant Coronary Artery Stenosis Using 320-slice Computed Tomography with Model-based Iterative Reconstruction in Cases with Severely Calcified Coronary Arteries

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Abstract:

Objective High-quality images can be obtained with 320-slice computed tomography (CT) with model-based iterative reconstruction (MBIR). We therefore investigated the diagnostic accuracy of 320-slice CT with MBIR for detecting significant coronary artery stenosis.

Methods This was a retrospective study of 160 patients who underwent coronary CT and invasive coronary angiography (ICA). The first 100 consecutive patients (Group 1) underwent 320-slice CT without MBIR or small-focus scanning. The next 60 consecutive patients (Group 2) underwent 320-slice CT with both MBIR and small-focus scanning. Patients who underwent coronary artery bypass surgery were excluded. The diagnostic performance of 320-slice CT without MBIR or small-focus scanning and 320-slice CT with both of them, with ICA regarded as a reference standard, was compared to detect significant coronary artery stenosis (≥70% on CT, ≥75% on ICA).

Results In a patient-based analysis, the sensitivity, specificity, and overall accuracy of detection of significant stenosis on CT against ICA were 95%, 85%, and 91% in Group 1, and 93%, 83%, and 90% in Group 2, respectively. No significant differences were observed between the two groups in the patient- and segment-based analyses. However, among cases with a severe coronary artery calcium score >400 (31 cases in Group 1 and 28 in Group 2), the specificity and overall accuracy were significantly higher (all p<0.01) in Group 2 than in Group 1 according to the segment-based analysis.

Conclusion The diagnostic accuracy of the detection of coronary artery stenosis on CT was improved using 320-slice CT with MBIR.

Key words: coronary artery disease, coronary angiography, computed tomography

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Introduction

Coronary computed tomography (CT) angiography has been widely used recently because of its high diagnostic accuracy for significant stenosis, especially its negative predictive value (1). The evaluation of significant stenosis has been difficult in cases with severely calcified lesions because of partial volume effects caused by calcified plaque. Coronary CT using contrast media for the evaluation of coronary artery stenosis is not recommended in cases with an Agatston coronary calcium score (CCS) >400 on non-contrast images obtained just before the injection of contrast media because of the increase in false positives caused by calcium

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Table 1. Details of Computed Tomographic Scanning Parameters.

	Group 1 (n=100)	Group 2 (n=60)	p value
Slice thickness	0.5 mm	0.5 mm	-
ECG gating	Retrospective (with dose modulation, if possible)	Retrospective (with dose modulation, if possible)	-
Speed of gantry rotation (ms)	**355±13**	**277±10**	**p<0.0001*****
Tube voltage (kV)	120	120	-
Tube current (mA)	**474±89**	**344±24**	**p<0.0001*****
Small focus scanning	**0 (0%)**	**100 (100%)**	**p<0.001*****
Image reconstruction	**FBP**	**FBP and MBIR**	**-**

FBP: filtered back projection, MBIR: model-based iterative reconstruction

artifacts on coronary arteries (2).

However, recent advancements have been made in CT technology. For example, the longitudinal coverage and maximum tube current have been increased, and the speed of gantry rotation speed has been improved (3). Forward Projected Model-based Iterative Reconstruction SoluTion (FIRST), a recently developed model-based iterative reconstruction (MBIR) technique, has been available for use with 320-slice CT, enabling the provision of high-quality CT images even in a low-radiation scan setting (4). We recently reported the improvement in the diagnostic performance of 320-slice CT with MBIR for detecting late iodinate enhancement in the left ventricular myocardium compared with the previous settings (5, 6).

In the present study, we intend to highlight the improvements in diagnostic accuracy for the detection of significant coronary artery stenosis using a combination of 320-slice CT and MBIR. To our knowledge, few reports have described the improvement in the image quality of coronary arteries using 320-slice CT and MBIR (4), and no report has discussed the improvement in the diagnostic accuracy.

Materials and Methods

This was a retrospective study of 160 patients (108 men; mean age 66±12 years old) who underwent both coronary CT and invasive coronary angiography (ICA) within a 3-month period. The study protocol conforms to the guidelines of the Declaration of Helsinki, and our institutional ethical committee approved this retrospective study (Reference number 2827).

The first 100 consecutive patients (Group 1) underwent 320-slice CT (Aquilion One; Canon Medical Systems, Otawara, Japan) without MBIR or small-focus scanning (Table 1), from December 2008 to 2013 in our institution. The next 60 consecutive patients (Group 2) underwent 320-slice CT (Aquilion One/ViSION Edition; Canon Medical Systems) with MBIR (FIRST cardiac sharp; Canon Medical Systems) at a standard strength level and small-focus scanning (Table 1), from December 2016 to 2019, in our institution. MBIR reconstructed coronary CT images of a patient in one cardiac phase in a few minutes. Patients with a history of coronary artery bypass surgery or who underwent CT using a different protocol from the one mentioned in the next paragraph were excluded. Patients with a high heart rate (HR) (>80 beats per minute) at CT scanning were also excluded, as short-acting intravenous β-blockers were only available in the era of Group 2, and any effects of the medicine were to be avoided.

The diagnostic performance of 320-slice CT without MBIR or small-focus scanning and 320-slice CT with both of them, with ICA regarded as a reference standard, was compared to detect significant coronary artery stenosis (≥70% on CT, ≥75% on ICA). in both patient- and segment-based analyses (defined by the American Heart Association) (7).

CT protocol

All subjects lay on the scanner table in the supine position. After a scout scan, a non-contrast electrocardiogram (ECG)-gated cardiac scan was performed using a prospective ECG-gated technique. After a non-contrast scan, conventional enhanced 320-slice CT was performed with a slice thickness of 0.5 mm and a tube voltage of 120 kV in both groups, using a retrospective ECG-gated with dose modulation technique and decreasing the radiation dose during the systolic phases (if possible) (Table 1) (8-10). The tube current during the scan was set based on the autoexposure control system (100-750 mA). All subjects with a heart rate >65 beats per minute received 10 mg of propranolol or 12.5 mg landiolol prior to scanning, except for those with contraindicated for β-blocker. Just prior to the scanning procedure, subjects were administered two doses of isosorbide dinitrate sublingually to facilitate dilation of the coronary arteries and enable the acquisition of clear images, even down to the small branches of the coronary arteries.

For contrast material injection, we employed a routine triphasic protocol. Right or left antecubital intravenous access using a 20- or 22-gauge needle was attained, and the system connected to a dual-syringe injector with a dual-flow option (Dual Shot; Nemoto, Tokyo, Japan). During the first phase, we injected 50-100 mL of undiluted contrast agent (350 or 370 mg/mL iodine contrast) at 3-4 mL/s, followed by 40-70 mL of a 50%/50% saline-to-contrast material mixture at 3-4.2 mL/s and 10-20 mL of pure saline at 2-4 mL/s. Time-resolved (every 1 second) single-section CT scans were acquired at the mid-left ventricle level in the first 10 to almost 40 seconds, just after the injection of media in order to determine the best scan timing. When the CT values in the descending aorta had increased to 200 HU, we started the actual examination scan while the subject held their breath.

Coronary CT angiography

CT images were reconstructed every 5% from 0% to 95% of the R-R interval using filtered back projection. The specific cardiac phase images with minimum motion artifact were also reconstructed, and the best cardiac phase images were reconstructed using MBIR only in Group 2. Significant stenosis (≥70%) of coronary arteries was evaluated on those images. Coronary arteries on the CT scans were divided into 15 segments based on the recommendations of the American Heart Association (11). All coronary artery segments with a diameter of >1.5 mm were analyzed. The evaluation of coronary arteries on CT was performed by an experienced cardiologist (H.T.) blinded to ICA results using both workstations mentioned above. There were several segments that were not fully diagnostic because of severe calcification; we judged them to have significant stenosis. For the first half of the cases in each group (n=50 in Group 1, n=30 in Group 2), another cardiologist (M.T.) evaluated CT images, and inter-observer agreement was assessed and compared between the two groups. The CCS was determined by an experienced cardiologist (H.T.) using a commercially available software program (Ziostation 2; Ziosoft, Tokyo, Japan). The effective scanning dose for the evaluation coronary arteries was calculated from the dose-length product in a dose report in both groups (conversion factor 0.014) (9, 12).

ICA protocol

ICA was performed according to standard clinical protocols. The interpretation of significant stenosis (≥75%) of coronary arteries on ICA was performed by experienced cardiologists. All coronary arteries were divided into 15 segments according to the same definition as was used for coronary CT interpretation (11).

Statistical analyses

Continuous variables are expressed as the mean±standard deviation (SD) or as the median (interquartile range) if not normally distributed. Categorical variables are reported as counts and percentages. Continuous variables were compared using Student's *t*-test when two samples had equal variance with a normal distribution, while Welch's *t*-test was used when two samples had unequal variances with a normal distribution. Wilcoxon's signed-rank test was used to compare continuous variables when two samples were not normally distributed. The chi-square test was used to compare categorical variables, including the diagnostic accuracy of CT for detection of the significant coronary artery stenosis, between the two groups (if any expected count was less than 5, Fisher's exact test was used). All tests were 2-sided, and p values <0.05 were considered to indicate statistical significance.

All statistical analyses were performed using the JMP software program, version 10.0.2 (SAS Institute Inc, Cary, NC, USA).

Results

The CT scanning parameters and patient background characteristics were compared between the two groups (Table 1, 2). The percentage of smokers was significantly higher (60% vs. 42%, p=0.007), and the patients were significantly older (69±11 vs. 64±12 years old, p=0.007) in Group 2 than in Group 1. Conversely, the percentages of patients with dyslipidemia and those taking statins, β-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers were significantly higher in Group 1 than in Group 2 (Table 2). The bodyweight of the patients in Group 2 was significantly lower than in Group 1 (56±9 kg vs. 64±14 kg, p<0.0001) (Table 2). The number of patients with CCS >400 was significantly higher in Group 2 than in Group 1 (47% vs. 31%, p=0.047) (Table 2). The number of patients with coronary stents was significantly higher in Group 1 than in Group 2 (21% vs. 5%, p=0.006) (Table 2). Patient height was not recorded in 2 cases in Group 1.

In the patient-based analysis, the sensitivity, specificity, positive and negative predictive values (PPV and NPV), and overall accuracy of detection of significant stenosis on CT against ICA as the gold standard were 95%, 85%, 90%, 92%, and 91% in Group 1, and 93%, 83%, 93%, 83%, and 90% in Group 2 (Fig. 1), respectively, with no significant differences observed between the two groups (p=0.69, 1.00, 0.67, 0.34, and 0.83, respectively) (Fig. 1).

In the segment-based analysis, the sensitivity, specificity, PPV and NPV, and overall accuracy of detection of significant stenosis on CT against ICA were 74%, 94%, 67%, 96%, and 92% in Group 1, and 70%, 96%, 67%, 96%, and 93% in Group 2, respectively, with no significant differences observed between the two groups (p=0.46, 0.14, 0.93, 0.71, and 0.24, respectively) (Fig. 2).

In the cases with severe CCS (CCS >400) (31 cases in Group 1 and 28 in Group 2), the sensitivity, specificity, PPV and NPV, and overall accuracy of detection of significant stenosis on CT against ICA were 96%, 57%, 88%, 80%, and 87% in Group 1, and 88%, 67%, 96%, 40%, and 86% in Group 2, respectively, in the patient-based analysis, with no significant differences observed between the two groups (p=0.61, 1.00, 0.61, 0.52, and 1.00, respectively). However, in the segment-based analysis, the sensitivity, specificity, PPV and NPV, and overall accuracy of detection of significant stenosis on CT against ICA were 73%, 87%, 60%, 92%, and 84% in Group 1, and 68%, 95%, 69%, 94%, and 91% in Group 2 (Fig. 3), respectively, with the specificity and overall accuracy significantly higher (p<0.001 and p=0.004, respectively) in Group 2 than in Group 1 (Fig. 3).

Typical coronary artery images with stents in a case from

Table 2. Patient Characteristics.

	Group 1	Group 2	p value
Age (years)	**64±12**	**69±11**	**p=0.007****
Males	66 (66%)	42 (70%)	p=0.60
Dialysis	2 (2%)	2 (3%)	p=0.63
Hypertension	65 (65%)	38 (68%)	p=0.83
Dyslipidemia	**58 (58%)**	**17 (38%)**	**p=0.0003*****
Familial history of CAD	8 (8%)	7 (11%)	p=0.44
Smoking	**42 (42%)**	**36 (60%)**	**p=0.007****
Diabetes	30 (30%)	10 (20%)	p=0.059
Administration of ARB or ACE-I	**62 (62%)**	**16 (27%)**	**p<0.0001*****
Administration of β-blocker	**40 (40%)**	**14 (23%)**	**p=0.031***
Administration of Statin	**48 (48%)**	**14 (23%)**	**p=0.0019****
Body Weight (kg)	**64±14**	**56±9**	**p=0.0001*****
Height (cm)	162±10	161±9	p=0.37
Atrial fibrillation at the scanning	3 (3%)	3 (5%)	p=0.68
Heart rate (beats per minute) at the scanning	60±10	59±8	p=0.41
The interval between CT and ICAG (days)	16±19	18±18	p=0.37
Coronary calcium score	457±703	766±1,331	p=0.056
Coronary calcium score >400	**31 (31%)**	**28 (47%)**	**p=0.047***
Coronary stents	**21 (21%)**	**3 (5%)**	**p=0.006****
Significant stenosis on coronary arteries	60 (60%)	42 (70%)	p=0.20
Radiation dose (mSv)	13.5±5.6	13.2±4.8	p=0.78

CAD: coronary artery disease, ARB: angiotensin II receptor blocker, ACE-I: angiotensin-converting enzyme inhibitor

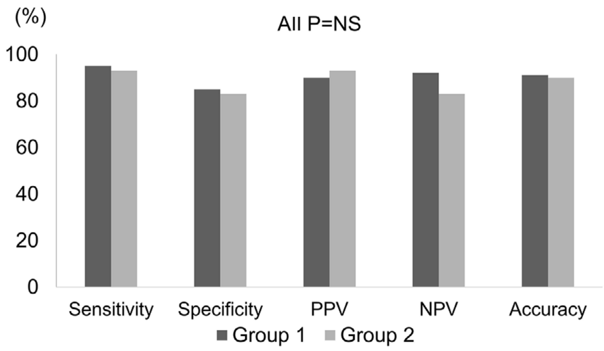

Figure 1. A comparison of the diagnostic accuracy of significant coronary artery stenosis between the two groups in a patient-based analysis. No significant differences were observed between the two groups in a patient-based analysis.

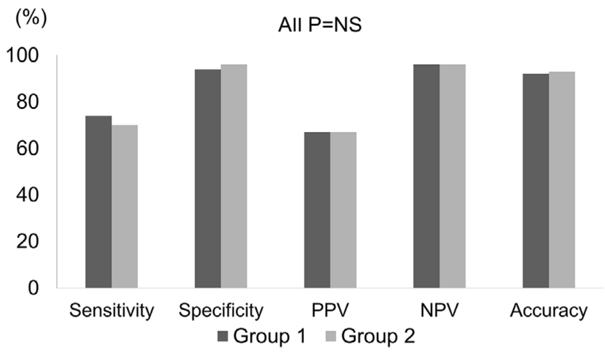

Figure 2. A comparison of the diagnostic accuracy of significant coronary artery stenosis between the two groups in a segment-based analysis. No significant differences were observed between the two groups in a segment-based analysis.

each group are shown in Figs. 4A and 4B, with magnified images shown in Figs. 4C and 4D, respectively. In both cases, 2.5-mm cypher stents were implanted at the white arrows, and the in-stent lumen and struts of the stent were more clearly depicted in Group 2 than in Group 1. Typical coronary artery images with severe calcifications in Groups 1 and 2 (CCS almost 2,300) were also shown (Fig. 5A, C, respectively), and their ICA findings are also shown (Fig. 5B, D, respectively). Significant stenosis was clearly ruled out only in the case from Group 2.

The between-group differences in patients' body weight and the number of patients with previous stents might have significantly influenced the diagnostic accuracy of coronary artery stenosis on CT. Therefore, we compared the overall diagnostic accuracy in the segment-based analysis between patients with a body weight ≥64 kg (median of all 100 patients; n=51) and those with a body weight <64 kg (n=49) in Group 1. However, there were no significant differences in the overall diagnostic accuracy between the groups (90% vs. 92%, p=0.21).

The number of segments with stents was 36 in 21 patients in Group 1 and 3 in 3 patients in Group 2. The number of patients with coronary stents was significantly higher in Group 1 than in Group 2, but there was no significant difference in the segment-based overall diagnostic accuracy between the segments with coronary stents (n=36) and all segments (n=1,415) in Group 1 (97% vs. 92%, p=0.36).

The inter-observer agreement was 0.92 in Group 1 and

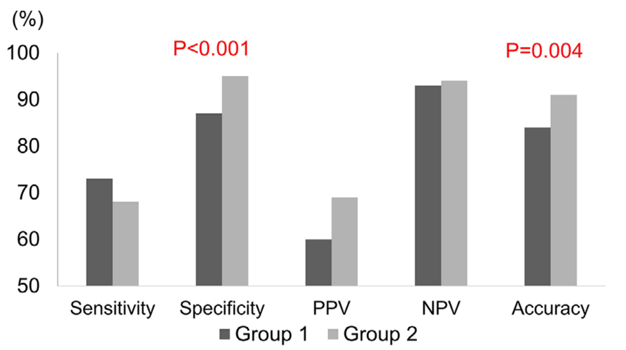

Figure 3. **A comparison of the diagnostic accuracy of significant coronary artery stenosis between the two groups in a segment-based analysis in only the cases with severely calcified coronary arteries (CCS>400). In a segment-based analysis, the specificity and accuracy were significantly higher (all p<0.01) in Group 2 than in Group 1.**

0.95 in Group 2, showing no significant difference between the groups (p=0.13). The effective dose of CT scan in the early contrast-phase for the evaluation of coronary arteries was 13.5±5.6 mSv in Group 1 and 13.2±4.8 mSv in Group 2 (p=0.78).

Discussion

The diagnostic accuracy of 320-slice CT with small-focus scan and MBIR for the detection of significant stenosis of the coronary artery was preserved in the population with a higher CCS and lower heart rate compared with 320-slice CT without small-focus scan or MBIR. This study also showed that the diagnostic performance of significant coronary stenosis on CT was improved with 320-slice CT with MBIR compared with 320-slice CT without MBIR in a segment-based analysis among cases with severely calcified

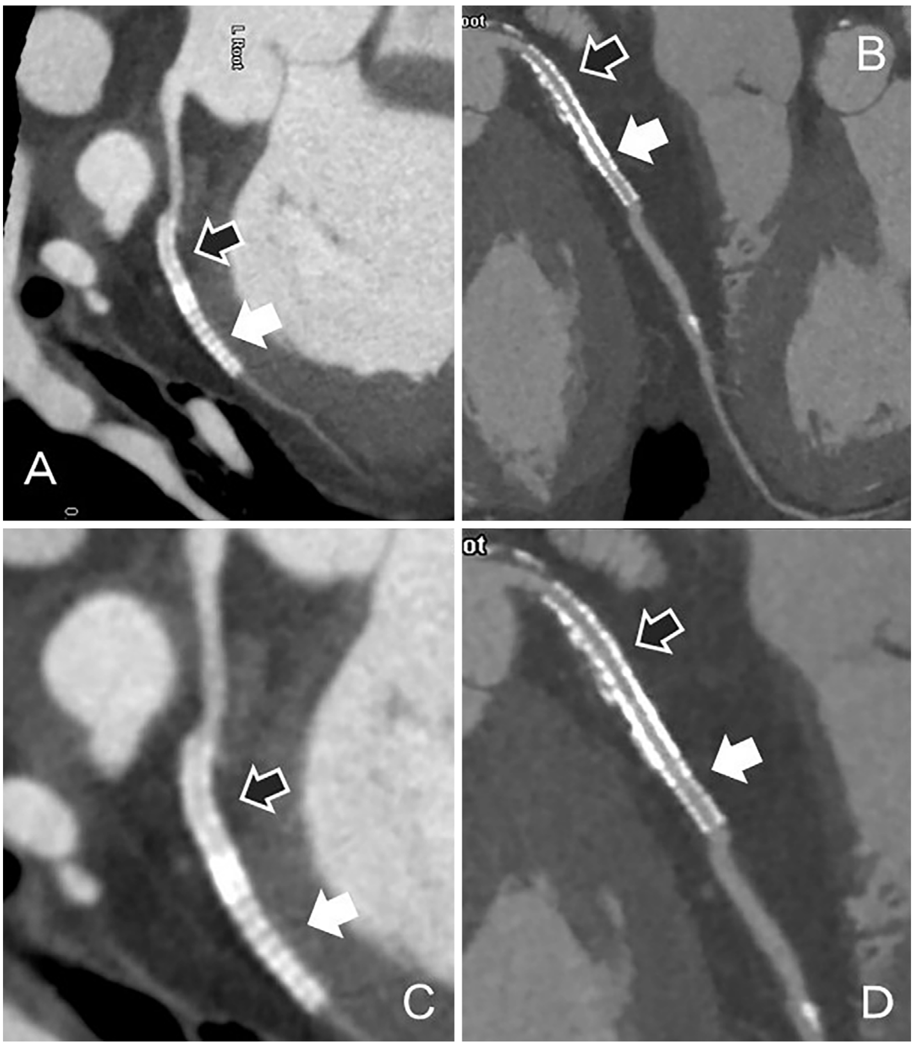

Figure 4. **Typical images of 2.5-mm cypher stents on 320-slice CT without MBIR (A, white arrow) and 320-slice CT with MBIR (B, white arrow), with magnification (C and D, respectively). In both cases, 2.5-mm cypher stents were implanted at the white arrows. In addition, a 3.5-mm cypher stent was also implanted at the proximal 2.5-mm cypher stent in the case from Group 1, and 2.5-mm xience sierra and zeta stents were implanted similarly at the proximal 2.5-mm cypher stent in the case from Group 2 (black arrows). The in-stent lumen and struts of the 2.5-mm cypher stent are more clearly depicted in the case of Group 2 than in that of Group 1.**

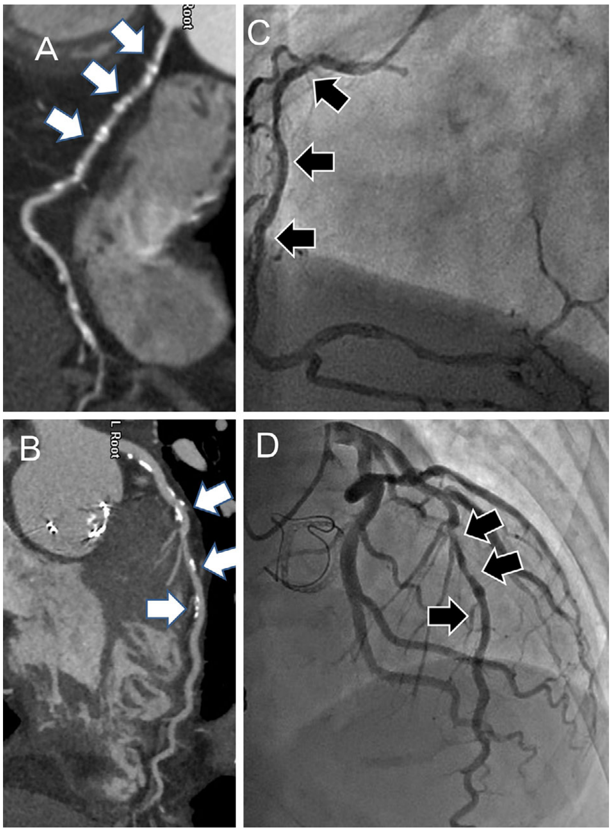

Figure 5. Typical images of coronary arteries with severe calcifications (patients' coronary calcium score almost 2,300) on 320-slice CT without MBIR (A, white arrow) and with MBIR (B, white arrow) and invasive coronary angiography of the same patient (C and D, black arrows). The stenosis in the segments with severe calcifications was complex, and the calcified stenotic lesion was over-diagnosed as significant stenosis (A, white arrows) with invasive coronary angiography regarded as a reference standard (C, black arrows). Because the blooming artifacts of calcification of the coronary artery were suppressed, and significant stenosis was correctly ruled out in the segments with severe calcifications on CT (B, white arrows) with invasive coronary angiography regarded as a reference standard (D, black arrows).

coronary arteries, especially with regard to the sensitivity and overall accuracy.

Based on the previous CT guideline, coronary CT was not recommended in cases with severe coronary artery calcification (3), as the specificity of the detection of significant stenosis was low in those patients. However, we must perform coronary CT in cases with severe atherosclerosis, especially just before trans-catheter aortic valve implantation. In addition, the number of patients who undergo cardiac CT has increased, so the improvement of diagnostic accuracy of coronary artery stenosis is necessary. We successfully detected the improvement in diagnostic accuracy of coronary CT in cases with severe calcification. However, this improvement was identified only in the segment-based analysis; it was not detected in the patient-based analysis because the number of patients was small in this study. Therefore, the diagnostic accuracy in patient-based analyses is expected to improve in daily clinical practice.

Diagnostic accuracy of significant stenosis on coronary arteries

In particular, the specificity for detection of coronary artery stenosis is known to be decreased in cases with CCS >400 (2). In the present report, we successfully revealed the improvement in the diagnostic accuracy of coronary CT using 320-slice CT with MBIR in cases with severely calcified coronary arteries. We suspect that the increased diagnostic accuracy of significant coronary artery stenosis in cases with severely calcified coronary arteries on 320-slice CT with MBIR was due to a reduction in blooming artifacts of calcium on coronary arteries because of the combination of 320-slice CT and MBIR.

We also suspected that the between-group differences in patients' body weight and the number of patients with previous stents might significantly influence the diagnostic accuracy of coronary artery stenosis on CT. Therefore, we compared the overall diagnostic accuracy in the segment-based analysis between patients with a body weight ≥64 kg (median of all 100 patients; n=51) and those with a body weight <64 kg (n=49) in Group 1. However, no significant difference between the groups was noted (91% vs. 92%, p=0.21), nor was there any significant difference in the segment-based overall diagnostic accuracy in the segments with coronary stents (n=36) and all segments (n=1,415) in Group 1 (97% vs. 92%, p=0.36). Therefore, we regarded the influence of the patients' body weight and history of coronary stenting on the segmental diagnostic accuracy on CT as negligible.

Utility of MBIR and small-focus scans for improving the diagnostic accuracy of significant coronary arteries

MBIR is a reconstruction technique known to be useful for reducing image noise on CT (4-6). The evaluation of significant stenosis of coronary arteries is sometimes difficult, especially in cases with severely calcified plaque, because of the plaque's blooming artifacts (13). The iterative reconstruction technique is useful for reducing artifacts of calcified plaque and improving the image quality of coronary arteries on CT (14). A small-focus scan is also useful for obtaining an increased spatial resolution on CT (15, 16), but the maximum tube current should be decreased. Therefore, while a low tube current acquisition with a small-focus scan may increase the image noise on CT, MBIR is useful for reducing the image noise. In addition, the maximum tube current during small-focus scanning was increased in Group 2 than in Group 1, because the scanner was evolved; such changes may also have affected the results of this study. In the era of Group 1, a decrease in the tube current for small-focus scanning was not recommended in most (98%) of the 100 consecutive cases who underwent both CT and ICA because of the risk of increment of image noise.

Recently, deep learning reconstruction (DLR) has become available, and radiation dose reduction and improvements in the image quality are consequently expected (17, 18). However, the number of scanners able to use DLR is still limited at present. Furthermore, DLR is performed via deep learning of CT images reconstructed using MBIR (18). Therefore, the clinical impact of this study is still preserved in daily clinical practice.

Role of the gantry rotation speed

A high gantry rotation speed might play a key role in improving the diagnostic accuracy in Group 2 because of the associated improvement in the temporal resolution of CT images. The image quality of coronary arteries on CT depends on the heart rate of the patients, and high-quality coronary artery images in cases with low heart rates can be expected because of the low number of motion artifacts (16). The short-acting intravenous β-blocker landiolol was newly released in the era of Group 2 and has been made available to patients who undergo cardiac CT. Some researchers have reported improvements in the image quality of coronary arteries on CT while using landiolol (19). However, this agent was not available during our evaluation of Group 1. Since we wished to avoid any effects of medication on our findings, patients with high heart rates at CT scanning were excluded.

Limitations

Several limitations associated with the present study warrant mention. This was a single-center retrospective study; therefore, a larger prospective study should be conducted to confirm our results. It is impossible to perform cardiac CT twice using different CT scanners in the same case at a similar clinical timing because of ethical issues. Therefore, the patient backgrounds differed between the two groups. The prevalence of significant coronary artery stenosis was relatively high (≥60%) because this study was a retrospective one, and the prevalence of the coronary artery disease might have differed from that in the cohort of candidates considered appropriate for coronary CT in daily clinical practice, based on the recent guideline.

Conclusion

The diagnostic accuracy of the detection of coronary artery stenosis on CT compared with ICA improved with the use of 320-slice CT with MBIR in cases with severely calcified coronary arteries.

The authors state that they have no Conflict of Interest (COI).

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