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Research paper

Comparison of quantitative stenosis characteristics at routine coronary computed tomography angiography with invasive fractional flow reserve for assessing lesion-specific ischemia

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ABSTRACT

Objective: To comprehensively evaluate quantitative parameters derived from routine coronary CT angiography (cCTA) for predicting lesion-specific ischemia in comparison to invasive fractional flow reserve (FFR).

Background: The ability of cCTA to gauge lesion-specific ischemia is limited. Several quantitative parameters have been proposed to enhance the specificity of cCTA, such as morphologic indices (lesion length/minimal lumen diameter^4 [LL/MLD^4]; percentage aggregate plaque volume [%APV]) and a measure of intracoronary contrast gradients (corrected coronary opacification [CCO]).

Methods: Forty-nine patients who had undergone cCTA followed by FFR within 3 months were included. An experienced observer visually assessed all cCTA studies and derived multiple measures characterizing the lesion of interest, including LL, MLD, minimal lumen area (MLA), LL/MLD^4, remodeling index, %APV, and CCO. Lesion-specific ischemia was considered with FFR <0.8.

Results: Among 56 lesions, 13 were flow-obstructing by FFR. On univariate analysis, LL, MLD, LL/MLD^4, and CCO showed discriminatory power. The area under the curve of LL/MLD^4 (0.909) was significantly greater compared with MLD (0.802, $P = 0.014$), LL (0.739, $P = 0.041$), and CCO (0.809), although the latter did not reach statistical significance ($P = 0.175$). On multivariate regression, LL/MLD^4 was the only independent predictor of lesion-specific ischemia (odds ratio 2.021, $P = 0.001$). Moreover, LL/MLD^4 compared favorably to visual cCTA evaluation.

Conclusion: LL/MLD^4 derived from routine cCTA can enhance the detection of lesion-specific ischemia and may be superior to other described quantitative parameters.

Abbreviations: AUC, area under the receiver operating characteristic curve; CAD, coronary artery disease; CCO, corrected coronary opacification; cCTA, coronary CT angiography; FFR, fractional flow reserve; LL/MLD^4, lesion length/minimal lesion diameter^4; MLA, minimal luminal area; %APV, percentage aggregate plaque volume.

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1. Introduction

Coronary computed tomographic angiography (cCTA) features robust diagnostic accuracy for coronary artery stenosis.[1,2] Although the high negative predictive value of cCTA allows for reliable exclusion of coronary artery disease, its moderate positive predictive value remains a limitation of this modality. Consequently, determining lesion-specific ischemia of anatomically identifiable coronary artery stenosis is regularly indeterminate by cCTA. Gauging the hemodynamic relevance of intermediate lesions is particularly unreliable.[3,4]

Invasive fractional flow reserve (FFR) demonstrably provides guidance for an improved patient care and is therefore suggested as the preferred test by the appropriate use criteria for diagnostic catheterization in order to assess the functional relevance of coronary lesions of stable patients with multivessel disease when evidence of ischemia is absent or previous findings are discrepant.[5–8] Aside from CT myocardial perfusion imaging and CT-based FFR derivation, ongoing, recent investigations have proposed several quantitative parameters for the characterization of coronary artery stenosis obtained at routine diagnostic cCTA that may have potential to increase the diagnostic performance of this test for the discrimination of hemodynamically relevant disease.[9–13] However, these parameters have largely been proposed and evaluated individually and to date their relative performance has never been compared in a systematic fashion and within the same patient population. Hence, the purpose of this study was to comprehensively evaluate and compare the diagnostic value of recently introduced quantitative characteristics of coronary artery stenoses, as derived from standard cCTA data, for the prediction of lesion-specific ischemia.

2. Material and methods

2.1. Patient population

The present study used a retrospective design; patients were eligible for inclusion if they had undergone cCTA followed by coronary catheter angiography with fractional flow reserve (FFR) interrogation from 01/2008 to 04/2014 because of suspected or known coronary artery disease. Patient data were excluded if the time interval between cCTA and invasive FFR exceeded 3 months. Baseline exclusion criteria further comprised previous revascularization (percutaneous coronary intervention with stent placement and coronary artery bypass graft surgery), occurrence of interprocedural complications (cardiac death, non-fatal myocardial infarction), and non-diagnostic cCTA image quality. Also, bifurcation lesions were excluded, because neither FFR nor quantitative cCTA-based parameters can be derived reliably. Our institutional review board approved the study and waived the need for written informed patient consent. This study was conducted in compliance with the Health Insurance Portability and Accountability Act.

2.2. Coronary catheter angiography with fractional flow reserve

Coronary catheter angiography was conducted as a standard procedure in our cardiac catheterization laboratory by an experienced interventional cardiologist per societal guidelines.[14] FFR was assessed intra-procedurally in intermediate lesions of patients without prior testing for myocardial ischemia, or with discrepancies of clinical presentation and non-invasive findings.[8] For this purpose, a dedicated pressure-monitoring guide wire was used. FFR was derived as the ratio of the mean coronary pressure distal to the stenosis over the mean aortic pressure at the time of pharmacologically-induced hyperemia (adenosine, 140 μg/kg/min). An FFR value < 0.80 was considered diagnostic for the presence of lesion-specific myocardial ischemia.

2.3. Coronary CT angiography acquisition

All cCTA examinations were performed on either first- or second-generation dual-source CT systems (Somatom Definition or Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). First, patients underwent a non-contrast medium enhanced calcium scoring scan (collimation, 32 × 1.2 mm; tube voltage 120 kV; tube current, 75 mA; slice thickness, 3 mm; increment, 1.5 mm).

Parameters of the cCTA protocol using first generation dual-source CT were as follows: gantry rotation time of 330 ms, 32 × 2 × 0.6 mm collimation with z-flying focal spot, tube voltage of 100 − 120 kV, and tube current of 320 to 650 mAs. With the second generation dual-source CT system the protocol involved a gantry rotation time of 280 ms, 2 × 64 × 0.6 mm collimation with z-flying focal spot, tube voltage of 80 − 120 kV, and tube current of 320 to 650 mAs. The acquisition techniques included retrospective electrocardiographic gating with default use of electrocardiography-dependent tube current modulation, prospective electrocardiographic triggering, and the high-pitch prospectively electrocardiography-triggered spiral mode. The acquisition technique was chosen individually for each patient with the goal of minimizing radiation exposure. Pharmacological rate control and nitroglycerin administration were available at the discretion of the attending physician of the day. The contrast agent was administered using a power injector (Stellant D, Medrad, Indianola, PA) at a rate of 4 − 6 mL/s for all phases through an 18 − 20 gauge antecubital intravenous line. A biphasic protocol was used with injection of 50 − 90 mL of contrast medium (Ultravist, 370 mgI/mL iopromide, Bayer, Wayne, NJ), followed by 30 mL of saline (0.9% sodium chloride) as a bolus chaser. Image reconstruction was performed for the cardiac phase with the least motion using the following parameters: 0.75 mm section thickness and 0.5 mm reconstruction increment using a vascular reconstruction algorithm (B26f).

2.4. Coronary CT angiography assessment

One observer used a 5-level Likert scale to grade the image quality of each cCTA dataset, with 0 = non-diagnostic; 1 = diagnostic despite impairment by image noise, artifacts and/or low vascular opacification; 2 = moderate image quality with sufficient intraluminal visibility, artifacts may be present; 3 = good vessel contrast in absence of major artifacts, low image noise; 4 = excellent image quality.

Axial images, cross-sectional views, and automatically generated curved planar reformations were used for evaluation. Lesion characterization was performed by one observer specialized in cardiovascular imaging (7 years of experience), who was blinded to the patients' clinical histories and the results of invasive angiography with FFR. The observer was only unblinded regarding the segmental location of the lesions of interest that had been interrogated by FFR. To obtain the vessel reference diameter and area, the average of non-diseased vessel dimensions proximal and distal to the lesion of interest were assessed at points where no atherosclerotic plaque could be detected.

Lesion length (LL) was measured on curved planar reformatted images and was measured as the maximum length between the proximal and distal extent of the lesion. Minimal lumen diameter (MLD) was determined as the smallest luminal diameter of a lesion of interest. Minimal lumen area (MLA) was measured manually at the narrowest level of the lesion on cross-sectional images. According to Li et al[11] LL divided by the fourth power of MLD resulted in an index (LL/MLD^4). Additionally, on cross-sectional vessel views,