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Utility of 64-MSCT in assessing acute non-reperfused myocardial infarct size

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Abstract

Objective To evaluate the utility of multi-slice computed tomography (MSCT) in assessing acute non-reperfused myocardial infarct size. **Methods** Seven domestic pigs (mean weight 17.3 ± 1.9 kg) underwent ligation of the distal left anterior descending artery to establish a model of acute myocardial infarction (MI). MSCT and triphenyltetrazolium chloride (TTC) staining were performed two hours later. The following data were acquired and analyzed: MI volume (%), CT values of the infarcted region, left ventricular cavity and normal cardiac tissue at various scanning time-points (1, 5, 10, 15, 20 min after contrast injection). **Results** Using MSCT, the overall MI volume showed a time-dependent decrease, with a reduction of 28.87% after 20 min. The greatest reduction occurred at the 5 min time-point. In TTC staining, MI volume was 9.87% ± 2.44%. When MI size, as determined by MSCT, was compared with that by TTC staining in Bland-Altman plots, there was a better agreement at 5, 10, and 15 min time-points at 1 and 20 min. **Conclusions** The study indicates that double-phase scanning examination using MSCT is a useful tool to assess MI size, and the optimal late-phase scanning time-point-set within 5–15 min of contrast injection.

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Keywords: Multi-slice computed tomography; Acute non-reperfused myocardial infarction; Time-factors; Animal model

1 Introduction

Multi-slice computed tomography (MSCT) has emerged as a promising new modality for non-invasive coronary imaging. The possibility to non-invasively examine significant coronary obstruction has rapidly increased the clinical use of this technique. Since 2004, the assessment of myocardial viability by means of late enhancement MSCT has evoked increasing interest.[1] Initial results were very promising,[1-13] and showed that double phase scanning with MSCT could be used to evaluate the size of the infarcted myocardium accurately, to assess different phases of myocardial infarction (MI) and to predict functional recovery in the affected arterial region by the late enhancement phenomenon. It might be a very useful non-invasive tool to assess MI size. MSCT can assess the infarcted myocardium accurately by contrast perfusion differentiation at different scanning phases after contrast injection.[2] Usually the first scanning time-point was set at 30–60 s after contrast injection. Nevertheless, there is still no consensus on the best suitable late scanning time-points. Both Lardo, *et al*.[5] and Brodoefe, *et al*.[9] set 5–10 min after contrast injection as the late phase scanning time-point, while Baks, *et al*.[6] set 15 min as the time-point. Although all studies reported good image quality, there was no consensus regarding the optimal time-point. Thus, the aim of this study was to determine the utility of MSCT in assessing MI size and the optimal late scanning time-point in an animal model of acute non-reperfused MI.

2 Methods

All procedures were approved by the Animal Ethics Committee at Shanghai Chest Hospital, Shanghai Jiaotong University.

2.1 Animal preparation and experimental protocol

Animals were fasted on the day of the operation. Seven healthy experimental pigs, aged 2–3 months and weighing 15.4–19.2 kg, were anesthetized with phenobarbital (30 mg/kg, *i.v.*) after intramuscular injection of diazepam

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(1 mg/kg) combined with ketamine (1.5 mg/kg) for basic anesthesia and electrocardiographic (ECG) monitoring. This was followed by intubation and mechanical ventilation. Parameters were set as follows: tidal volume 540 mL; frequency 12 breaths per minute; oxygen saturation 30%–50%; and inspiration/expiration ratio 1: 2. Left lateral thoracotomy was performed along the fourth intercostal space, and the pericardium was excised. The distal one-third of the left anterior descending (LAD) was ligated. Prior to the ligation, an infusion of 100 mg lidocaine was given via the ear vein to prevent ventricular fibrillation (VF). A 20–30 joule intracardiac, non-synchronized shock was delivered in case of VF. The thorax was closed subsequently, and after 2 h, the animals were transported to the CT suite to serve as acute MI models for imaging studies.

2.2 MSCT imaging protocol

MSCT imaging was performed with a 64-detector, single-source CT scanning system (Philips Medical Systems Corporation). Beta-blockade was used to achieve a heart rate of < 120 beats/min and additional sedation was given as needed. Scanning parameters were as follows: tube voltage, 80 kV; tube current, 800 mA; slice thickness, 0.8 mm; increment, 1 mm. A 100 mL bolus of Ultravist 370 was injected intravenously at a rate of 5 mL/s. MSCT images were acquired at 1, 5, 10, 15, 20 min after bolus injection, and raw data were stored for analysis. Source images were analyzed using software at 75% of the R-R interval with a retrospective multi-cycle ECG gating algorithm, slice thickness 3 mm and reconstruction increment 3.0 mm. Axial slices were reconstructed for assessment of the infarct volume, and various myocardial signal intensities.

2.3 MSCT image and data analysis

From the raw data, 3 mm double-oblique, short-axis images without an inter-slice gap were reconstructed at 75% of the R-R interval. Then the MI area and the CT value of different tissues in each slice at different scanning stages were determined.

To quantify the CT value, a standardized 10 mm^2 region of interest was positioned within the areas of perfusion deficit and normal areas in the interventricular septum, and in the posterior and lateral walls at a single mid-infarct image location. To quantify perfusion deficits, the endo- and epicardial contours of the left ventricle and the contours of perfusion deficit were drawn manually in each section. Definitions were as follows:

(1) Left ventricle (LV) mass (g) = (∑LV epicardial area – ∑LV endocardial area) × slice thickness × 1.06

(2) Hypo-enhanced mass (g) = ∑Hypo-enhanced area × slice thickness × 1.06

(3) Hypo-enhanced extent (%) = Hypo-enhanced Mass (g) / LV mass (g) × 100%

2.4 Triphenyltetrazolium chloride (TTC) measurements

Animals were subsequently euthanized using 10% potassium chloride, and the hearts were immediately removed and sectioned into 5 mm thick short-axis slices from the apex towards the base of the heart. Myocardial sections were stained with TTC for 15–20 min at 37°C, then photographed digitally under room light. Regions that failed to stain were designated as ischemic/infarcted regions. Images were loaded into Image-Pro Plus 6.0 software.

2.5 Statistical analysis

Continuous variables were expressed as mean ± SD. A comparison of CT values of the same segment on the multi-phase MSCT images was carried out using the paired Student *t*-test. Agreement between MSCT- and TTC-derived infarct size was assessed using Pearson's correlation coefficient and Bland-Altman analysis.[14] Statistical analysis was performed with SPSS 13.0 software. For Bland-Altman analysis, MedCalc® software was used. The infarct area measurement in pathological slices was completed using Image-Pro Plus 6.0 software. Statistical significance was defined as a two-sided probability value < 0.05.

3 Results

Acute myocardial infarction was successfully induced in all seven pigs. However, one pig died of VF at 1 h after LAD ligation and another pig died of anesthesia overdose. Data were thus available for five pigs.

MSCT myocardial images at 1, 5, 10, 15, 20 min after contrast injection are shown in Figure 1, and the corresponding data are presented in Table 1. Overall MI volume showed a time-dependent reduction, decreasing by 28.87% at the 20 min time-point. The greatest reduction, of 17.61%, occurred from 1 min to 5 min, while the reduction from 5 min to 10 min was quite small at 2.18% and not significant. There was a significant reduction of 9.37% between 10 min and 15 min, and no significant reduction between 15 min and 20 min (6.22%), (Table 2).

The CT value of the infarcted region at the 5 min time-point increased significantly compared with that at 1 min ($P = 0.008$) (Table 1). There was no significant change in the CT value at later time-points. The CT value of the left ventricular cavity declined with time, with a reduction of 62.47% at the 20 min time-point. The decrease diminished

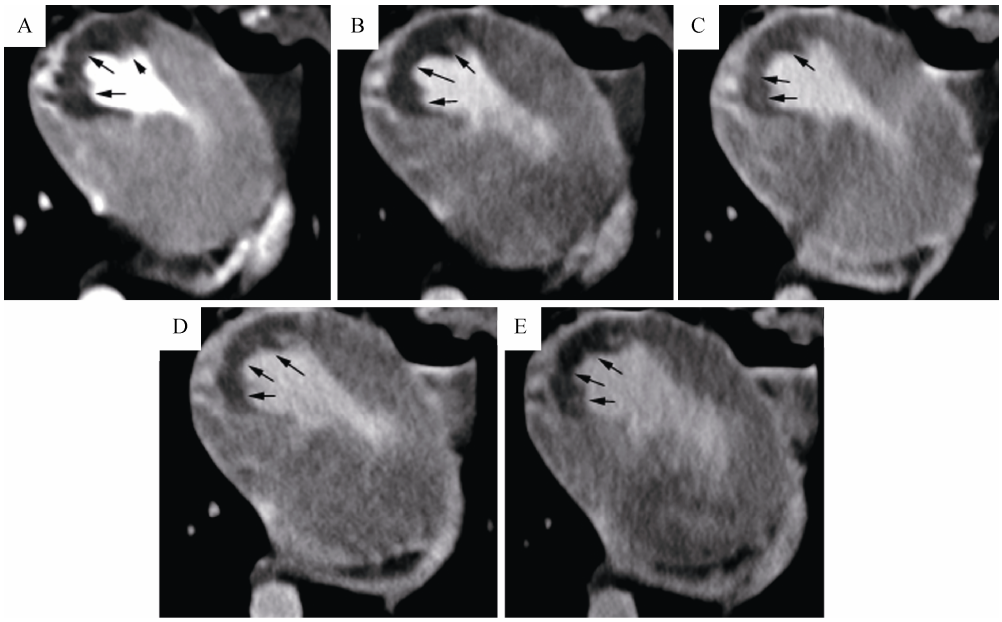

Figure 1. Multi-slice computed tomography (MSCT) myocardial image at various time-points. Images at 1 min (A), 5 min (B), 10 min (C), 15 min (D), and 20 min (E) after contrast injection. Dark zone (black arrows) indicates perfusion defects in the infarcted region.

Table 1. Volume of infarction (%) and CT value of different cardiac tissues at various time-points.

	1 min	5 min	10 min	15 min	20 min
MI volume (%)	11.87 ± 3.54	9.78 ± 2.88*	9.57 ± 2.88*	8.99 ± 2.69$^{*,\dagger,\#}$	8.51 ±2.93$^{*,\dagger,\#}$
CT value of infarcted region (HU)	26 ± 15	68 ± 11*	66 ± 6*	64 ± 7*	69 ± 18*
CT value of LV cavity (HU)	620 ± 39	383 ± 26*	302 ± 27*,†	245 ± 25$^{*,\dagger,\#}$	232 ± 22$^{*,\dagger,\#}$
CT value of normal myocardium (HU)	253 ± 32	179 ± 23*	150 ± 10*	129 ± 5$^{*,\dagger,\#}$	128 ± 20$^{*,\dagger,\#}$

*Significant difference compared with that at 1 min; †significant difference compared with that at 5 min; $^{\#}$significant difference compared with that at 10 min. LV: left ventricle; MI: myocardial infarction.

Table 2. Percentage reductions in measurements between various time-points.

	1–20 min	1–5 min	5–10 min	10–15 min	15–20 min
MI volume	28.87%	17.61%	2.18%	9.37%	6.22%
CT value of LV cavity	62.47%	37.95%	21.25%	18.75%	4.88%
CT value of normal myocardium	48.11%	27.85%	14.76%	13.56%	0.27%

MI: myocardial infarction; LV: left ventricle.

with time, and the smallest change was between 15 min and 20 min. The CT value of normal cardiac tissue decreased overall by 48.11%, with the largest decrease at 5 min (27.85%) and the smallest between 15 min and 20 min (0.27%).

With TTC staining (Figure 2), MI volume was calculated as 9.87% ± 2.44%. When MI size determined by late-phase MSCT was compared with that by TTC staining in Bland-Altman plots there was a better agreement at 5 min, 10 min, and 15 min time-points than that at 1 and 20 min (Figure 3).

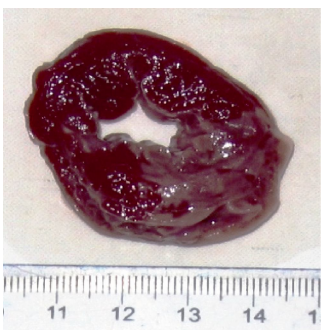

Figure 2. Triphenyltetrazolium chloride (TTC)-stained slice. White zone indicates infarcted region.

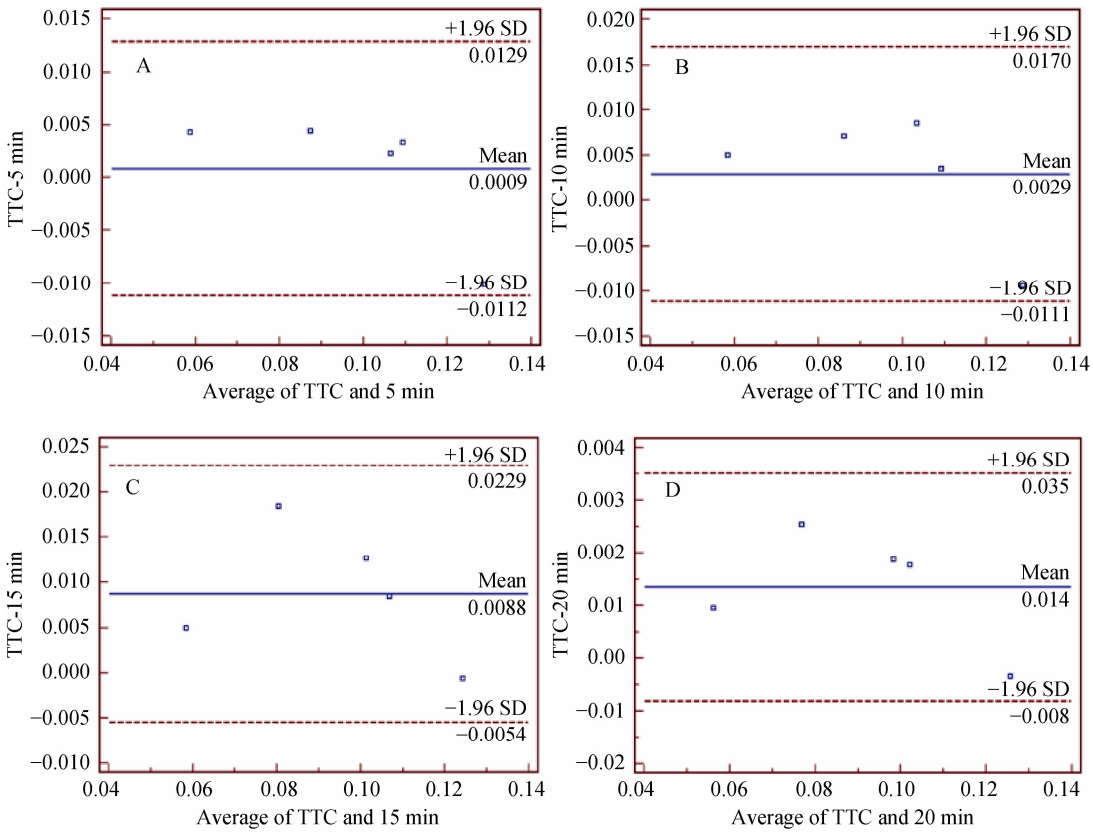

Figure 3. Comparison of myocardial infarct size between triphenyltetrazolium chloride (TTC) staining and multi-slice computed tomography (MSCT) using Bland-Altman plots at various time-points.

4 Discussion

Because of insufficient spatial and temporal resolution of single-slice CT, the use of CT to assess MI size had not previously been viable. In 2004, with the advent of new generation detectors, Hoffmann, *et al*.[1] assessed the size of acute non-reperfused MI by 4-MSCT. Because of good agreement between TTC staining and MSCT, interest in the usefulness of MSCT to assess the myocardium was evoked again. After that, the double-phase scanning modality was used to assess the myocardium. Although initial results were promising,[1-13] there was still no consensus on the most suitable CT protocols, including optimal late scanning time-points, optimal contrast dose and injection mode, and optimal CT parameters. Some studies set 5–10 min after contrast injection as the late scanning time-points,[9,10] others set 15 min.[6] However, specific studies about optimal time-points are sparse.

This study examined four sets of late scanning time-points and compared the MI size determined by MSCT at the various time-points with that determined by TTC staining. Results showed that MI size decreased with time in the acute non-reperfused MI with the greatest reduction between 1 min and 5 min. MI size determined by MSCT at 5 min, 10 min, and 15 min time-points showed a good agreement with that measured by TTC staining. Accordingly, 5–15 min after contrast injection were determined as the optimal time-points to measure the size of the acute non-reperfused MI accurately. This result is in agreement with Brodoefel's study,[9] although the latter studied a reperfused MI model.

The change in MI size at various scanning time-points is closely related with the micro-circulation. Usually, the speed of contrast wash-in and wash-out are very different in the infarct core, periphery, and non-infarcted remote region over time. Gerber, *et al*.[3] showed that the wash-in time was 0.8 ± 0.4 min and wash-out time was 2.3 ± 0.9 min in normal non-infarcted regions, while they were slower at 1.2 ± 0.2 min and 10 ± 4 min, respectively, in the periphery, and 6.9 ± 3.5 min and 15 ± 15 min, respectively, in the infarct core. Consequently, during the first scanning at 30–60 s, wash-in had started in the normal non-infarcted region, and in the periphery, but not in the infarct core. The early scan of MSCT demonstrates the non-reperfusion area, including the necrotic core area and the peri-necotic area. The early scan, in most circumstances, might over-estimate the infarct

size by the fact that the existence of the collaterals allows the slow penetration of the contrast. However, as time goes by, the delayed enhancement by contrast retention causes the separation between necrotic area and peri-necrotic area. As a result, the delayed scan of MSCT is more accurate than the early one in assessing the infarct size. The theory based on the micro-circulation was supported by our study.

The reperfusion animal model is different from the non-reperfusion animal model in terms of contrast perfusion phenomenon. In the farctate rim, the slow perfusion rate made the contrast shift from extracellular to intracellular, hence demonstrating the "late enhancement" phenomenon. In the infarcted core, there was no contrast perfusion even no delayed imaging. The residual perfusion deficit reflected the presence of severe microcirculation obstruction with poor long-term prognosis. This phenomenon is common in reperfusion animal model, while in acute non-reperfusion animal model late enhancement (LE) is hardly noted with the fact that collaterals and antegrade flow is limited. However, in the delayed scanning phase, viable myocardium will be reperfused which makes the infarct zone estimation much more reliable than the early scan phase.

The CT value of the left ventricular cavity and normal non-infarcted region both decreased over time in this study. Consequently, the ratio of CT value in the infarcted region to that in the left ventricular cavity and normal non-infarcted region decreased so that image quality decreased also. Because of the poorer image quality, MI size determined by MSCT was less accurate at longer times. Edelman, *et al*.[10] found a similar result, and their study showed that, because of contrast wash-out, the acquired image quality was poorer when the scanning time-point was set at times after 15 min. Thus, better quality images can be acquired, and also the most accurate estimates of MI size can be obtained if the scanning time-point is set within 5–15 min of contrast injection.

Actually the time frame after the culprit infarct does little on the ability of this technique for assessing the infarct sizing, though we agree, the establishment of the collaterals might affect, to some extent, the exact sizing via this technique. Our previous data[15] showed MSCT was a valid modality for assessing the infarct size in the chronic phase.

There are some limitations about this study. Firstly, the number of experimental animals is too small. This could decrease the power of the conclusion. Secondly, in our study, we compared the accuracy of MSCT in testing MI size only with that of TTC staining, which is the widely accepted golden criterion for MI size evaluation. Surely, there is no significant advantage of MSCT in assessing infarct size compared with that of magnetic resonance imaging. However, the early scanning phase of MSCT shows the distribution of coronary tree, while the late one gives information on myocardial perfusion. A single MSCT examination may provide some valuable information on the nature of the coronary artery, and myocardial perfusion, which would be helpful for subsequently designing appropriate revascularization strategy in these subjects.

In conclusion, this study indicates that double-phase scanning examination using MSCT is a useful tool to assess MI size, and the optimal late-phase scanning time-point is set within 5–15 min after contrast injection.

Acknowledgement

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