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Additional Value of Transluminal Attenuation Gradient in CT Angiography to Predict Hemodynamic Significance of Coronary Artery Stenosis

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OBJECTIVES The current study evaluates the incremental value of transluminal attenuation gradient (TAG), TAG with corrected contrast opacification (CCO), and TAG with exclusion of calcified coronary segments (ExC) over coronary computed tomography angiogram (CTA) alone using fractional flow reserve (FFR) as the gold standard.

BACKGROUND TAG is defined as the contrast opacification gradient along the length of a coronary artery on a coronary CTA. Preliminary data suggest that TAG provides additional functional information. Interpretation of TAG is hampered by multiple heartbeat acquisition algorithms and coronary calcifications. Two correction models have been proposed based on either dephasing of contrast delivery by relating coronary density to corresponding descending aortic opacification (TAG-CCO) or excluding calcified coronary segments (TAG-ExC).

METHODS Eighty-five patients with intermediate probability of coronary artery disease were prospectively included. All patients underwent step-and-shoot 256-slice coronary CTA. TAG, TAG-CCO, and TAG-ExC analyses were performed followed by invasive coronary angiography in conjunction with FFR measurements of all major coronary branches.

RESULTS Thirty-four patients (40%) were diagnosed with hemodynamically-significant coronary artery disease (i.e., FFR $\leq$0.80). On a per-vessel basis (n = 253), 59 lesions (23%) were graded as hemodynamically significant, and the diagnostic accuracy of coronary CTA (diameter stenosis $\geq$50%) was 95%, 75%, 98%, and 54% for sensitivity, specificity, negative predictive value, and positive predictive value, respectively. TAG and TAG-ExC did not discriminate between vessels with or without hemodynamically significant lesions (–13.5 $\pm$ 17.1 HU [Hounsfield units] $\times$ 10 mm^{-1} vs. –11.6 $\pm$ 13.3 HU $\times$ 10 mm^{-1}, p = 0.36; and 13.1 $\pm$ 15.9 HU $\times$ 10 mm^{-1} vs. –11.4 $\pm$ 11.7 HU $\times$ 10 mm^{-1}, p = 0.77, respectively). TAG-CCO was lower in vessels with a hemodynamically-significant lesion (–0.050 $\pm$ 0.051 10 mm^{-1} vs. –0.036 $\pm$ 0.034 10 mm^{-1}, p = 0.03) and TAG-ExC resulted in a slight improvement of the net reclassification index (0.021, p < 0.05).

CONCLUSIONS TAG did not provide incremental diagnostic value over 256-slice coronary CTA alone in assessing the hemodynamic consequences of a coronary stenosis. Correction for temporal nonuniformity of contrast delivery or exclusion of calcified coronary segments slightly enhanced the results. (J Am Coll Cardiol Img 2014;7:374–86) © 2014 by the American College of Cardiology Foundation

Coronary computed tomography angiography (CTA) is increasingly used as a noninvasive diagnostic imaging tool for detection and exclusion of coronary artery disease (CAD) (1–3). A well-recognized limitation of coronary CTA, similar to the anatomical evaluation during invasive coronary angiography (ICA), is its moderate ability to assess the hemodynamic significance of a given coronary stenosis (4–6). Therefore, functional evaluation of coronary lesions deemed significant by coronary CTA is warranted to avoid excess referral for ICA and to guide revascularization therapy in a judicious manner (6,7). Although computed tomography (CT) stress perfusion and coronary CTA-derived estimation of fractional flow reserve (FFR_{CT}) based on computational fluid dynamics have been developed for this purpose, these methods require additional contrast/radiation exposure or extremely complex off-line analysis, respectively, hampering their implementation in routine clinical practice (8–11). Alternatively, linear regression analysis of the attenuation gradient along the course of a coronary artery has been proposed to evaluate the functional relevance of a coronary lesion. The rationale behind the transluminal attenuation gradient (TAG) is that contrast opacification should fall off more rapidly in the presence of a functionally-significant stenosis (12). Preliminary data, obtained using a 320-row CT, have shown incremental value of TAG over coronary CTA assessment alone (13). However, TAG interpretation is complicated by multiple heartbeat acquisitions (64- to 256-slice CT) resulting in a lack of temporal uniformity. In addition, distortions due to highly calcified coronary plaques may influence results. Two correction models have been proposed based on either dephasing of contrast delivery by relating coronary density to corresponding descending aortic opacification (TAG corrected contrast opacification [CCO]) or excluding nonlinear values provoked by coronary calcifications (TAG excluding calcified coronary segments [ExC]) (14,15). Studies that have evaluated these models are scarce, and the results are conflicting (14–17). The current study aims to explore the diagnostic potential of TAG, including its correction models, obtained with a 256-slice CT scanner. Imaging results were prospectively compared with ICA in conjunction with invasive FFR.

METHODS

Patient population. A total of 91 patients with an intermediate probability of CAD, determined according to the criteria of Diamond and Forrester (18), were prospectively enrolled. Exclusion criteria were previous percutaneous coronary intervention, coronary artery bypass graft surgery, a previous myocardial infarction, atrial fibrillation, second- or third-degree atrioventricular block, impaired renal function, symptomatic asthma, or pregnancy. Electrocardiography and echocardiography confirmed normal global left ventricular systolic function and the absence of previous myocardial infarction or regional wall motion abnormalities in all patients. The protocol consisted of cardiac CT with coronary artery calcium (CAC) score and coronary CTA, followed by ICA in conjunction with FFR measurements of all major coronary branches within 5 days. Coronary CTA was not performed in case of persistent elevated heart rate above 65 beats/min despite pretreatment with beta-blocking agents (n = 4). Two patients refused ICA after coronary CTA. The study population, therefore, comprised 85 patients. No cardiac events were documented between coronary CTA and ICA in these patients. The study was approved by the ethics committee, and written informed consent was obtained from all patients.

ABBREVIATIONS AND ACRONYMS

CAC = coronary artery calcium
CAD = coronary artery disease
CCO = corrected contrast opacification
CTA = computed tomography angiography
DS = diameter stenosis
ExC = excluding calcified coronary segments
FFR = fractional flow reserve
HU = Hounsfield units
ICA = invasive coronary angiography
TAG = transluminal attenuation gradient
TIMI = Thrombolysis In Myocardial Infarction

Cardiac CT. Patients underwent CAC scoring and coronary CTA on a 256-slice CT scanner (Philips Brilliance iCT, Philips Healthcare, Best, the Netherlands). A stable low heart rate <65 beats/min was achieved prior to the scanning protocol, either spontaneously or after administration of oral and/or intravenous metoprolol. A standard scanning

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