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Original article

Comparison of 3-dimensional and 2-dimensional quantitative coronary angiography and intravascular ultrasound for functional assessment of coronary lesions

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ABSTRACT

Background: Three-dimensional quantitative coronary angiography (3D-QCA) reportedly allows more accurate delineation of true vessel geometry when compared with standard two-dimensional (2D) QCA and has been validated by intravascular ultrasound (IVUS). This study sought to compare diagnostic efficiency of 2D- and 3D-QCA, and IVUS in identifying hemodynamically significant coronary stenoses as determined by fractional flow reserve (FFR).

Methods: Forty-two lesions in 40 patients were assessed by FFR, IVUS, and 2D- and 3D-QCA. Correlations between FFR values and anatomical parameters obtained by 2D- and 3D-QCA and IVUS were analyzed. The receiver operating characteristic (ROC) curves were used to compare the diagnostic accuracy of the parameters for predicting FFR $\leq$ 0.80.

Results: Mean FFR value was 0.75 ± 0.13. FFR $\leq$ 0.80 was observed in 28 lesions (67%). Of IVUS measurements, minimum lumen area (MLA) well correlated with FFR values ($r = 0.71$, $p < 0.001$). Of 3D- and 2D-QCA measurements, minimum lumen diameter (MLD) correlated best with FFR values ($r = 0.79$, $p < 0.01$; $r = 0.68$, $p < 0.01$, respectively), followed by MLA ($r = 0.76$, $p < 0.01$; $r = 0.67$, $p < 0.01$, respectively). The area under the ROC curve for 3D-QCA MLD was greater than those for 2D-QCA MLD ($p = 0.03$) and 2D-QCA MLA ($p = 0.03$). On the other hand, the AUC for 3D-QCA MLD, 3D-QCA MLA, and IVUS MLA were not significantly different.

Conclusions: 3D-QCA is more useful than 2D-QCA and possibly comparable to IVUS in the assessment of functional stenosis severity. When FFR is not available, 3D-QCA MLA and MLD may assist in the assessment of functional severity of intermediate lesions.

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Introduction

The functional significance of coronary artery stenoses with intermediate severity, which are defined angiographically as 40–80% luminal narrowing, is important in determining strategy in patient care [1]. Fractional flow reserve (FFR) is considered the gold standard for the physiological assessment of coronary artery stenosis with a cut-off FFR value of $\leq$0.80 (currently proposed to indicate functional significance) [1–3]. Visual estimation on angiography, or even measurement using conventional two-dimensional quantitative coronary angiography (2D-QCA), cannot accurately determine the physiological severity of coronary stenosis [4], since their abilities to depict three-dimensional (3D) vascular structures of the coronary arterial tree are limited [5,6]. Intravascular ultrasound (IVUS) is the most widely used intracoronary imaging tool for the quantitative assessment of coronary artery disease, which yields more accurate measurements of vessel geometry and lesion severity than conventional angiography [7]. The efficiency of IVUS in determining the functional status of coronary lesions has been previously examined in numerous studies [1,8–12]. In particular, the minimum lumen area (MLA) obtained by IVUS was shown to be one of the independent correlates for ischemic FFR value [1]. However, IVUS is more invasive, costly, and time-consuming than coronary angiography.

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3D-QCA using 3D reconstruction techniques based on routine 2D projections has been developed [13,14], and reported to allow more accurate delineation of true vessel geometry compared with conventional 2D-QCA [14,15]. However, few data are available regarding the relationship between anatomical 3D-QCA parameters and functional FFR results. Moreover, 2D- and 3D-QCA, and IVUS have not been compared for measuring FFR in the same patients. The objective of the present study was to compare diagnostic efficiency of 2D- and 3D-QCA, and IVUS in identifying hemodynamically significant coronary stenoses as determined by FFR.

Methods

Study population

Between August 2012 and July 2014, 42 lesions in 40 patients with intermediate angiographic severity (40–80% on visual estimation) were assessed using FFR, IVUS, and 2D- and 3D-QCA. Exclusion criteria were: multiple stenoses (>40% of diameter stenosis on visual estimation) within the target vessel, lesions located at the origin of the right coronary ostium or in the left main coronary artery, vessels with supply of coronary collaterals, lack of ≥2 angiographic projections separated by 30°, poor image quality, prior myocardial infarction in the territory supplied by the target vessel, prior coronary artery bypass surgery, unstable angina, recent myocardial infarction (within 7 days), severe valvular heart disease, decompensated heart failure, advanced renal failure (estimated glomerular filtration rate ≤30 ml/min), obvious left ventricular hypertrophy or cardiomyopathy, and contraindication to both adenosine 5′-triphosphate and papaverine.

Written informed consent was obtained from all patients for all examinations. The ethics committee of Chiba University approved the study (approval No. 2307).

Measurement of fractional flow reserve

Coronary angiography was performed using a 5 or 6 French guide catheter without side holes by a radial approach. After coronary angiography, FFR measurements were performed using a 0.014-inch pressure monitoring guidewire (Volcano Inc., Rancho Cordova, CA, USA). The pressure monitoring guidewire was externally calibrated and introduced into the guiding catheter. The pressure transducer was advanced just outside the tip of the guide catheter, and the pressure measured by the sensor was then equalized to that of the guide catheter. The wire was then advanced distally to the target coronary stenosis. After checking the correct position of both the guide catheter and the pressure wire and after the pressures had stabilized, intracoronary papaverine (8 mg for right coronary artery and 12 mg for left coronary artery) or intravenous adenosine 5′-triphosphate (140 μg/kg/min) was then administered to induce maximal hyperemia. FFR was calculated as the ratio of the mean distal coronary pressure divided by the mean aortic pressure obtained after achievement of maximal hyperemia. In all patients, intracoronary isosorbide dinitrate (at least 0.5 mg) was administered before coronary angiography and before FFR measurement. An FFR value of ≤0.80 was considered the significant ischemic threshold. The decision for treatment of any lesion was left to operator's discretion.

Quantitative coronary angiography analysis

Angiographic images were acquired at 15 frames per second. Two angiographic images separated by a viewing angle ≥30° with the least foreshortening and the best depiction were selected at end-diastolic frames. The view with the most severe stenosis was then used for 2D-QCA using standard commercial software (CAAS QCA 5.11, Pie Medical Imaging BV, Maastricht, the Netherlands). For 3D-QCA analysis, both images were used, and it was performed by a trained analyst blinded to the FFR results using dedicated 3D reconstruction software (CAAS QCA 5.11, Pie Medical Imaging BV). After calibration performed in the same frame as 2D-QCA, the major steps of 3D-QCA were contour detection on two angiographic projections of the involved vessel segments and identification of a common image point. The rest of the reconstruction was performed automatically by the system as shown in Fig. 1, although fine adjustments were possible with manual edge detection, according to the judgment of the operator. The QCA software provided automatic contour detection and automated identification of the sites of maximal luminal obstruction and the start and end of the stenosis. All diameter values reported by 3D-QCA were based on the equivalent diameter concept, being calculated as the diameter of a circle with the same cross-sectional area as the ellipse. The following angiographic parameters were obtained in the target lesion: minimum lumen diameter (MLD), MLA, reference vessel diameter, reference vessel area, % diameter stenosis, % area stenosis, and lesion length.

IVUS assessment

IVUS studies were performed with the 40 MHz IVUS catheter (ViewIT, Terumo Corp., Tokyo, Japan) after administration of intracoronary isosorbide dinitrate. The transducer was pulled back automatically at a speed of 0.5 mm/s up to the guide catheter with the use of a validated motorized device. Offline analysis of the IVUS images was performed by an experienced cardiologist blinded to the FFR results using computerized planimetric software (VisiWave, Terumo Corp.). Lumen area was measured at the site of the narrowest luminal cross section (MLA), and at the reference site with the largest luminal cross section within 10 mm of the proximal or distal to the MLA site with no intervening branches [16]. Vessel area was also measured at these sites. Lesion was defined as the site of stenosis due to accumulation of atherosclerotic plaque that compromises the lumen by at least 50% by cross-sectional area. The lesion length was calculated as the length from the most proximal to the most distal site of the stenosis. Plaque burden at the MLA site and lumen area stenosis were calculated according to the validated IVUS guidelines [16].

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentages. Correlations were calculated using the Pearson correlation coefficient for parametric data. Receiver-operating characteristics (ROC) curve analysis was used to examine IVUS and QCA parameters as a predictor of the functional significance of lesions (FFR ≤ 0.80). The resulting sensitivity and specificity were calculated. The best cut-off value was determined by the maximum sum of sensitivity and specificity. The area under the ROC curve (AUC) was compared using a nonparametric approach proposed by DeLong et al. [17]. All statistical analyses were performed with JMP Pro 11 (SAS Institute, Cary, NC, USA) or SAS version 9.4 (SAS Institute). A value of $p < 0.05$ was considered statistically significant.

Results

Baseline clinical, angiographic, and IVUS characteristics are shown in Tables 1 and 2. The mean FFR value was 0.75 ± 0.13 and 28 vessels (67%) had an FFR value of ≤0.80. The mean target vessel reference diameter measured 2.70 ± 0.63 mm by 2D-QCA, and

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