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Three-dimensional quantification of myocardial perfusion during regadenoson stress computed tomography

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ABSTRACT

Background: There is no accepted methodology for CT-based vasodilator stress myocardial perfusion imaging and analysis. We developed a technique for quantitative 3D analysis of CT images, which provides several indices of myocardial perfusion. We sought to determine the ability of these indices during vasodilator stress to identify segments supplied by coronary arteries with obstructive disease and to test the accuracy of the detection of perfusion abnormalities against SPECT.
Methods: We studied 93 patients referred for CT coronary angiography (CTCA) who underwent regadenoson stress. 3D analysis of stress CT images yielded segmental perfusion indices: mean X-ray attenuation, severity of defect and relative defect volume. Each index was averaged for myocardial segments, grouped by severity of stenosis: 0%, <50%, 50–70%, and >70%. Objective detection of perfusion abnormalities was optimized in 47 patients and then independently tested in the remaining 46 patients.
Results: CTCA depicted normal coronary arteries or non-obstructive disease in 62 patients and stenosis of >50% in 31. With increasing stenosis, segmental attenuation showed a 7% decrease, defect severity increased 11%, but relative defect volume was 7-fold higher in segments with obstructive disease ($p < 0.001$). In the test group, detection of perfusion abnormalities associated with stenosis >50% showed sensitivity 0.78, specificity 0.54, accuracy 0.59. When compared to SPECT in a subset of 21 patients (14 with abnormal SPECT), stress CT perfusion analysis showed sensitivity 0.79, specificity 0.71, accuracy 0.76.
Conclusions: 3D analysis of vasodilator stress CT images provides quantitative indices of myocardial perfusion, of which relative defect volume was most robust in identifying segments supplied by arteries with obstructive disease. This study may have implications on how CT stress perfusion imaging is performed and analyzed.

1. Introduction

Abnormal or equivocal computed tomography coronary angiography (CTCA) tests in patients with acute chest pain frequently trigger downstream testing [1–4]. In an effort to improve efficiency and reduce costs, a growing number of studies have been focusing on the potential of multidetector computed tomography (MDCT) for simultaneous evaluation of coronary anatomy and the hemodynamic significance of stenosis in a single test, by adding the assessment of myocardial perfusion during vasodilator stress. Several studies have tested the feasibility of detecting perfusion abnormalities induced by adenosine stress by visual identification of areas of reduced X-ray attenuation during peak stress [5–11]. However, visual interpretation is challenging due to the need for manual optimization of contrast windows, in order to minimize the risk of missing small or less pronounced perfusion defects. Also, current methodology fails to capitalize on the three-dimensional (3D) nature of the MDCT datasets and is limited to visual assess-

Abbreviations: 3D, three-dimensional; CTCA, computed tomography coronary angiography; LV, left ventricular; MDCT, multidetector computed tomography; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic; SPECT, single photon emission computed tomography.

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ment of multiple planes. Accordingly, improved image analysis tools and quantitative indices of myocardial perfusion are needed.

In the current study, we used recently developed software for quantitative 3D analysis of myocardial perfusion from MDCT images, designed to take into account the entire myocardium, rather than individual slices, and to avoid the need for manual optimization of contrast windows [12]. This approach is based on 3D analysis of spatial distribution of myocardial X-ray attenuation and provides several indices of myocardial perfusion in addition to mean segmental X-ray attenuation, including severity of defect, relative defect volume, and a combined index of severity and extent of perfusion abnormality. We previously investigated the utility of the latter index and found that this approach not only compared well against SPECT under resting conditions [13], but also showed good accuracy for the detection of significant coronary artery stenosis in a group of patients undergoing vasodilator stress [12]. However, its diagnostic performance was not confirmed in an independent group of patients, validated against other myocardial perfusion imaging tests under vasodilator stress, or compared with that of other possible indices of myocardial perfusion. Furthermore, the relationship between the degree of coronary stenosis and the severity and extent of perfusion abnormalities detected by 3D analysis of CT images remains to be determined.

Accordingly, the present study was designed to further test the clinical usefulness of our quantitative 3D perfusion analysis of MDCT images during regadenoson stress. Our specific goals were: (1) to study the relationship between the individual component indices of myocardial perfusion, namely defect size and severity, and the degree of coronary stenosis; (2) to test the accuracy of our technique for objective detection of perfusion abnormalities in an independent group of patients; and (3) to test the accuracy of this analysis against SPECT in a subset of patients.

2. Methods

2.1. Population

The study was approved by the Institutional Review Board, and each patient signed an informed consent prior to participation. We prospectively studied a cohort of 103 patients undergoing clinically indicated CTCA, who agreed to have an additional MDCT scan during vasodilator stress. Patients with relative contraindications to CTCA, including known allergies to iodine, renal dysfunction (creatinine >1.6 mg/dl), inability to perform a 10 sec breath-hold, and contraindications to beta-blockers or vasodilators, such as chronic obstructive pulmonary disease, advanced heart block or systolic blood pressure <90 mmHg, were excluded. In addition, patients who had history of cardiothoracic surgery or pacemaker implantation were excluded. Although previous myocardial infarction was not among exclusion criteria, patients with a history of infarction are usually not referred for CTCA in our institution, and accordingly we did not have such patients in this study. Patients were instructed to abstain from caffeine consumption over 12 h leading to the test.

2.2. Imaging protocol

Patients received the beta-blocker metoprolol orally (50–100 mg, 1 h prior to imaging) and/or intravenously (5–15 mg immediately prior to imaging), as necessary to achieve a target heart rate of <70 bpm. Sublingual nitroglycerin (0.4–0.8 mg) was also administered, provided that systolic blood pressure was >100 mmHg. Images were acquired during suspended respiration using an MDCT system: 103 patients using a 256-channel Philips iCT scanner. After resting imaging was performed according to a standard clinical CTCA protocol, regadenoson (Astellas), a specific A_{2A} receptor agonist with an improved side-effect profile, was administered (0.4 mg, i.v.) at least 15 min later to ensure contrast clearance. An additional set of images was acquired 1 min after the administration of regadenoson to ensure imaging during peak effect.

Imaging was performed using tube voltage of 100–120 kV, using prospective gating without phase tolerance, when possible, to minimize radiation exposure [14]. Imaging parameters included: gantry rotation time: 270 ms, slice thickness 0.625 mm, and tube currents 600–1000 mA (depending on body weight). Patients received 55–90 ml of nonionic iodinated contrast agent (Omnipaque-350, Amersham, Milwaukee WI; 4–6 ml/sec depending on scan duration), which was injected into the right antecubital vein and followed by a 20 ml chaser bolus (70% saline, 30% contrast). Image acquisition was triggered by the appearance of contrast in the descending thoracic aorta, 5 sec after attenuation increased >50 Hounsfeld units (HU).

2.3. CTCA reference for significant coronary artery disease

CTCA interpretation of coronary anatomy, performed on the resting images by an experienced reader (10 years of CTCA experience), included the determination of presence, location and extent of stenosis in percent of luminal narrowing. To allow comparisons of regional myocardial MDCT perfusion indices against coronary stenosis, coronary anatomy depicted on each patient's MDCT volume rendering was used to determine the perfusion territory of each artery and its major branches. This approach was chosen, rather than using standardized perfusion maps, to avoid assigning myocardial segments to incorrect vascular territories. The specific location of stenosis, when detected on CTCA, was used to determine which myocardial segments would be affected. Myocardial segments were then divided into four categories, according to CTCA findings: (0) segments supplied by arteries without detectable stenosis or with stenosis located distally to the segment, and segments supplied by coronary arteries with stenosis located proximally to the specific segment and causing: (1) <50% luminal narrowing on CTCA, (2) 50–70% luminal narrowing, and (3) >70% luminal narrowing.

2.4. Stress MDCT image analysis

MDCT images obtained during vasodilator stress were analyzed using custom software for volumetric analysis and visual display of myocardial perfusion, as previously described in detail [12–14]. Briefly, following manual initialization of endo- and epicardial boundaries in 4–5 slices, the endo- and epicardial 3D surfaces were automatically estimated using the level-set technique [15], and displayed using 3D rendering. The 3D region of interest confined between the endocardial and epicardial surfaces was identified as left ventricular (LV) myocardium and divided into 17 wedge-shaped 3D myocardial segments, according to standard AHA segmentation: 6 basal, 6 mid-ventricular, 4 apical and an apical cap (AHA segment 17, which was excluded from analysis). Coronary arteries and contrast-filled inter-trabecular spaces were excluded from the myocardial segments and papillary muscles and trabeculae were excluded from the LV cavity by setting thresholds on the histograms of X-ray attenuation to discard voxels represented by a separate peak/tail outside normal distribution of the myocardium and the blood pool, respectively [12–14].

The visualization component of the software uses a color-coded display of subendocardial attenuation normalized by mean LV cavity attenuation, calculated across the inner 50% of the myocardial thickness to optimize the visualization of stress-induced subendocardial perfusion defects. To further facilitate visual interpretation of the perfusion information in relationship to the individual coro-