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Physiological Severity of Coronary Artery Stenosis Depends on the Amount of Myocardial Mass Subtended by the Coronary Artery

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ABSTRACT

OBJECTIVES This study investigated the role of fractional myocardial mass (FMM), a vessel-specific myocardial mass, in the evaluation of physiological severity of stenosis. Using computed tomography angiography, the study investigated fractional myocardial mass, a concept of myocardial mass subtended by specific vessel, which could reduce anatomical-physiological mismatch.

BACKGROUND Discordance between anatomical stenosis and physiological severity is common but remains poorly understood.

METHODS This multicenter study enrolled 463 patients with 724 lesions, who underwent coronary computed tomography angiography (CCTA) and invasive coronary angiography with fractional flow reserve (FFR) measurement. FMM was assessed by allometric scaling analysis of arterial tree length and myocardial mass from CCTA.

RESULTS FFR $<$0.80, a criteria for vessel-specific physiological stenosis, was found in 281 vessels (39%). FMM decreased consistently according to the vessel downstream ($p < 0.001$, all). The frequency of FFR $<$0.80 increased in proportion to FMM and inverse proportion to angiographic minimal luminal diameter (MLD) ($p < 0.001$). In per-vessel analysis, FMM per MLD (FMM/MLD) showed good correlation with FFR ($r = 0.61$) and was superior to diameter stenosis (DS) for FFR $<$0.80 by receiver operating characteristic and reclassification analysis (C-statistics = 0.84 versus 0.74, net reclassification improvement [NRI] = 0.63, integrated discrimination improvement [IDI] = 0.18; $p < 0.001$, all). The optimal cutoff of FMM/MLD was 29 g/mm, with sensitivity = 75%, specificity = 77%, positive predictive value = 68%, negative predictive value = 83%, and accuracy = 77%. Addition of FMM/MLD to DS could further discriminate vessels with FFR $<$0.80 (C-statistic = 0.86 vs. 0.84, NRI = 0.34, IDI = 0.03; $p < 0.005$, all). In per-range classification analysis, agreement between FFR and FMM/MLD maintained $>$80% when the severity of disease was away from cutoff.

CONCLUSIONS FMM/MLD could find physiological severity of coronary artery with higher accuracy than anatomical stenosis. FMM may explain the anatomical-physiological discordance. (J Am Coll Cardiol Intv 2016;9:1548–60)

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Evaluation of myocardial ischemia or physiological severity of coronary artery disease is the most important criterion for predicting prognosis and decision of revascularization. Coronary angiography (CAG) is being used as a standard for decision of treatment strategy or revascularization in daily practice. However anatomical stenosis visualized by CAG is a poor predictor of physiological severity and frequently underestimates or overestimates physiological severity of stenosis. Fractional flow reserve (FFR) <0.80, a widely accepted gold standard of vessel-specific physiologically significant stenosis which may evoke myocardial ischemia, is identified in less than one-half of vessel with significant stenosis defined by diameter stenosis (DS) ≥50%. This discordance between anatomical stenosis and physiological severity is found in as high as 40% of stenotic coronary arteries but is still poorly understood (1). Hence physiology-guided revascularization is considered superior to anatomy-guided revascularization in terms of improved clinical outcome and saving medical cost (2,3), understanding and reducing anatomical-physiological discordance has important implications for performing appropriate revascularization procedure.

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FFR can be described as a pressure gradient across stenotic segment during maximal myocardial blood flow. Anatomical stenosis, myocardial mass, and microvascular resistance are major constituents of FFR value (4). The major unknowns in anatomical measurement are myocardial mass and microvascular resistance. Therefore, we reasoned that the anatomical-physiological discordance can be reduced by addition of downstream myocardial mass to anatomical stenosis of the supplying artery. We developed fractional myocardial mass (FMM), a concept defined by vessel-specific myocardial mass, and investigated its implication in the anatomical-physiological discordance.

METHODS

STUDY DESIGN. This study was a prospective multicenter registry of 5 university teaching hospitals in Korea. From January 2010 to May 2015, the study enrolled 466 patients who underwent clinically indicated coronary computed tomography angiography (CCTA) and followed elective CAG with physiological assessment without intervening coronary events. Patients with ST-segment elevation myocardial infarction (MI), uncompensated heart failure, bypass surgery with patent graft, contraindication to adenosine therapy, complex structural or congenital heart disease, prosthetic valves, or any clinical instability or life-threatening disease were not included. The study protocol was approved by the institutional review board at each institute. All data were anonymized and independently analyzed by core laboratory in Samsung Medical Center.

ABBREVIATIONS AND ACRONYMS

CAG = coronary angiography
CCTA = computed tomography angiography
DS = diameter stenosis
FFR = fractional flow reserve
FMM = fractional myocardial mass
MLD = minimal luminal diameter
QCA = quantitative coronary angiography
RD = reference diameter

FFR AND QCA. CAG and FFR measurements were made according to the standard protocol of each institute as described previously (5). Briefly, a minimum of 2 optimized projections were obtained for each major coronary artery after administration of intracoronary nitroglycerin. FFR was measured using a pressure wire (PressureWire Certus, St. Jude Medical Systems, San Francisco, California; ComboWire, Philips Healthcare, Baltimore, Maryland) under adenosine-induced maximal hyperemia. An FFR value <0.80 was considered physiologically significant stenosis. Quantitative coronary angiography (QCA) was performed by independent experienced technicians who were told of the location of FFR measurement but were blinded to the result of FFR and the other data. A computer-assisted automatic arterial contour detection system (Centricity CA-1000, GE Healthcare, Little Chalfont, United Kingdom) was used. Lesion length, DS, and minimal luminal diameter was measured in the end-diastolic angiographic image with optimal projection showing minimal foreshortening of the lesion. Decision to revascularize was made by agreement of attending physician and interventional cardiologist.

ACQUISITION AND ANALYSIS OF CCTA. CCTA was performed using multivendor CT scanners equipped with 64 or more detectors (Aquilion One or Aquilion 64, Toshiba Medical Systems, Tokyo, Japan; Somatom Definition, Siemens Medical Solution, Austin, Texas; Lightspeed VCT, GE Healthcare). Oral nitroglycerin and metoprolol were administered before subjects were scanned, if required. Prospective or retrospective

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