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Original article

Peak enhancement ratio of myocardium to aorta for identification of myocardial ischemia using dynamic myocardial computed tomography perfusion imaging

Yuki Tanabe (MD)[a,*], Teruhito Kido (MD, PhD)[a], Akira Kurata (MD, PhD)[a], Takahiro Yokoi (MD)[a], Naoki Fukuyama (MD)[a], Teruyoshi Uetani (MD, PhD)[b], Hikaru Nishiyama (MS)[a], Naoto Kawaguchi (MD, PhD)[a], Enver Tahir (MD)[c], Masao Miyagawa (MD, PhD)[a], Teruhito Mochizuki (MD, PhD)[a]

[a] Department of Radiology, Ehime University Graduate School of Medicine, Shitsukawa, Toon City, Ehime, Japan
[b] Department of Cardiovascular Internal Medicine, Ehime University Graduate School of Medicine, Shitsukawa, Toon City, Ehime, Japan
[c] Department of Diagnostic and Interventional Radiology and Nuclear Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

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ABSTRACT

Background: This study aimed to evaluate the feasibility of peak enhancement (PE) ratio of myocardium to aorta (PER) derived from stress dynamic computed tomography myocardial perfusion imaging (CTP) for the detection of myocardial ischemia assessed by magnetic resonance (MR) imaging.
Methods: Forty-four patients who underwent stress dynamic CTP and MR imaging were retrospectively evaluated. From the time-attenuation curve, myocardial PE, PER, and myocardial blood flow (MBF) were calculated on a segment-based analysis. The correlation between myocardial and aortic PE was assessed by Spearman's correlation, and the differences in myocardial PE and PER between normal and ischemic myocardium were assessed by the Mann–Whitney *U*-test. The diagnostic accuracies of myocardial PE, PER, and MBF for detecting myocardial ischemia were compared by receiver operating characteristic analysis.
Results: Of 704 segments, 258 segments (37%) were diagnosed as myocardial ischemia with MR imaging. Myocardial and aortic PE were significantly correlated in both normal and ischemic segments ($r = 0.76$ and 0.58; $p < 0.05$, in each). The myocardial PE and PER of ischemic segments were significantly lower than those of normal segments ($p < 0.05$, in each). Sensitivity and specificity were 61% [95% confidence interval (CI), 55–70%] and 83% (95% CI, 73–87%) for myocardial PE, 78% (67–88%) and 82% (95% CI, 70–91%) for PER, and 81% (95% CI, 73–87%) and 85% (95% CI, 79–92%) for MBF. There was a significantly larger area under the curve for PER (0.87; 95% CI, 0.84–0.90) and MBF (0.88; 95%CI, 0.85–0.91), compared to myocardial PE (0.75; 95% CI, 0.70–0.79) ($p < 0.05$, in each). There was no significant difference in area under the curve between PER and MBF.
Conclusions: The semi-quantitative parameter of PER showed a high diagnostic accuracy for the detection of myocardial ischemia, comparable to that of MBF.

Introduction

Physiological assessment of myocardial perfusion is important for the therapeutic strategy and long-term prognosis in patients with coronary artery disease (CAD) [1,2]. In current practice, myocardial perfusion imaging (MPI) by single-photon emission computed tomography (SPECT), magnetic resonance (MR) imaging, or positron emission tomography (PET) is widely used for the assessment of myocardial ischemia.

Recently, myocardial computed tomography perfusion imaging (CTP) has emerged as a useful method for the detection of myocardial ischemia [3–5]. CTP has higher spatial resolution than SPECT, and this is preferable for detecting myocardial ischemia as well as cardiac MR [6–9]. Moreover, dynamic CTP allows for quantifying myocardial perfusion parameters [e.g. myocardial blood flow (MBF), upslope, time to peak] [10–15]. In these quantitative parameters, myocardial peak enhancement (PE) was

* Corresponding author at: Department of Radiology, Ehime University Graduate School of Medicine, Shitsukawa, Toon City 791-0295, Japan. Fax: +81 89 960 5375.
E-mail address: yuki.tanabe.0225@gmail.com (Y. Tanabe).

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an easily assessable semi-quantitative parameter for detecting myocardial ischemia with diagnostic accuracy comparable to full-quantitative parameter of MBF [14]. However, the myocardial PE substantially varies according to the physical status, cardiac function, and scanning parameters [16,17]. Therefore, we hypothesized that the PE ratio of myocardium to aorta (PER) was more relevant than myocardial PE for the detection of myocardial ischemia. This study aimed to evaluate the feasibility of PER for the detection of myocardial ischemia using stress dynamic CTP.

Materials and methods

Study population

This retrospective study was approved by the institutional review board and registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN000019509). We enrolled 44 patients who underwent stress dynamic CTP and cardiac MR imaging within 2 months of each other between January 2013 and August 2016. Patients were screened for CAD because of effort or resting angina diagnosed by electrocardiogram (ECG) change or relief of symptoms upon administration of nitroglycerin, or multiple coronary risk factors. Indications for cardiac CT and MR imaging were determined at the discretion of the attending physician. The exclusion criteria were as follows: history of acute/old myocardial infarction; cardiomyopathy; left ventricular (LV) ejection fraction <20%; atrial fibrillation; atrioventricular block greater than first degree; left complete bundle branch block; valvular heart disease; and history of percutaneous coronary intervention or coronary artery bypass graft. The radiation dose was calculated from the dose-length product mentioned in dose reports (conversion factor, 0.014) [18].

CT scan protocol

This study employed an established comprehensive cardiac CT protocol [15]. A 256-slice multi-detector CT unit (Brilliance iCT, Philips Healthcare, Cleveland, OH, USA) and an automatic dual injector (Stellant DualFlow, Nihon Medrad KK, Osaka, Japan) were used. A timing bolus scan was performed with a 20%-diluted contrast medium (370 mg iodine/mL; Iopamidol, Bayer Yakuhin, Ltd., Osaka, Japan; 5 mL/s for 10 s), followed by saline chaser (5 mL/s for 4 s). The time delay for the start of dynamic CTP was set as 6 s before the arrival of contrast medium at the proximal ascending aorta. Three minutes after adenosine triphosphate loading (Adetphos-L KOWA injection 20 mg; Kowa Company Ltd., Tokyo, Japan; 0.16 mg/kg/min, for 5 min), dynamic CTP was performed for 30 consecutive heartbeats, with the prospective ECG-gated dynamic mode targeting a phase of 40% RR interval (systolic phase) under a single breath-hold in the expiration position to shorten the cranio-caudal length of the heart, by using contrast medium (5.0 mL/s for 10 s) followed by a saline chaser (5.0 mL/s for 4 s). Coronary CT angiography was then performed using the optimized contrast medium dilution individually, based on the contrast enhancement of the test bolus scan, as previously described [16]. Data acquisition was performed in the prospective or retrospective ECG-gated mode with dose modulation, targeting a 75% RR interval (mid-diastolic phase), at scan heart rates of <65 or ≥65 beats/min, respectively. The scan parameters for dynamic CTP were as follows: detector collimation, 64 mm × 1.25 mm; tube voltage, 100 kV; and tube current-time product, 80 mAs.

Cardiac CT post processing and image analysis

A series of dynamic CTP axial images of 1.25-mm thickness were reconstructed using a 360° reconstruction algorithm (temporal resolution, 270 ms) on a dedicated workstation (IntelliSpace Portal, Philips Healthcare), using elastic registration for motion compensation and a spatio-diffusion filter for reduction of noise spikes over time. Contiguous 8-mm-thick short-axial sections were generated from the apex to the base of the LV without spatial and temporal gaps. All CTP images were quantitatively analyzed on another dedicated workstation (Synapse Vincent, Fuji Medical Systems, Tokyo, Japan).

Three representative short-axial CTP images (basal, mid, and apical) corresponding to the subsequent MR-MPI were selected per patient by a cardiologist with 13 years of experience in cardiac CT and MR imaging. Quantitative analysis was blindly performed by two radiologists with 6 and 15 years of experience in cardiac CT. Based on the 16-segment model excluding the apex [19], regions of interest were set in the ascending aorta (size, 100–150 mm^2) and myocardial segment (size, 30–50 mm^2), and the PE, PER, and MBF were analyzed with the time attenuation curve as follows: PE (Hounsfield units: HU) was defined as the difference between baseline and peak CT attenuation; PER (%) was calculated as the ratio of myocardial to aortic PE (Fig. 1); MBF (mL/g/min) was calculated by model-independent deconvolution analysis [15]. Myocardial segments were diagnosed as myocardial ischemia when each parameter was lower than the cut-off value obtained by receiver operating characteristic (ROC) analysis.

Coronary CT angiography was assessed by vessel-based analysis in accordance with the CAD-RADS guidelines [20]. Coronary lesion with more than moderate stenosis was defined as significant stenotic vessel. When the vessel was not evaluated due to any reasons such as calcification, motion artifact, and so on, the vessel was assumed as significant stenotic vessel.

Cardiac MR protocol and image analysis

Cardiac MR was performed according to a comprehensive protocol with a 3 T MR system (Achieva 3.0 T Quasar Dual; Philips Healthcare, Best, Netherlands), as previously described [21]. Stress and rest dynamic MR-MPI were performed for 35 s, with every heartbeat data acquisition during the first pass of a gadolinium-based contrast medium (0.1 mmol/kg gadopentetate dimeglumine; Magnevist, Bayer HealthCare Pharmaceuticals Inc., Leverkusen, Germany) with and without the ATP infusion (0.16 mg/min/kg for 5 min). Image data were retrieved from three cardiac cross sections (basal, mid, and apical), as well as stress dynamic CTP. Late gadolinium enhancement (LGE) images were acquired using an

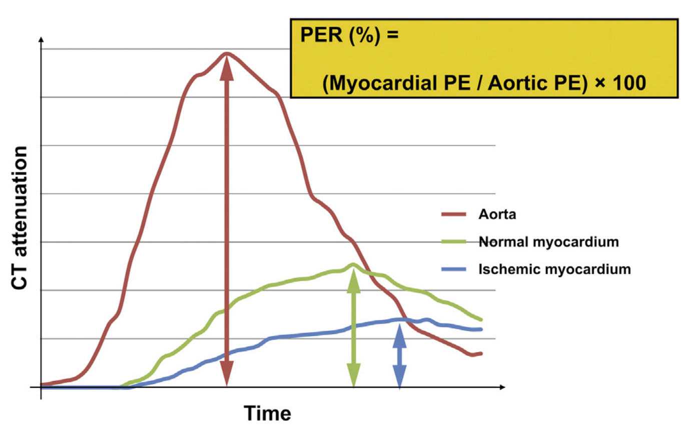

Fig. 1. Analysis of PER derived from dynamic myocardial CT perfusion imaging. PE was defined as the difference between baseline and peak CT attenuation of the aorta and myocardium. PER (%) was calculated as the following: PER = (myocardial PE/aortic PE) × 100. CT, computed tomography; PE, peak enhancement; PER, peak enhancement ratio.

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