JACC: CARDIOVASCULAR IMAGING
VOL. 6, NO. 12, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2013.05.018

ORIGINAL RESEARCH

Myocardial CT Perfusion Imaging in a Large Animal Model

Comparison of Dynamic Versus Single-Phase Acquisitions

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OBJECTIVES This study sought to compare dynamic versus single-phase high-pitch computed tomography (CT) acquisitions for the assessment of myocardial perfusion in a porcine model with adjustable degrees of coronary stenosis.

BACKGROUND The incremental value of the 2 different approaches to CT-based myocardial perfusion imaging remains unclear.

METHODS Country pigs received stent implantation in the left anterior descending coronary artery, in which an adjustable narrowing (50% and 75% stenoses) was created using a balloon catheter. All animals underwent CT-based rest and adenosine-stress myocardial perfusion imaging using dynamic and single-phase high-pitch acquisitions at both degrees of stenosis. Fluorescent microspheres served as a reference standard for myocardial blood flow. Segmental CT-based myocardial blood flow (MBF_{CT}) was derived from dynamic acquisitions. Segmental single-phase enhancement (SPE) was recorded from high-pitch, single-phase examinations. MBF_{CT} and SPE were compared between post-stenotic and reference segments, and receiver-operating characteristic curve analysis was performed.

RESULTS Among 6 animals (28 $\pm$ 2 kg), there were significant differences of MBF_{CT} and SPE between post-stenotic and reference segments for all acquisitions at 75% stenosis. By contrast, although for 50% stenosis at rest, MBF_{CT} was lower in post-stenotic than in reference segments (0.65 $\pm$ 0.10 ml/g/min vs. 0.75 $\pm$ 0.16 ml/g/min, $p < 0.05$), there was no difference for SPE (128 $\pm$ 27 Hounsfield units vs. 137 $\pm$ 35 Hounsfield units, $p = 0.17$), which also did not significantly change under adenosine stress. In receiver-operating characteristic curve analyses, segmental MBF_{CT} showed significantly better performance for ischemia prediction at 75% stenosis and stress (area under the curve: 0.99 vs. 0.89, $p < 0.05$) as well as for 50% stenosis, regardless of adenosine administration (area under the curve: 0.74 vs. 0.57 and 0.88 vs. 0.61, respectively, both $p < 0.05$).

CONCLUSIONS At higher degrees of coronary stenosis, both MBF_{CT} and SPE permit an accurate prediction of segmental myocardial hypoperfusion. However, accuracy of MBF_{CT} is higher than that of SPE at 50% stenosis and can be increased by adenosine stress at both degrees of stenosis. (J Am Coll Cardiol Img 2013;6:1229–38) © 2013 by the American College of Cardiology Foundation

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JACC: CARDIOVASCULAR IMAGING, VOL. 6, NO. 12, 2013
DECEMBER 2013:1229–38

The increase in detector width and temporal and spatial resolution over the last decade has contributed enormously to the establishment of coronary computed tomography angiography (CTA) as the noninvasive modality of choice for morphological imaging of the coronary artery system. When compared with invasive coronary angiography, coronary CTA has shown high diagnostic accuracy, particularly for patients with low-to-intermediate pre-test probability for coronary artery disease (1).

In parallel, clinical evidence favoring the hemodynamic relevance of a coronary lesion over the degree of stenosis as the most important parameter for prognosis and clinical decision making has accumulated over the last few years (2). However, there is a large body of evidence indicating that the hemodynamic relevance cannot be estimated by the degree of stenosis as measured by invasive coronary angiography or coronary CTA (3). Thus, comprehensive assessment of the hemodynamic significance remains beyond the capabilities of routine coronary CTA.

Several studies have shown that the detection of myocardial perfusion defects at rest and pharmacological stress is feasible using state-of-the-art computed tomography (CT) technology employing 2 different approaches: "single-phase CT acquisitions" at rest or adenosine-induced stress rely on a single CT acquisition after injection of an iodinated contrast agent and are characterized by relatively low radiation exposure (4). However, assessment of myocardial perfusion is limited to a qualitative or semiquantitative evaluation on the basis of mere comparisons of enhancement between apparently post-stenotic versus normal myocardial segments (single-phase enhancement [SPE]). Sequential CT acquisitions, on the other hand, enable dynamic imaging of contrast agent kinetics and permit a truly quantitative evaluation of myocardial blood flow (CT-derived MBF [MBF_{CT}]) and other parameters at stress and at rest (5). The latter approach, however, typically is associated with higher radiation exposure. Although both approaches have been evaluated separately, a direct comparison including the evaluation of potential intrinsic limitations in an experimental setting is lacking.

The aim of this in vivo animal study was to compare dynamic with single-phase CT acquisition techniques for myocardial perfusion imaging in a large animal model with different degrees of coronary artery stenosis.

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

CT = computed tomography

CTA = computed tomography angiography

FM = fluorescent microsphere(s)

HU = Hounsfield units

MBF_{CT} = computed tomography–derived myocardial blood flow

MBF_{MIC} = microsphere-derived myocardial blood flow

ROC = receiver-operating characteristic

ROI = region of interest

SPE = single-phase enhancement

METHODS

The study was approved by the governmental animal protection committee and the institutional review board for the care of animal subjects. All animal studies were performed in accordance with the "Position of the American Heart Association on Research Animal Use."

Animal experiments. All experiments were performed at the Walter-Brendel-Centre of Experimental Medicine, Ludwig-Maximilians-University (Munich, Germany).

Experiments included 6 young country pigs of either sex weighing between 25 and 30 kg; all animals were fed 75 mg of clopidogrel (Ratiopharm, Ulm, Germany) daily for 2 days before the experiment. General anesthesia was induced by intramuscular administration of acepromazine (Vetranquil, Biokema, Crissier, Switzerland), atropine (B. Braun, Melsungen, Germany), and ketamine (B. Braun), followed by a bolus of intravenous midazolam (0.1 mg/kg) (Dormicum, Roche Pharma, Basel, Switzerland). After endotracheal intubation, anesthesia was maintained by continuous intravenous administration of fentanyl (6 μg/kg/h) (B. Braun) and propofol (2%, 10 to 15 ml/h) (MCT, Fresenius, Bad Homburg, Germany) using perfusion pumps connected to an intravenous drip of normal saline and hydroxyethyl starch plasma expander (50%/50%). Automatic mechanical ventilation was performed with a tidal volume of 150 ml and a breathing frequency of 40 breaths/min. To ensure adequate oxygenation, a pulse oximeter was attached to the tail tip. A 4-lead electrocardiogram was recorded continuously throughout the experiment and synchronized with the CT scanner. After intravenous administration of 500 mg of aspirin (Aspirin i.v., Bayer Healthcare, Berlin, Germany) and 1,000 IE of heparin (Heparin-Calcium, Ratiopharm), 2 catheters (8-F sheath) were introduced through the carotid

Drs. Wintersperger and Nikolaou are on the Speakers' Bureau for Bayer Healthcare and Siemens Healthcare. Dr. Bamberg is on the Speakers' Bureau for Siemens Healthcare and Bayer Healthcare; and has received an unrestricted research grant from Bayer Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received February 18, 2013; revised manuscript received May 2, 2013, accepted May 23, 2013.