Detection of Coronary Artery Disease Using Coronary Flow Velocity Reserve by Transthoracic Doppler Echocardiography versus Multidetector Computed Tomography Coronary Angiography: Influence of Calcium Score

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Background: There have been no clinical data specifying the degree of calcium deposition at which coronary flow velocity reserve (CFVR) measurement using transthoracic Doppler echocardiography surpasses 320-row multidetector computed tomographic coronary angiography (CTCA) in detecting obstructive coronary artery disease.

Methods: One hundred seventy patients who underwent invasive coronary angiography, transthoracic Doppler echocardiography, and CTCA were prospectively enrolled. Coronary artery stenosis was defined as percentage diameter stenosis $\geq$ 50% on invasive coronary angiography. CFVR < 2.0 and narrowing $\geq$ 50% measured with CTCA were the thresholds indicating the presence of coronary artery stenosis. The degree of coronary artery calcification was also assessed using the Agatston calcium score method by computed tomography.

Results: The majority of patients (89%) were classified as having either high or intermediate pretest probability of coronary artery disease. Significant coronary artery stenoses by invasive coronary angiography were found in 71 patients and 104 vessels. Although the overall diagnostic performance of CTCA was comparable with that of CFVR measurement for detecting coronary artery stenosis, only the diagnostic performance of CTCA was negatively affected by the extent of a patient's coronary artery calcification. Receiver operating characteristic curve analysis indicated that only CFVR measurement is diagnostically accurate when calcium scores are >319 in the patient-based assessment, 189 for the left anterior descending coronary artery, 98 for the left circumflex coronary artery and 282 for the right coronary artery.

Conclusions: Transthoracic Doppler echocardiography and 320-row multidetector CTCA successfully diagnosed significant coronary artery stenosis with high feasibility and accuracy. However, only the diagnostic performance of CTCA was negatively affected by the extent of a patient's coronary artery calcification, and therefore the diagnostic performance of CFVR measurement for detecting coronary artery stenosis surpassed that of CTCA when the calcium score exceeded specified cutoff values. (J Am Soc Echocardiogr 2014;■:■-■.)

Keywords: Coronary artery disease, Calcification, Coronary flow velocity reserve, Echocardiography, 320-row multidetector computed tomographic coronary angiography

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Noninvasive coronary angiography is being increasingly performed using computed tomographic coronary angiography (CTCA) in assessing obstructive coronary artery disease (CAD).[1-3] The ability of 320-slice technology to incorporate 16-cm anatomic coverage allows imaging of the entire heart in a single gantry rotation, which improves image quality, reduces artifacts, and enables better visualization of the coronary artery lumen.[4-6] However, coronary artery calcification degrades image quality and limits the diagnostic accuracy of CTCA.[7,8] Coronary flow velocity reserve (CFVR) using transthoracic Doppler echocardiography (TTDE) is another useful, noninvasive measurement for predicting significant coronary artery stenosis,[5,9] and the diagnostic performance of this method is unaffected by the presence and severity of coronary artery

Abbreviations

CAD = Coronary artery disease

CFVR = Coronary flow velocity reserve

CI = Confidence interval

CS = Calcium score

CTCA = Computed tomographic coronary angiography

DS = Diameter stenosis

FFR = Fractional flow reserve

ICA = Invasive coronary angiography

LAD = Left anterior descending coronary artery

LC = Left circumflex coronary artery

RCA = Right coronary artery

TTDE = Transthoracic Doppler echocardiography

calcification. However, there have been no clinical data specifying the degree of calcium deposition at which CFVR measurement surpasses CTCA in detecting obstructive CAD. Therefore, we investigated the diagnostic accuracy of CFVR measurement for detecting obstructive CAD with various degrees of coronary artery calcification in the left anterior descending coronary artery (LAD), the left circumflex coronary artery (LC), and the right coronary artery (RCA) in comparison with that of CTCA.

METHODS

Patient Selection

The study group consisted of 182 patients >20 years of age who underwent invasive coronary angiography (ICA) to evaluate CAD in Yokkaichi Social Insurance Hospital between January 2009 and July 2012. All patients had reported either typical or atypical chest symptoms of angina pectoris. Patients with known histories of CAD or previous coronary intervention were excluded from the present study. After 10 patients were excluded for renal insufficiency (serum creatinine > 2.0 mg/dL) and two patients for severe respiratory insufficiency, the remaining 170 patients underwent TTDE and CTCA. ICA was performed in all patients within 2 weeks after TTDE and CTCA, regardless of the results. Written informed consent was obtained from all subjects, and the protocol was approved for use by the Human Studies Subcommittee of Yokkaichi Social Insurance Hospital.

Measurements of CFVR Using TTDE

All patients underwent a complete routine transthoracic echocardiography with CFVR measurement using a Sonos 7500 system and an HD15 system (Philips Medical Systems, Andover, MA). Left ventricular ejection fraction and wall thickness were measured by two-dimensional echocardiography. Patients were defined as having left ventricular hypertrophy if interventricular septal or posterior wall thickness was ≥12 mm.[5]

Coronary flow velocity was measured both at rest (Figure 1) and during intravenous infusion of adenosine triphosphate (0.14mg/kg/min) in the 3 major coronary arteries using TTDE, as previously described.[5,9-13] CFVR was defined as the ratio of mean diastolic velocity at peak flow response to mean diastolic velocity at baseline, and CFVR < 2.0 was defined as abnormal flow reserve indicative of significant coronary artery stenosis.[5,9] Two experienced and blinded investigators measured CFVR by tracing the contour of the spectral Doppler signal using the computer incorporated in the ultrasound system. All measurements for calculating CFVR were averaged over three cardiac cycles. The mean time required to complete a coronary flow velocity measurement, including CFVR calculation, was about 10 min for each coronary artery and therefore 30 min for each patient.[5]

Coronary Angiography with 320-Row computed Tomography

Patients underwent two computed tomographic scans (coronary calcium scoring and angiography) using a 320-row scanner with 0.5-mm detector elements, 350 msec of gantry rotation time, and up to 16 cm of coverage in the z direction (Aquilion ONE; Toshiba Medical Systems, Otawara, Japan).[5,14] An evaluating calcium score (CS) was performed on the postprocessing workstation (Calcium Scoring software; Toshiba Medical Systems). Coronary calcium was defined as an area of at least three "face-connected" voxels in the axial plane in the course of a coronary artery, with an attenuation threshold value of ≥130 Hounsfield units. Three in-axial-plane face-connected voxels correspond to a minimum lesion area of >1 mm^2, which is used as reference value in calcium scoring.[15] Because we aimed to compare the diagnostic utility of the two modalities for detecting CAD in the three major coronary arteries, we excluded the left main trunk, the septal branch, the diagonal branch, the obtuse marginal branch, and the atrioventricular branch from the calcium scoring. For CTCA, 6 to 11 mL iodine was injected at a flow rate of 3 to 5.5 mL/sec as a test bolus for determining the arrival time in the ascending aorta, which was followed by a 20-mL saline chaser at the same flow rate. An initial data set was reconstructed at 75% to 80% of the RR interval, with a slice thickness of 0.50 mm and a reconstruction interval of 0.25 mm. Two blinded and experienced investigators assessed coronary artery stenosis on a commercially available workstation (ZIO STATION System 1000; Amin/ZIOSOFT, Tokyo, Japan). Lesions causing ≥50% reductions of the lumen were considered obstructive.[16]

Invasive Coronary Angiographic Procedure and Analysis

Selective ICA was performed using standard techniques. Quantitative analysis of the results (QAngio XA version 7.1.14.0; Medis Medical Imaging, Leiden, The Netherlands) was performed, and the results were interpreted independently by another two readers unaware of the results of CFVR measurement and CTCA.[5] Binary coronary artery stenosis was defined as percentage diameter stenosis (DS) ≥ 50%.

Comparing the Diagnostic Accuracy of CFVR Measurement and CTCA

Both patient-based and vessel-based analyses were performed to directly compare the utility of CFVR measurement with that of CTCA for the diagnosis of coronary artery stenosis. Therefore, a patient was considered to either be misdiagnosed or to have nonassessable image quality if at least one of the coronary arteries was inaccurately diagnosed in the patient-based assessment. In addition, the severity of segmental coronary artery calcification was quantified using an adapted cross-sectional arc calcification method in the segment-based analyses using CTCA.[16] In brief, coronary artery segments were visually examined in cross-section, and the greatest circumferential extent of calcium within the coronary segment (arc calcification) was assessed in degrees according to the following ordinal scale: 1 = noncalcified segments, 2 = mild calcification (cross-sectional arc calcium < 90°), 3 = moderate calcification (cross-sectional arc calcium of 90°–180°), and 4 = severe calcification (cross-sectional arc calcium > 180°). Because only CTCA is suitable for the segment-based assessment of coronary artery stenosis