Does Reduced Radiation Dose Adversely Affect the Ability to Detect Abnormal Myocardial Perfusion on Computed Tomography during Vasodilator Stress?

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Abstract

The ability of multidetector computed tomography (MDCT) to detect stress-induced myocardial perfusion abnormalities is of great clinical interest as a potential tool for the combined evaluation of coronary stenosis and its significance. However, stress testing requires repeated scanning, which is associated with additional radiation exposure and iodine contrast. Our goal was to determine the effects of reduced tube voltage and contrast dose on the ability to detect perfusion abnormalities. We studied 40 patients referred for CT coronary angiography (CTCA). Images were acquired at rest and during regadenoson stress (256-channel scanner, Philips) using 120kV tube voltage with 80-90 ml contrast in 20 patients and 100kV with 55-70 ml contrast in the remaining 20 patients. Custom software was used to define 3D myocardial segments and measure segmental x-ray attenuation. In each group of patients, myocardial attenuation was averaged for segments supplied by arteries with stenosis causing >50% narrowing on CTCA, and separately for segments supplied by arteries without significant stenosis. In both groups, myocardial attenuation was equally reduced in segments supplied by diseased arteries, despite the 74% reduction in radiation and the 28% reduction in contrast. Regadenoson stress MDCT imaging can detect hypoperfused myocardium even when imaging settings are optimized to provide a significant reduction in radiation and contrast doses.

1. Introduction

It is well established that multidetector computed tomography (MDCT) is a powerful tool to rule out the presence of significant coronary artery stenosis due to its high negative predictive value (reported to be 90% to 100%) [1]. However, several investigators have demonstrated that MDCT has a limited specificity and positive predictive value for detecting significant stenosis. An increasing number of studies have been focusing on the potential of MDCT to assess myocardial perfusion in the same test, which could be useful for both the diagnosis of coronary artery disease (CAD) and evaluation of its functional significance. Many initial studies reported dark areas corresponding to myocardial scar visualized on MDCT images in patients with prior myocardial infarction (MI) and in animal models of acute ischemia [2]. More recently, several studies have tested the feasibility of detecting perfusion abnormalities induced by vasodilator stress [3-6].

While the body of evidence for MDCT perfusion imaging is steadily growing, concerns about additional radiation exposure and iodine contrast associated with stress testing remain to be addressed. Our hypothesis was that both radiation and contrast doses, delivered to a patient to allow stress imaging, could be reduced without significantly compromising the ability to detect stress-induced myocardial ischemia. We studied two groups of patients undergoing regadenoson stress MDCT with two different levels of contrast dose and radiation dose achieved by reducing tube voltage and by minimizing coverage. In these two groups, we studied x-ray attenuation, as well as a 3D quantitative index of severity and extent of perfusion abnormality, calculated in myocardial segments supplied by coronary arteries with stenosis causing >50% luminal narrowing on CTCA, as compared with segments supplied by arteries without significant stenosis.

2. Methods

2.1. Population and protocol

We prospectively studied 40 patients (age: 54±11, 29 males, body mass index: 29.3±5.1 kg/m²) who underwent clinically indicated CT coronary angiography (CTCA) for the evaluation of CAD and agreed to undergo an additional scan during vasodilator stress. Patients with contraindications to CTCA, including allergies to iodine, renal dysfunction (creatinine >1.6 mg/dL), inability to perform a 10 sec breath-hold, and contraindications to

beta-blockers, were excluded from the study. In addition, patients who had prior cardiothoracic surgery were excluded. Each patient received the beta-blocker metoprolol to achieve a target heart rate of <70 bpm. After resting imaging was performed, A_{2A}-agonist, regadenoson (Astellas) was administered (0.4mg, i.v.) at least 15 minutes later to ensure contrast clearance, and an additional set of images was acquired 1 minute after administration of regadenoson to ensure its peak effect.

2.2. MDCT imaging

Images were acquired during suspended respiration using an MDCT system (256-channel iCT scanner, Philips). Iodinated contrast agent was injected into a right antecubital vein and followed by a 20 ml chaser bolus (70% saline, 30% contrast, at 4-6 ml/sec).

Resting images were acquired according to a standard clinical CTCA protocol using prospective gating at a 75% phase of the cardiac cycle, with phase tolerance to allow reconstruction of additional phases in diastole. Contrast dose varied between 65 and 90 ml and was infused at a rate of 5-6 ml/sec with tube voltages set between 100 and 140 kV, depending on multiple patient's characteristics, according to standard clinical criteria. Resultant radiation dose was 8.0±3.7 mSv.

Stress images were acquired using prospective gating without phase tolerance, in order to minimize radiation exposure. Patients were randomized into two groups: Group 1 (N=20) was imaged during regadenoson stress using tube voltage of 120 kV and received 80-90 ml of iodinated contrast agent at a rate of 5-6 ml/sec, and Group 2 (N=20) using 100 kV with 55-70 ml of contrast at 4-5 ml/sec. While in Group 1 stress images were acquired at a 75% phase of the cardiac cycle, in Group 2 acquisition was performed at 40% cardiac cycle, i.e. approximately during end of systole, when the long-axis dimension of the ventricle reaches its minimum. As a result, while three slabs were usually needed in Group 1, two slabs were usually sufficient to cover the left ventricle in Group 2, resulting in further radiation dose reduction.

2.3. MDCT image analysis

Clinical CTCA interpretation was performed on the resting images by an experienced reader, whose interpretation included determination of presence, location and extent of stenosis. For the purposes of this study, luminal narrowing >50% was considered as significant stenosis.

Myocardial perfusion was analyzed both at rest and during vasodilator stress. Images were reformatted to generate a 3D dataset of 1 mm thick short-axis slices of the left ventricle from just above the mitral annulus to just below the apex. These 3D datasets were analyzed using custom software for volumetric analysis as described previously [7]. Briefly, following manual initialization of endo- and epicardial boundaries in a small number of slices, the endo- and epicardial 3D surfaces were automatically estimated using the level-set technique [8], and displayed using 3D rendering. The 3D region of interest confined between the endocardial and epicardial surfaces was identified as LV myocardium and divided into seventeen 3D wedge-shaped myocardial segments of equal height, 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 the normal distribution of the myocardium and the blood pool, respectively [7].

For each myocardial segment, mean x-ray attenuation value was measured in Hounsfeld units (HU). In addition, for each myocardial segment, a quantitative index of extent and severity of perfusion abnormality, Q_h, was calculated as a mathematical product of the number of voxels with low attenuation in % of the total volume of the segment (reflecting the extent of the defect) and the difference between the attenuation in these voxels and the previously determined normal attenuation in the same anatomic location (reflecting the severity of the defect) [7].

2.4. Inter-group comparisons

In each group of patients, myocardial x-ray attenuation was averaged for segments supplied by coronary arteries with stenosis located proximally to the specific segment and causing >50% luminal narrowing on CTCA, and separately for segments supplied by arteries without significant stenosis or with stenosis located distally to the segment. Similarly, segmental values of index Qh were averaged separately for the normally perfused and for the hypoperfused segments. Student's t-tests were used to test the significance of the differences between normal and hypoperfused myocardial segments in these two indices.

3. Results

CTCA detected stenosis >50% in 23/120 coronary arteries in 16/40 patients. Figure 1 shows examples of MDCT images obtained during regadenoson stress in two patients one from each group, both with normal coronary arteries and no visible perfusion defects (top panels), and with perfusion defects caused by significant coronary stenosis (bottom panels).

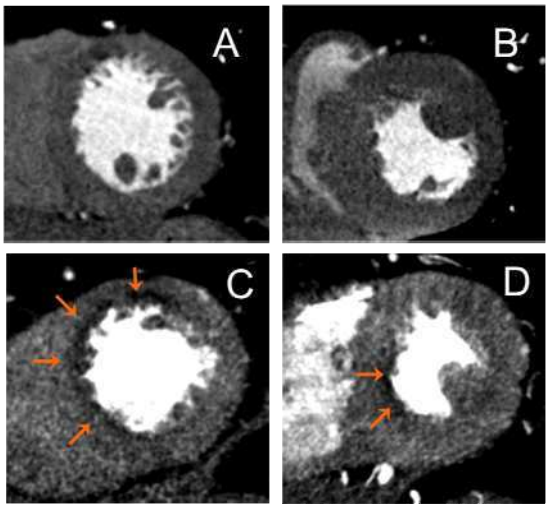

Figure 1. Example of MDCT images obtained during regadenoson stress in four patients: two with normal coronary arteries and no visible perfusion defects (A and B) and the other two with perfusion defects (arrows) caused by significant coronary stenosis (C and D). Of note these images were obtained using 120 kV tube voltage with 80 ml iodine contrast at end-diastole (A and C), and 100 kV tube voltage with 60 ml contrast at end-systole (B and D).

In all patients combined, mean myocardial attenuation increased from 86±9 HU at rest to 110±17 HU with stress, reflecting an increase in tissue blood flow. This is despite the decrease in left ventricular cavity attenuation (347±72 to 281±55 HU), reflecting the decrease in contrast concentration as a result of the increase in cardiac output and the decrease in infusion rate.

Table 1 presents the summary of radiation doses and contrast doses delivered to patients in the two groups during the stress scan, as well as myocardial attenuation in segments supplied by normal coronary arteries and separately in segments supplied by arteries with stenosis >50%. Mean radiation dose was reduced by 74% and mean contrast dose by 28% in group 2 compared to group 1 ($p<0.05$).

Importantly, in both groups, myocardial attenuation was reduced in segments supplied by diseased arteries, compared to normally perfused segments ($p<0.001$) (Table 1), despite the above reduction in radiation and in contrast dose. Although these differences were relatively small (7 and 10% in groups 1 and 2, respectively), they were highly statistically significant ($p<0.001$).

Figure 2 shows the differences between normally perfused and hypoperfused myocardial segments for both x-ray attenuation (reported in Table 1) side-by-side with the index of severity and extent of perfusion abnormality, Qh. Of note, Qh was considerably elevated in abnormally perfused segments, as reflected by an increase of two- to three-fold from the value of this index in the normal segments. Importantly, similar to the raw x-ray attenuation, these differences were seen in both groups of patients, irrespective of tube voltage and contrast dose.

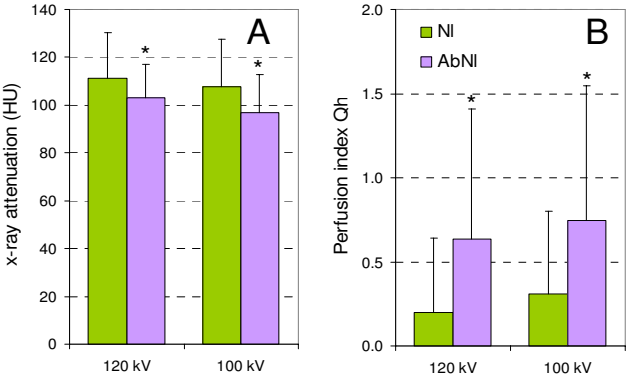

Figure 2. X-ray attenuation (A) and the quantitative index of severity and extent of perfusion abnormality, Qh (B), both averaged separately for normally perfused and hypoperfused segments during regadenoson stress (*$p<0.0003$). Data are shown side-by-side for two groups of patients, who were imaged using higher tube voltage (120 kV) and lower voltage (100 kV).

4. Discussion and conclusions

Several recent MDCT studies have tested the feasibility of detection of myocardial ischemia induced by vasodilator stress [3-6]. While the results of these studies are very promising, they were limited by the two-dimensional nature of image analysis methodology they used, which relies on subjective selection of a small number of slices and manual manipulation of contrast

	Stress scan radiation dose (mSv)	Contrast dose (ml)	Attenuation in normal segments (HU)	Attenuation in abnormal segments (HU)	Percent difference in attenuation (%)
Group 1	7.43±2.82	84±7	119±19	103±14 *	7
Group 2	1.90±0.45 ^	60±7 ^	108±20	97±16 *	10

^ $p<0.05$ vs. Group 1 * $p<0.001$ vs. normal segments

Table 1. Summary of radiation doses and contrast doses delivered to patients in the two groups during the stress scan, as well as myocardial attenuation in segments supplied by normal coronary arteries and separately in hypoperfused segments.

windows necessary to visualize perfusion abnormalities.

To circumvent these limitations, we developed a technique for 3D analysis that takes into account x-ray attenuation in the entire myocardial volume to quantitatively assess myocardial perfusion, without relying on subjective choice of slices and contrast windows. This approach was shown to accurately determine the presence, location, extent and severity of fixed perfusion abnormalities in agreement with nuclear myocardial perfusion imaging [7].

Importantly, irrespective of analysis technique used, concerns about additional radiation exposure and iodine contrast associated with MDCT stress testing remain to be addressed. These concerns led us to design this study, which was aimed at determining to what extent reduced tube voltage and reduced contrast dose would affect the ability of 3D analysis of myocardial x-ray attenuation to detect stress-induced myocardial ischemia. An underlying assumption for our study design was that perfusion imaging does not necessarily require optimal image quality such as needed for CTCA, which is usually performed on resting images, and that segmental x-ray attenuation can be reliably measured on images of potentially even slightly inferior quality. In addition to the raw attenuation values, we studied a quantitative 3D index of severity and extent of perfusion abnormality. This was done in order to take into account the fact that stress-induced perfusion defects are subendocardial rather than transmural, resulting in only modest decrease in overall segmental attenuation in ischemic segments. Unlike the raw attenuation values, perfusion index Q_h directly reflects the relative size and severity of the perfusion defect, and is thus expected not to be as affected by the presence of the non-ischemic tissue within the same segment.

Our results showed that reducing tube voltage by as little as 20 kV (from 120 to 100kV) combined with reduced coverage resulted in savings of almost ¾ of the radiation dose. Importantly, irrespective of tube voltage and contrast dose, myocardial attenuation was significantly reduced in segments expected to be hypoperfused based on CTCA findings of significant stenosis in the relevant coronary artery. As anticipated, perfusion index Q_h showed even larger differences between normal and ischemic segments than the averaged attenuation values. Importantly, the differences in Q_h between normal and ischemic segments were equally prominent irrespective of radiation and contrast doses, confirming the hypothesis that this study was designed to test. These findings confirmed that the strategy used in this study to reduce radiation and contrast doses is indeed effective and images obtained under conditions used in group 2 are suitable for quantitative 3D analysis of myocardial perfusion.

One might view the lack of direct perfusion assessment by an independent technique such as SPECT as a limitation of our study. While we agree that the study could be strengthened by SPECT data, such data is not available in the majority of patients referred for CTCA in our institution.

In conclusion, volumetric analysis of x-ray attenuation on MDCT images obtained during regadenoson stress can detect hypoperfused myocardium, even when imaging settings are optimized to provide a significant reduction in radiation and contrast doses. These findings may have implication on future MDCT stress perfusion protocols.

References

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