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Non-Invasive Detection of Coronary Artery Disease in Patients With Left Bundle Branch Block Using 64-Slice Computed Tomography

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OBJECTIVES The goal of this study was to evaluate the diagnostic accuracy of 64-slice computed tomography (CT) to identify coronary artery disease (CAD) in patients with complete left bundle branch block (LBBB).

BACKGROUND Left bundle branch block increases risk of cardiac mortality, and prognosis is primarily determined by the underlying coronary disease. Non-invasive stress tests have limited performance, and conventional coronary angiography (CCA) is usually required.

METHODS Sixty-six consecutive patients with complete LBBB and sinus rhythm admitted for CCA were enrolled. Computed tomography was performed 3 ± 3.9 days before CCA. The accuracy of 64-slice CT to detect significant stenosis (>50% lumen narrowing) was compared with quantitative coronary angiography. All segments were analyzed regardless of image quality from coronary calcification or motion artifacts. Results were analyzed by patient and by coronary segment (990) using the American Heart Association 15-segment model.

RESULTS Lower heart rates were associated with improved image quality. Computed tomography correctly identified 35 of 37 (95%) patients without significant stenosis and 28 of 29 (97%) patients with significant stenosis on CCA. Computed tomography correctly assessed 68 of 94 (72%) significant stenosis. Overall, accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 64-slice CT for identifying CAD by patient was 95%, 97%, 95%, 93%, and 97%, respectively, and by segment was 97%, 72%, 99%, 91%, and 97%, respectively.

CONCLUSIONS In a routine clinical practice, 64-slice CT detects with excellent accuracy a significant CAD in patients with complete LBBB. A normal CT in this clinical setting is a robust tool to act as a filter and avoid invasive diagnostic procedures. (J Am Coll Cardiol 2006;48:1929–34) © 2006 by the American College of Cardiology Foundation

Left bundle branch block (LBBB) correlates strongly to age (1,2) and increases risk of cardiac mortality (1–7). Prognosis is primarily determined by the underlying cardiac pathology (3–5). Left bundle branch block is most commonly associated with atherosclerotic coronary artery disease (CAD) (3,5). Thus, the identification of chronic CAD in patients with LBBB is important to stratify the risk and manage the therapy. Non-invasive stress tests have limited performance, and conventional coronary angiography (CCA) is usually required to confirm diagnosis (8–12).

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Multislice computed tomography (MSCT) is a promising non-invasive technique to detect and characterize stenotic and non-stenotic plaque in CAD (13–23). The 64-slice computed tomography (CT) offers an improved spatial and temporal resolution (21–23). The aim of the present study was to evaluate in a routine clinical practice the diagnostic accuracy of 64-slice CT to identify CAD in patients with complete LBBB compared with CCA.

METHODS

Patients. From September 2004 to November 2005, 66 consecutive patients with complete LBBB, without a history of CAD, admitted for CCA in our institution were enrolled in the study. Multislice CT was performed 3 ± 3.9 days before angiogram. Exclusion criteria were suspicion of acute coronary syndrome, known history of CAD, arrhythmia, renal insufficiency (serum creatinine >150 μmol/l), iodine allergy, and pregnancy. All patients were in sinus rhythm and received oral beta-blocker medication if not contraindicated (metoprolol 100 mg, 1 h before acquisition) in order to lower heart rate below 70 beats/min. However, no patient was excluded due to a higher heart rate. Nitroglycerine was not used before CT acquisition. The local ethics committee approved the study, and a signed informed consent was obtained from all patients.

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Abbreviations and Acronyms

CAD = coronary artery disease
CCA = conventional coronary angiography
CT = computed tomography
LAD = left anterior descending coronary artery
LBBB = left bundle branch block
LCX = left circumflex artery
LVEF = left ventricular ejection fraction
MSCT = multislice computed tomography
QCA = quantitative coronary angiography
RCA = right coronary artery

LBBB criteria. Left bundle branch block was recorded on a 12-lead electrocardiogram (ECG) and defined as set by the Criteria Committee of the New York Heart Association (24): QRS interval ≥120 ms; slurred/notched wide and predominant R waves in leads I, aVL, V_5, and V_6; slurred/notched and broad S waves in V_1 and V_2 with absent or small R waves; mid-conduction delay defined as notching or a plateau in the mid-QRS wave; ventricular activation time >50 ms at the onset of the QRS interval; M-shaped QRS variants with occasionally wide R waves in V_5 and V_6; no initial Q-wave over the left precordium; and absence of pre-excitation.

Left ventricular ejection fraction (LVEF). Transthoracic echocardiography (Philips Sonos 7500, Amsterdam, the Netherlands) was performed with a multifrequency transducer and harmonic imaging as appropriate. Two-dimensional echocardiography was performed from the apical 4- and 2-chamber views. The LVEF was computed using biplane Simpson's methodology (25).

MSCT technique. All examinations were performed with a 64-slice CT (Sensation 64, Siemens, Erlangen, Germany). The acquisition protocol included a gantry rotation time of 330 ms, a theoretical collimation of 0.4 mm (combining 64 × 0.6 mm slice collimation with the new z-sharp double sampling technology allowing dual focal spots per detector row) (26), and a table feed of 18 mm/s. The ECG was monitored during the scanning, and 70 to 90 ml of contrast medium were injected (flow rate 4 ml/s) (Iopamidol 400 mg/ml, Schering SA, Berlin, Germany). Acquisition started automatically at a threshold of 100 HU within the region of interest over the descending aorta. A tube voltage of 120 kV and a current of 600 mAs were applied with individual adaptation according to the patient's morphology. The ECG-pulsed current modulation was activated. Dose-length product was obtained from the protocol that summarized each CT. The effective radiation dose was estimated by a method proposed by the European Working Group for Guidelines on Quality Criteria in CT as derived from the product of the dose-length product and a conversion coefficient for the chest as the investigated anatomic region ($k = 0.017$ mSv · mGy^{-1} · cm^{-1}) averaged between male and female models (27). In our study, the estimated effective radiation was 7 ± 2 mSv.

Reconstruction process. Transverse images were reconstructed retrospectively from the raw CT data and electrocardiographic tracings. The reconstruction was gated at −350 ms of RR interval for each cardiac cycle to generate diastolic phase cardiac images, using a slice thickness of 0.75 mm to minimize image noise and optimize signal-to-noise ratio and a reconstruction increment of 0.5 mm, with a smooth kernel (B30). The quality of image volumes was immediately judged in the frontal, axial, and sagittal plans. In cases of artifacts, additional sets of images were created for various points of the cardiac cycle, and the dataset with the minimum artifact was selected for further analysis.

Interpretation. Multislice CT scans were analyzed by consensus of 2 examiners blinded to the results of CCA and all clinical information. Image quality was classified with a 5-point scale as: 5 = excellent (no motion artifacts present); 4 = good (minor motion artifact present); 3 = moderate (substantial motion artifacts present, but luminal assessment regarding significant stenosis still possible); 2 = heavily calcified (vessel lumen obscured by calcification); and 1 = blurred (only contrast visualization inside the vessel possible, no luminal assessment regarding significant stenosis possible) (15).

A previously described 15-segment American Heart Association model of the coronary tree was used (28). In case of a single lesion per segment, side branches or bifurcation were used as markers for the location. In case of multiple lesions per segment, the worst lesion was defined as eligible. Each lesion identified was examined using maximum intensity projection and multiplanar reconstruction techniques along longitudinal plane using the scanner standard workstation (Wizard, Siemens). Each lesion was examined by the minimal and normal adjacent lumen diameter seen in any view in the same segment. A significant stenosis was defined by visual estimation >50% on maximum intensity projection images for non-calcified lesions and on multiplanar reconstruction images for partially or heavily calcified lesions. Patients were considered as having a significant CAD in cases of at least 1 stenosis >50%.

CCA. Selective coronary angiogram was performed by conventional technique, using 5-F catheters. Intracoronary injection of nitrates (1 mg of isosorbid dinitrate) was systematically used after identification of stenosis. The same 15-segment model employed for MSCT was used. Angiograms were reviewed by an experienced operator blinded to clinical and MSCT findings. Quantitative coronary angiography (QCA) was performed using the CAAS II algorithm (a second generation system for offline and online QCA) (29). A significant stenosis was defined as a mean diameter reduction >50% in 2 orthogonal views.

Statistics. Effect of heart rate, LVEF, and body mass index on image quality was assessed by analysis of variance and procedure of least significant difference method Fisher test post-hoc analysis. The accuracy of MSCT to detect significant stenosis was compared with QCA as the standard of reference. Statistical analysis was performed with StatView

Table 1. Patient Characteristics

Total number of patients	66
Men, n (%)	40 (61)
Women, n (%)	26 (39)
Age (yrs)	69 ± 13
Heart rate (beats/min)	67 ± 13
Body mass index (kg/m^2)	27.4 ± 3.3
Angina pectoris, n (%)	18 (27)
Atypical chest pain, n (%)	7 (11)
Silent ischemia, n (%)	8 (12)
Isolated LBBB, n (%)	4 (6)
Syncope, n (%)	1 (2)
Congestive heart failure, n (%)	28 (42)
LVEF (%)	52 ± 16
Hypertension, n (%)	48 (73)
Diabetes, n (%)	15 (23)
Hypercholesterolemia, n (%)	32 (48)
Smoker, n (%)	26 (39)
Exlusion CAD, n (%)	37 (56)
1-vessel disease, n (%)	14 (21)
2-vessel disease, n (%)	4 (6)
3-vessel disease, n (%)	11 (17)

CAD = coronary artery disease; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction.

5.0 software (SAS Institute Inc., Cary, North Carolina). Percentages were expressed with a 95% confidence interval. Continuous variables were expressed as mean values ± SD and nominal variables as counts and percentages. A p value <0.05 was regarded as statistically significant.

RESULTS

No patient was excluded from the study. Multislice CT was performed without complication in all patients. Ten patients (15%) were already under beta-blocker therapy, but additional treatment was needed in 56 patients (85%) before scanning. The mean heart rate during the scan was 67 ± 13 beats/min (range 46 to 119 beats/min). The total scan time was 12 ± 2 s. The clinical characteristics of the patients are summarized in Table 1.

Conventional coronary angiography revealed no significant stenosis in 37 patients (56%), 1-vessel disease in 14 patients (21%), 2-vessel disease in 4 patients (6%), and 3-vessel disease in 11 patients (17%). Five patients had significant left main stenosis.

Image quality. Image quality score was good on average (3.8 ± 1.4) (Fig. 1). Score 5 (n = 32), 4 (n = 10), 3 (n = 6), 2 (n = 14), and 1 (n = 4) were for a heart rate of 60 ± 8, 67 ± 8, 71 ± 3, 72 ± 10, and 101 ± 13 beats/min, respectively. According to heart rate, image quality was significantly impaired among patients in score 1 and better among patients in score 5 when compared with patients in score 2, 3, and 4 ($p < 0.05$). All the patients with a heart rate >90/min presented blurred image quality (score 1). Four patients presented respiratory artifacts, 2 patients had an initial tachycardia during the scanning, and 8 patients had important diffuse calcifications impairing image quality to score 2. No relationship between image quality and LVEF or body mass index was noted.

Patient-based analysis. Multislice CT correctly identified 35 of 37 (95%) patients without significant stenosis on CCA and 28 of 29 (97%) patients with significant stenosis on CCA (Table 2). One patient with a significant stenosis on the right posterior descending artery was classified as normal on MSCT. However, all 15 patients with multivessel disease were correctly detected by MSCT. Two patients without significant stenosis were classified as positive on MSCT regarding stenosis detected on mid-right coronary artery (RCA) and proximal left circumflex artery (LCX). Overall, accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 64-slice CT for identifying patients with or without CAD was 95%, 97%, 95%, 93%, and 97%, respectively.

Lesion-by-lesion analysis. Of 990 coronary segments, CCA detected 94 significant stenoses; MSCT correctly detected 68 (72%) (Table 2, Fig. 2). Multislice CT detected relatively less stenosis than CCA especially in multilesion patients. Twenty-six stenoses (28%) were missed or underestimated: 14 stenoses were missed because of motion artifacts (5) or important calcifications (9), and 12 lesions were underestimated. The distribution of missed lesions per vessel was as follows: left main, 0 of 5 (0%); left anterior descending artery (LAD), 5 of 42 (12%); LCX, 9 of 22 (41%); RCA, 12 of 25 (48%).

Seven lesions were overestimated by MSCT because of motion artifacts (3) and important calcifications (4). Three of these lesions were on LCX and the 4 others on RCA.

On a per-artery analysis, MSCT had excellent specificity (99% to 100%), but sensitivity was, respectively, 100% for left main, 88% for LAD, and only 59% for LCX and 52% for RCA.

Overall, accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 64-slice CT for detecting significant stenosis was 97%, 72%, 99%, 91%, and 97%, respectively.

DISCUSSION

To our knowledge, this is the first study comparing MSCT and CCA in patients with LBBB. Our data demonstrates that 64-slice CT provides a high diagnostic accuracy to

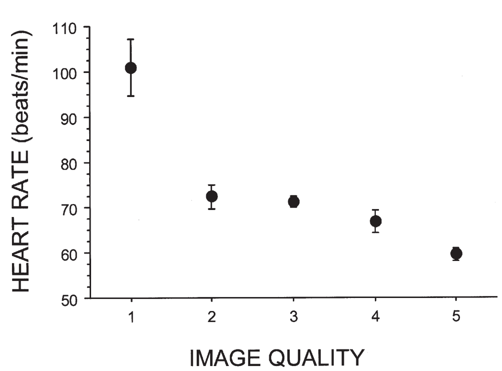

Figure 1. Plot showing comparison between image quality score and heart rate (beats/min) during scanning.

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Table 2. Detection of Significant Coronary Artery Stenosis (>50%) With 64-Slice Computed Tomography

	n	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy	PPV	NPV
Patients	66	28	35	2	1	97 (82–100)	95 (82–99)	95 (87–99)	93 (78–99)	97 (85–100)
Coronary segment overall	990	68	889	7	26	72 (62–81)	99 (98–100)	97 (95–98)	91 (82–96)	97 (96–98)
LM	66	5	61	0	0	100 (48–100)	100 (94–100)	100 (95–100)	100 (48–100)	100 (94–100)
LAD	330	37	288	0	5	88 (74–96)	100 (99–100)	98 (96–100)	100 (91–100)	98 (96–99)
Proximal	66	15	50	0	1	94 (70–100)	100 (93–100)	98 (92–100)	100 (78–100)	98 (90–100)
Mid-	66	16	47	0	3	84 (60–97)	100 (92–100)	95 (87–99)	100 (79–100)	94 (83–99)
Distal	66	0	66	0	0	—	100 (95–100)	100 (95–100)	—	100 (95–100)
First diagonal	66	6	59	0	1	86 (42–100)	100 (94–100)	98 (92–100)	100 (54–100)	98 (91–100)
Second diagonal	66	0	66	0	0	—	100 (95–100)	100 (95–100)	—	100 (95–100)
LCX	264	13	239	3	9	59 (36–79)	99 (96–100)	95 (92–98)	81 (54–96)	96 (93–98)
Proximal	66	5	58	3	0	100 (48–100)	95 (86–99)	95 (87–99)	63 (24–91)	100 (94–100)
Distal	66	3	61	0	2	60 (15–95)	100 (94–100)	97 (89–100)	100 (29–100)	97 (89–100)
First obtuse marginal	66	4	58	0	4	50 (16–84)	100 (94–100)	94 (85–98)	100 (40–100)	94 (84–98)
Second obtuse marginal	66	1	62	0	3	25 (1–81)	100 (94–100)	95 (87–99)	100 (3–100)	95 (87–99)
RCA	330	13	301	4	12	52 (31–72)	99 (97–100)	95 (92–97)	76 (50–93)	96 (93–98)
Proximal	66	2	61	1	2	50 (7–93)	98 (91–100)	95 (87–99)	67 (9–99)	97 (89–100)
Mid-	66	7	53	3	3	70 (35–93)	95 (85–99)	91 (81–97)	70 (35–93)	95 (85–99)
Distal	66	2	63	0	1	67 (9–99)	100 (94–100)	98 (92–100)	100 (16–100)	98 (92–100)
RPDA	66	1	62	0	3	25 (1–81)	100 (94–100)	95 (87–99)	100 (3–100)	95 (87–99)
PLA	66	1	62	0	3	25 (1–81)	100 (94–100)	95 (87–99)	100 (3–100)	95 (87–99)

FN = false negative; FP = false positive; LAD = left anterior descending artery; LCX = left circumflex; LM = left main; NPV = negative predictive value; PLA = posterolateral artery; PPV = positive predictive value; RCA = right coronary artery; RPDA = right posterior descending artery; TN = true negative; TP = true positive.

detect significant CAD if any, in patients with complete LBBB and sinus rhythm.

LBBB features. The prevalence of complete LBBB increases from 1% at age 50 years to 17% at age 80 years in a general male population (1). In the onset of acute myocardial infarction, LBBB is related to ischemia in the distribution of LAD (30), but chronic block is a marker of a slowly progressing degenerative disease that also affects the myocardium (1). Currently, atherosclerotic CAD is associated in nearly one-half of patients with LBBB (3,5). Patients with LBBB are at increased risk of cardiac death (1–7), but the impact of CAD on mortality has yielded conflicting results. Previous studies found that LBBB is an independent predictor of mortality in chronic CAD (6,7) but was associated with more extensive CAD and worse left ventricular function (7). However, in other studies, the underlying cardiac pathology predicts the prognosis (3–5). The higher risk of sudden death is due to tachyarrhythmia and myocardial infarction (5), highlighting the importance of identifying CAD to stratify the risk and manage the therapy.

Non-invasive stress tests have limited performance to identify CAD in patients with complete LBBB (8–12). Exercise-induced ST-segment changes are non-specific for ischemia (8). Myocardial perfusion studies often suffer from false-positive anteroseptal or septal perfusion defects in the absence of LAD stenosis (9,11). Dobutamine stress echocardiography is a highly specific test (10,12), but sensitivity is moderate for septal ischemia in case of abnormal rest septal thickening (12). However, myocardial contrast echocardiography with adenosine seems to improve diagnostic accuracy (31). Finally, most studies excluded patients with a history of myocardial infarction or ventricular tachyarrhythmia or structural valve disease (10,12).

Conventional coronary angiography is usually required to confirm diagnosis of CAD in patients with complete LBBB. Cardiac catheterization is a relatively safe procedure but has a well-defined risk of morbidity (1.7%) and mortality (0.1%) (32).

Clinical implications. In a routine clinical setting, including limitations of heart rate and calcifications, 64-slice CT correctly assessed 95% of patients with CAD (35 of 37) and identified all the patients (21 of 21) who needed revascularization. Regarding the false-negative patient, the missed lesion may be explained by the distal localization on side branch.

Furthermore, CCA could have been avoided in 57% of the cases (35 of 66 patients) with a negative predictive value of 97%. This high negative predictive value is comparable to that of other studies (13–15,17,21,23).

Lesion detection. Complete visualization of all clinically important coronary segments is a prerequisite for MSCT coronary angiography to become an accepted clinical tool for the assessment of patients with suspected CAD (14). Our findings confirm the high diagnostic accuracy (97%) and specificity (99%) of 64-slice CT in detecting coronary stenosis. However, sensitivity was moderate (72%). Four hypotheses could explain such results.

Firstly, in our study all the segments were analyzed including distal and side branches with diameter <1.5 mm. Side branches were less accurate than in other localization (13 false negative [FN]/26; 7 lesions in obtuse marginal, 3 in right posterior descending artery, and 3 in posterolateral artery), possibly due to lower diameter and insufficient contrast opacification (23) (Fig. 2). These results are consistent with prior studies of 64-slice CT. Leber et al. (22) found a sensitivity of 75% without excluding small vessels. Raff et al. (21) found a sensitivity of 86% but failed to

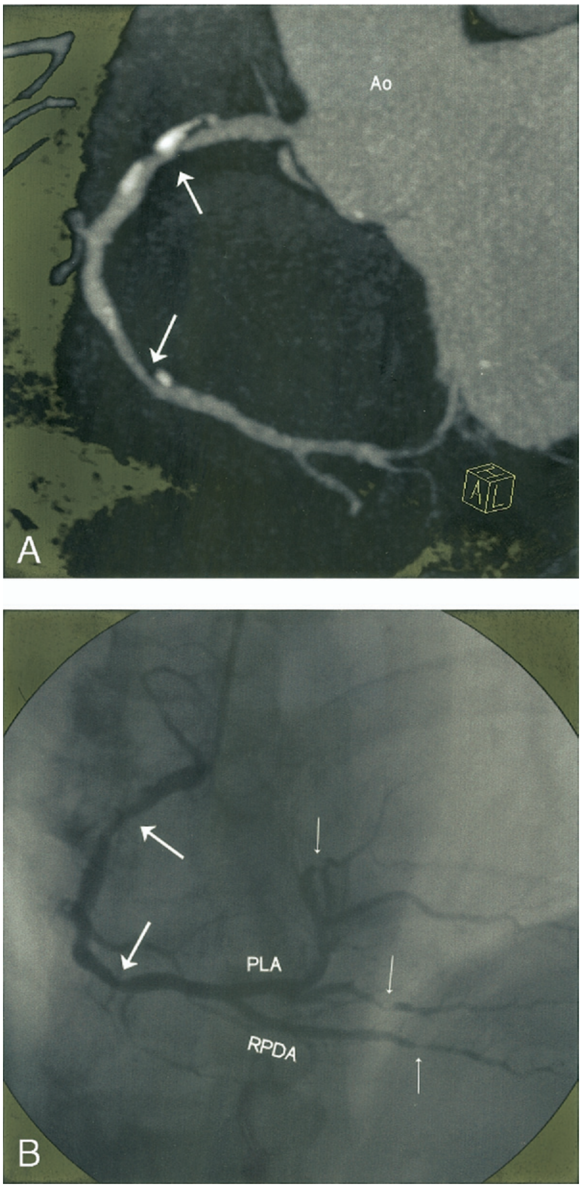

Figure 2. Sixty-four-slice computed tomography in a 68-year-old man admitted for suspected coronary artery disease **(A)**. Curved multiplanar reconstruction image of right coronary artery demonstrates significant stenosis on the proximal and distal portion **(thick arrows)** correctly assessed by coronary angiography **(B)**. Note that 3 lesions were missed on side branches **(thin arrows) (B)**. Ao = aorta; PLA = posterolateral artery; RPDA = right posterior descending artery.

evaluate 12% of segments that were excluded. In contrast, Leschka et al. (23) found an excellent sensitivity of 94% with only 6% false-negative lesions (11 of 176). However, this discrepancy between our results could be explained by the high incidence of false-positive lesions: 14% (24 of 176) were overestimated versus 7% (7 of 94) in our study (23).

Secondly, heavily calcified segments led to 9 missed lesions (35% FN), 12 underestimated lesions (46% FN), and 4 overestimated lesions. Calcified plaque creates blooming artifacts and partial volume effects that blurred the delineation of the coronary lumen (14,16,17,21–23). Partial volume effect is due to averaging different densities within a single voxel, but this problem may be alleviated by decreasing voxel size or increasing spatial resolution (17,21). Currently, 64-slice CT with 0.4-mm z resolution remains highly accurate with moderate calcification, but segments with massive calcifications remain challenging to assess (21).

Thirdly, in our study exams with motion, artifacts were not excluded. When premature ventricular contraction or respiratory artifacts occurred, they rarely affected all the coronary segments: only 5 lesions were missed (19% FN) and 3 lesions were overestimated. The RCA (12 FN/26) and LCX (9 FN/26) were more commonly affected by missed lesion than LAD (5 FN/26) or left main artery (0 FN/26) probably due to curved anatomy of these arteries and their greater cardiac motion (14,17,23). Note that septal wall abnormalities usually observed in patients with LBBB hampered non-invasive stress tests and had no effect on the MSCT accuracy in analyzing the LAD segments (sensitivity and specificity were 100% and 88%, respectively).

Finally, in multilesion patients (but not necessarily multivessel patients), MSCT detected relatively less stenosis than CCA. This could be primarily explained due to the lack of sensitivity of MSCT for detecting side branch stenosis, and, secondly, multilesion analysis in clinical practice is time-consuming and should refer the patient for CCA for revascularization management.

Study limitations. All our patients with LBBB were referred for catheterization, and CAD was identified in nearly one-half of our cohort. This could have influenced MSCT sensitivity, but this high prevalence of CAD in this population is consistent with previous studies (3,5).

The need for beta-blocker therapy to reduce heart rate in our experience is still recommended.

Previous studies showed high sensitivity and specificity for the detection of CAD when restricting analysis to patients with a low calcium scoring (15,21). The coronary calcification score has been shown to correlate strongly with the presence and severity of coronary atherosclerosis (33). However, the lack of specificity of this score (34) partially explained why this score was not assessed in our high-risk population.

In our study, no segment was excluded, but in a clinical screening practice, heavy calcifications or motion artifacts blurring the luminal assessment in some non-interpretable segments should cause the patient to be referred for cardiac catheterization.

Radiation exposure of MSCT remains a matter of concern. However, we have systematically used the ECG-pulsed current modulation to reduce radiation dose during systole (35). We have also applied individual adaptation according to the patient's morphology. Thus, in our study, the estimated effective radiation (7 $\pm$ 2 mSv) was 30% to 50% lower than that reported in previous studies with 64-slice CT (21,22). Our data are consistent with that of Hausleiter et al. (36) who found 5.4 $\pm$ 1.1 mSv when low tube voltage and ECG-dependent dose modulation were applied with 64-slice CT.

Conclusions. In a routine clinical practice, 64-slice CT detects with excellent accuracy a significant CAD in patients with complete LBBB. A normal MSCT in this clinical setting is a robust tool to act as a filter and avoid invasive diagnostic procedures. Severe calcifications and cardiac rhythm remain common limitations. Sixty-four-slice CT may be proposed as an alternative method to stress tests in screening patients with LBBB.

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