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Reduction of the Body Weight-adapted Volume of Contrast Material by Increasing the Injection Rate in 320-detector Row Coronary CT Angiography

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Abstract: Background: 320-detector row dynamic volume computed tomography (CT) scanner was widely applied in coronary CT angiography (CCTA)，which made it possible to reduce the volume of contrast material (CM) used. Some studies have reported the feasibility of reducing the CM in 320-detector row CCTA using a weight-adapted injection protocol. However, it hasn't been studied to investigate what was the significance of increasing the injection rate with a lower volume of CM. Objective: To investigate the feasibility of reducing the body weight-adapted volume of CM by increasing the injection rate in 320-detector row CCTA. Methods: A total of 116 patients who underwent 320-detector row CCTA were divided into three groups. Group A received 0.7 ml/kg of CM (350 mg I/ml) at an injection rate of 5.0 ml/s (n = 40); group B received 0.6 ml/kg of CM at 5.5 ml/s (n = 39); group C received 0.5 ml/kg of CM at 6.0 ml/s (n = 37). A 30-ml 0.9% saline chaser was administered after the CM. Enhancement values of the cardiovascular territories and coronary arteries were measured and compared. Image quality was also evaluated and compared among the three groups. Result: Enhancement values of the proximal coronary arterial segments for group C were significantly lower than those for groups A and B (all, $P < 0.05$), whereas there were no significant differences between groups A and B (all, $P > 0.05$). Similar statistical results were found in the proportion of proximal coronary arterial segments with enhancement values ≥ 300 HU, image quality ratings and the proportion of the main of coronary arterial segments with image quality scores ≥ 3 on both per-vessel and per-patient analyses. Conclusion: At least 0.6 ml/kg with 350 mg I/ml of CM at 5.5 ml/s injection rate was required to achieve sufficient and credible evaluation of the coronary artery in 320-detector row CCTA.

Keywords: Coronary CT Angiography, 320-detector Row CT, Contrast Material, Injection Rate, Image Quality

1. Introduction

With the rapid advancement of multi-detector computed tomography (CT) and improvements in image quality and acquisition speed, coronary CT angiography (CCTA) has become a standard noninvasive imaging modality, with high spatial and temporal resolution, for the diagnosis of coronary artery disease [1,2]. Unfortunately, patients undergoing CCTA are inevitably exposed to iodinated contrast media (CM) [3]. It has been reported that contrast-induced nephropathy (CIN) is an important iatrogenic complication from use of the CM [4], can have a poor prognosis, and may result in additional healthcare costs [5]. A number of studies have focused on how to prevent CIN, and the core recommendation is to use the lowest possible volume of CM because the incidence of CIN is highly associated with the volume of CM used [6]. Therefore, minimizing the total volume of CM used in CCTA is important, especially for patients with significant coronary artery stenosis who may be exposed to more CM during subsequent coronary artery stenting or angioplasty [7].

In recent years, the 320-detector row dynamic volume CT scanner was widely applied in clinical practice. It has a

z-coverage width of 160-mm and allows acquisition of the entire heart in a single rotation and within a single heartbeat with a minimum temporal resolution of 175 ms [8]. The non-helical volume scan mode of the entire heart makes it possible to reduce the volume of CM used [9, 10]. Some studies have reported the feasibility of reducing the CM volume in 320-detector row CCTA using a weight-adapted injection protocol [11, 12]. However, to our knowledge few studies have investigated what was the significance of increasing the injection rate with a lower volume of CM in 320-detector row CCTA. Our study was therefore designed to investigate the feasibility of using the lowest possible volume of CM with a body weight-adapted injection protocol, by increasing the CM injection rate and precisely determining the CM bolus arrival time, to achieve sufficient and credible evaluation of the coronary artery with 320-detector row CCTA.

2. Materials and Methods

2.1. Patients

This study was performed according to the principles of the Declaration of Helsinki and was approved by our institutional review board. Informed consent was obtained from all patients before the CCTA examination. Before this clinical study, a preliminary retrospective investigation was performed to determine the lowest possible CM volume and injection rate in 320-detector row CCTA.

From February 2019 to September 2019, a total of 116 patients (68 males and 48 females; mean age, 60.42 ± 12.35 years; range, 29 - 86 years) who were scheduled to undergo 320-detector row CCTA were consecutively recruited for this study. All patients were suspected of having coronary artery disease based on electrocardiography (ECG) findings or clinical symptoms, and had no history of coronary artery stenting or bypass surgery. Patients who had a previous allergic reaction to iodinated CM, respiratory failure, severe arrhythmias, congestive heart failure, renal failure (serum creatinine > 1.5 mg/dl [133 mol/l]), or an inability to achieve a heart rate below 75 beats per minute (bpm) with the use of beta-blocking agents, as well as women who were potentially pregnant, were excluded. Metoprolol (Metoprolol tartrate tablets, AstraZeneca AB, Sweden) 25 mg or 50 mg as a single dose was administered orally to 23 patients 1 - 2 hours before examination in order to meet the heart rate inclusion criterion.

The 116 enrolled patients were randomly divided into three groups using a table of random numbers. Group A (n = 40) received 0.7 ml/kg of CM at an injection rate of 5.0 ml/s, group B (n = 39) received 0.6 ml/kg of CM at 5.5 ml/s, and group C (n = 37) received 0.5 ml/kg of CM at 6.0 ml/s. All patients received nonionic CM (Optiray, Ioversol Injection; 350 mg of iodine per milliliter; Tyco Healthcare, Quebec, Canada). A 30-ml 0.9% saline chaser was administered with the same injection rate after the injection of CM. They were injected using a dual shot injector (Dual Shot Alpha; Nemoto-Kyorindo, Tokyo, Japan) through a 20-gauge or 18-gauge (injection rate of 6.0 ml/s) intravenous injection catheter (BD Intima II; Becton Dickinson Medical Devices, New Jersey, USA) inserted into an antecubital vein.

2.2. CT Scanning

CCTA was performed using a 320-detector row dynamic volume CT scanner (Aquilion ONE; Toshiba Corporation Medical Systems, Tokyo, Japan). Nitroglycerin spray (0.5 mg, glycerol trinitrate; Jing-wei Pharmaceutical Corp. Ltd. Shandong, China) was administered sublingually 3 - 5 minutes prior to the examination. Prospective ECG gating (Cardiac Trigger Monitor 3000; IVY Biomedical Systems Inc., Branford, USA) was used. The CCTA scanning parameters were: 320×0.5-mm collimation, 0.35-s gantry rotation time, 120-kV tube voltage, and 350 - 550 mA tube current.

The delay between the start of the CM injection and scanning was set with the help of automatic bolus-tracking technology (Real Prep technique; Toshiba Corporation Medical Systems, Tokyo, Japan). Dynamic monitoring scanning (120 kV, a tube current of 50 mA) was performed at the midlevel of the heart. Two regions of interest (ROIs) were placed in the left ventricle (LV) and the descending aorta (DA), and the threshold values were set at 100 and 280 Hounsfield units (HU), respectively. Twelve seconds after the initiation of intravenous CM injection, dynamic monitoring scanning was started to obtain the dynamic monitoring image of every second. The patient was instructed to take a breath and hold it when the enhancement value in the LV reached 100 HU (first threshold). After approximately 5.5 s, when the enhancement value in the DA reached 280 HU (second threshold), diagnostic scanning was performed automatically when the patient held his/her breath (Figure 1).

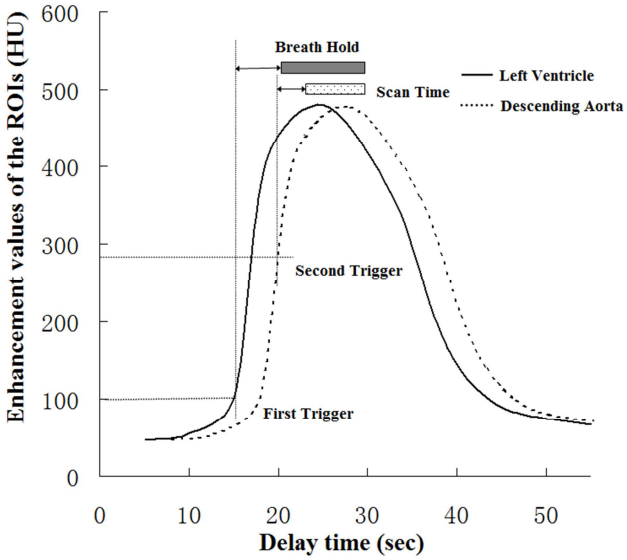

Figure 1. *Two regions of interest (ROIs) were placed in the left ventricle (LV) (real line) and the descending aorta (DA) (dashed line).*

Reconstruction phase was determined at the system's console by using cardiac-phase search software (Phase Navi; Toshiba Corporation Medical Systems, Tokyo, Japan). Images were reconstructed by using a segmented reconstruction

algorithm at 75% of the R-R interval or auto-choose best phase with a slice thickness of 0.5 mm and a reconstruction interval of 0.25 mm (image matrix 512 × 512). If motion artifacts were still present in any coronary artery at this phase, additional reconstructions were performed with the reconstruction window offset by 5% toward the beginning or end of the cardiac cycle, or at intervals of 10 ms. The image with the fewest motion artifacts among all of the reconstructed images was chosen to transfer to an off-line 3D workstation (Vitrea FX; Vital Images, Minnesota, USA) for post-processing.

2.3. Data Measurement and Image Quality Evaluation

Enhancement values of vascular structures were measured in all patients by an experienced radiologist using a manually defined circular ROI cursor. The radiologist was blinded to the injection protocol performed and to the patient grouping. Enhancement values of the cardiovascular territories were measured on axial images at two representative slice levels: level 1 at the origin of the left main coronary artery (LMCA) was used to measure the enhancement values of the ascending aorta (AA) and pulmonary trunk (PT) (Figure 2a), and level 2 at the midlevel of the heart was used to measure the enhancement values of the right atrium (RA), right ventricle (RV), left atrium (LA), LV, and DA (Figure 2b). The mean enhancement values based on two measurements by the radiologist were used for analysis. Enhancement values of the coronary arteries were measured at the following five points on cross-sectional images in which the vessel lumen was easily identified: LMCA, proximal segments of the left anterior descending artery (LAD), left circumflex artery (LCX), right coronary artery (RCA), and distal segments of the RCA. The mean enhancement values based on three measurements obtained from three ROIs in each target point were used for analysis. Figure 2c depicted the methods of measurement for the point of the proximal RCA (RCA-p). Calcifications, soft plaques, papillary muscles, and areas of stenosis were carefully avoided. To avoid the influence of partial volume effects, the coronary arteries were required to be more than 2 mm in diameter.

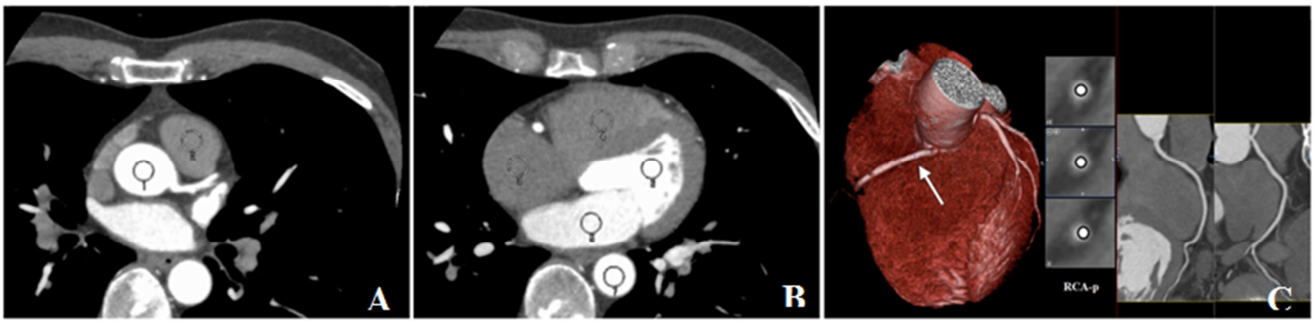

Figure 2. *Enhancement values of the cardiovascular territories were measured at the following two representative slice levels: A: level 1 at the origin of the left main coronary artery for the ascending aorta (ROI 1) and pulmonary trunk (ROI 2); B: level 2 at the midlevel of the heart for the right atrium (ROI 3), right ventricle (ROI 4), left atrium (ROI 5), left ventricle (ROI 6), and descending aorta (ROI 7); C: the point of the proximal right coronary artery (RCA-p).*

Image quality was evaluated independently by another two cardiovascular radiologists with more than 5 years of experience in cardiac CT imaging using a 5-point grading scale for the main coronary arterial segments: 5=excellent, 4=good, 3=acceptable, 2=suboptimal, and 1=nondiagnostic. The main segments of the coronary arteries were assessed qualitatively by scoring of all vessels with a diameter of at least a 1.5 mm, including the LMCA and proximal, middle, and distal segments of the LAD, LCX, and RCA. Every segment of the coronary artery with a score of 3 or higher was considered a diagnosable image.

2.4. Statistical Analysis

Statistical analysis was performed using SPSS software version 21.0 (SPSS, Chicago, IL, USA). The quantitative data were expressed as the mean ± standard deviation (SD). The means were compared with one-way analysis of variance (ANOVA) among the three groups. To evaluate the homogeneity of contrast enhancement in the entire coronary artery, a paired *t*-test was used to compare the enhancement value between the proximal and distal portions of the RCA in each group. Statistical significance was accepted at a value of $P < 0.05$. Image quality ratings of the main of coronary arterial segments for the three groups were compared using the nonparametric Kruskal-Wallis test, and pair-wise comparisons of groups were performed using the Mann-Whitney *U* test. Inter-observer agreements of the image quality ratings were calculated using kappa statistics. Pearson Chi-Square test was performed to examine the difference in the proportions of the proximal coronary arterial segments with enhancement values ≥ 300 HU and the proportion of the main of coronary arterial segments with a score of 3 or higher on per-vessel and per-patient analyses. On the per-patient analysis, the proportion of patients with all proximal segments ≥ 300 HU and all the assessed coronary arterial segments with a score ≥ 3 were calculated. In pair-wise comparisons, statistical significance was accepted at a value of $P < 0.05/3 = 0.017$ by Bonferroni correction.

3. Results

CCTA was performed successfully in all 116 patients without any technical problems or adverse reactions to the CM. Significant coronary artery stenosis (lumen obstruction of ≥

50%) were noted in 34 patients (29.31%). There were no significant differences in demographic characteristics or CT scanning parameters including scan delay, scan time, breath-holding time (BHT), and dose-length product (DLP) among the three groups (all, $P > 0.05$) (Table 1). The mean total volume of CM used was 46.53 ± 6.64 ml in group A, 40.59 ± 6.12 ml in group B, and 33.92 ± 4.47 ml in group C. The injection duration was 9.70 ± 1.44 s in group A, 7.85 ± 1.18 s in group B, and 6.14 ± 0.75 s in group C.

Table 1. *Patients' characteristics and treatment method of CT scanning for the three groups.*

	Group A	Group B	Group C	Statistic	*P*
No. of patients	40	39	37	--	--
Male/female ratio	23/17	23/16	22/15	0.033*	0.983
Age (years)	63.20±11.01	59.15±13.63	58.76±12.12	1.568	0.213
Weight (kg)	65.82±9.53	67.18±10.37	67.46±8.87	0.322	0.725
Height (cm)	164.35±6.76	162.56±7.35	163.27±9.45	0.513	0.600
BMI (kg/m²)	24.31±2.72	25.33±2.97	25.38±3.31	1.596	0.207
Heart rate (bpm)	61.92±5.78	60.97±5.83	61.51±6.16	0.256	0.775
Volume of CM (ml)	46.53±6.64	40.59±6.12	33.92±4.47	44.620	0.000
Injection rate (ml/s)	5.0	5.5	6.0	-	-
Injection duration (s)	9.70±1.44	7.85±1.18	6.14±0.75	89.920	0.000
Scan delay time (s)	19.86±2.79	19.88±2.26	20.11±3.01	0.100	0.905
Scan time (s)	3.02±0.42	3.03±0.41	3.07±0.48	0.140	0.870
BHT (s)	8.22±0.69	8.23±0.73	8.27±0.80	0.055	0.947
DLP (mGy·cm)	245.47±58.93	248.47±57.45	258.31±57.42	0.510	0.602

Unless otherwise specified, the data are the means ± SD; *Statistic of the male/female ratio is χ^2 value.
BMI Body mass index, *bpm* beats per minute, *CM* contrast material, *BHT* breath-holding time, *DLP* dose-length product, *SD* standard deviation.

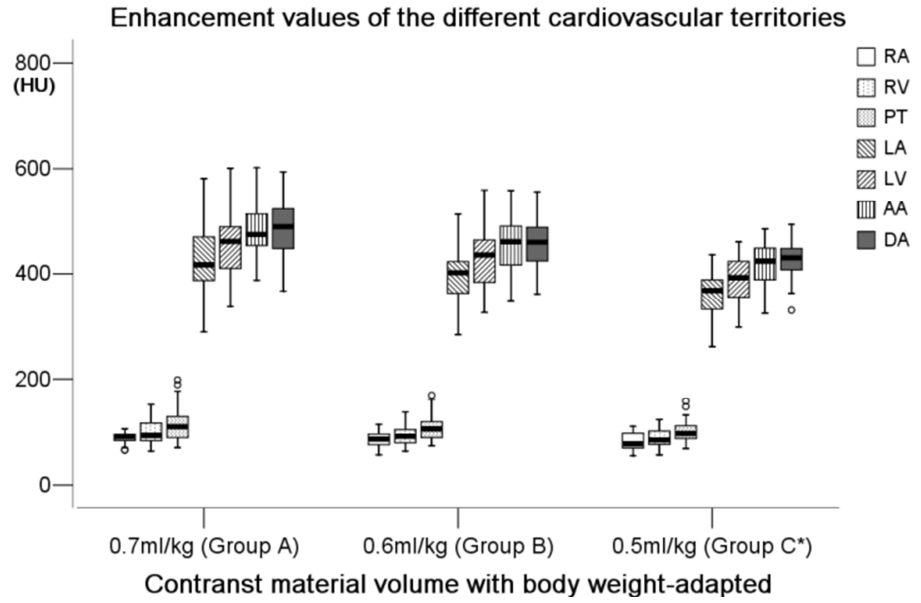

Figure 3. *Box plot illustrated enhancement values within the different cardiovascular territories. *P < 0.05 for group C vs. group A and group B with the mean enhancement values of the LA, LV, AA and DA.*

Enhancement values of the cardiovascular territories are shown in Figure 3. There were no significant differences in the mean enhancement values of the RA, RV, and PT among the three groups (all, $P > 0.05$). The mean enhancement values of the LA, LV, AA, and DA exhibited a declining trend from group A to group B to group C, which for group C were lower than those for groups A and B (all, $P < 0.05$), whereas there were no significant differences between group A and group B (all, $P > 0.05$).

The mean enhancement values of the LMCA, proximal LAD (LAD-p), proximal LCX (LCX-p), proximal RCA (RCA-p), and distal RCA (RCA-d) for group C were lower than those for groups A and B (all, $P < 0.05$), whereas there were no significant differences between group A and group B (all, $P > 0.05$) (Table 2). There were no significant differences in the enhancement values between the RCA-p and RCA-d in groups A and B ($P = 0.319$, $P = 0.941$, respectively), whereas a significant difference was noted in group C ($t = 3.269$, $P = 0.002$). The proportions of the proximal coronary arterial segments with enhancement values ≥ 300 HU on per-vessel and per-patient analysis were 71.17% (79/111) and 62.16% (23/37) in group C as compared to 90.83% (109/120) and 90.00%

(36/40) in group A, and 88.89% (104/117) and 87.18% (34/39) in group B, respectively. Those proportions in group C were significantly lower than those in groups A and B on both per-vessel and per-patient analysis (all, $P < 0.012$), but there were no significant differences between group A and group B ($\chi^2 = 0.248$, $P = 0.620$; $\chi^2 = 0.156$, $P = 0.693$).

Table 2. *The mean enhancement values of the coronary arteries for the three groups.*

	Group A	Group B	Group C	*F*	*P*
LMCA	405.58±51.79	382.55±43.74	351.86±37.94	13.725	0.000*
LAD-p	376.89±51.53	353.56±42.26	320.63±40.31	15.035	0.000*
LCX-p	353.74±52.94	329.68±43.68	302.88±40.98	11.589	0.000*
RCA-p	400.64±50.18	376.36±43.48	335.11±39.01	21.077	0.000*
RCA-d	399.03±44.85	376.26±41.57	369.35±50.51	26.813	0.000*

Data are the means ± SD; *$P < 0.05$ for group C vs. group A and group B
LMCA left main coronary artery, *LAD-p* proximal left anterior descending artery, *LCX-p* proximal left circumflex artery, *RCA-p* proximal right coronary artery, *RCA-d* distal right coronary artery

Image quality ratings of the main coronary arterial segments were 4.60 ± 0.83 or 4.52 ± 0.92 in group A, 4.54 ± 0.95 or 4.44 ± 1.04 in group B, and 3.87 ± 1.39 or 3.72 ± 1.41 in group C by reader 1 or reader 2, respectively. The image quality for group C was significantly worse than that for groups A and B (all, $P < 0.000$), but there were no significant differences between group A and group B ($Z = 0.467$, $P = 0.641$ or $Z = 0.509$, $P = 0.611$) with reader 1 or reader 2. Inter-observer agreements regarding image quality ratings of each measured segment of the coronary arteries were all good ($\kappa \geq 0.730$). The results of the proportion of the main of coronary arterial segments with a score of 3 or higher on per-vessel and per-patient analysis by reader 1 or reader 2 are shown in Table 3. The proportions of coronary arteries with a score ≥ 3 on per-vessel and per-patient analysis for group C were significantly lower than those for groups A and B (all, $P < 0.012$), but there were no statistically significant differences between group A and group B ($\chi^2 = 2.907$, $P = 0.088$; $\chi^2 = 2.414$, $P = 0.120$ or $\chi^2 = 0.614$, $P = 0.433$; $\chi^2 = 0.156$, $P = 0.693$).

Table 3. *Proportion of the main coronary arterial segments with image quality scores ≥ 3 for the three groups.*

	LMCA	LAD (p, m, d)	LCX (p, m, d)	RCA (p, m, d)	Per-vessel analysis	Per-patient analysis
Group A						
Reader 1	40/40	114/120	111/120	120/120	385/400 (96.25%)	37/40 (92.50%)
Reader 2	40/40	112/120	108/120	120/120	380/400 (95.00%)	36/40 (90.00%)
Kappa	0.895	0.798	0.730	0.877		
Group B						
Reader 1	38/39	111/117	102/117	114/117	365/390 (93.59%)	34/39 (87.18%)
Reader 2	38/39	108/117	102/117	112/117	360/390 (92.31%)	34/39 (87.18%)
Kappa	0.799	0.778	0.768	0.797		
Group C						
Reader 1	34/37	78/111	71/111	96/111	279/370 (75.41%)*	23/37 (62.16%)*
Reader 2	32/37	82/111	69/111	94/111	277/370 (74.86%)*	23/37 (62.16%)*
Kappa	0.802	0.775	0.762	0.765		

*$P < 0.012$ for group C vs. group A and group B on per-vessel and per-patient analysis
LMCA Left main coronary artery, *LAD* left anterior descending artery, *LCX* left circumflex artery, *RCA* right coronary artery, *p* proximal segment, *m* middle segment, *d* distal segment.

4. Discussion

In 320-detector row CCTA, volume data acquisition is completed at once by the CT scanner when the coronary artery enhancement arrive peak, and then reconstructs three-dimensional images of the coronary artery with computer post-processing [13]. In general, consistent and high enough vascular contrast enhancement is considered a prerequisite to sufficiently evaluate the coronary artery. And most studies tend to believe this enhancement value shall not be less than 300 HU [14]. Enhancement values of the coronary arteries are suffered from numerous interacting factors, including scan delay, scan time, scan direction and scan mode; CM concentration, volume, injection rate, injection duration, injection mode; patient age, body weight, cardiac output and other factors [15]. Some researchers think body weight is a cardinal patient-related factor affecting the magnitude of vascular contrast enhancement [11, 16], and suggest that the CM volume is adjusted according to patient body weight in CCTA. On the other hand, injection rate is another primary CM injecting factor affecting the magnitude of vascular contrast enhancement.

In the current study, we compared the three groups according to the volume of CM administered with a body weight-adapted injection protocol: patients received 0.7 ml/kg of CM at an injection rate of 5.0 ml/s (group A), 0.6 ml/kg of CM at 5.5 ml/s (group B), or 0.5 ml/kg of CM at 6.0 ml/s (group C). The results showed there were no significant differences in the mean enhancement values of the coronary artery and the image quality between group A and group B. This demonstrates that increasing the CM injection rate allows a 12.77% reduction in the total volume of CM from 0.7 ml/kg (mean 46.53 ml) to 0.6 ml/kg (mean 40.59 ml) for CCTA

without affecting the imaging quality. We tried to reduce the volume of CM to 0.5 ml/kg (mean 33.92 ml). But the mean enhancement values in the cardiovascular territories and coronary arteries all decreased significantly, and the image quality was also destroyed.

Using a lower CM volume and higher injection rate implies that the injection duration and peak time of contrast enhancement in the coronary artery will be shorter [13]. If the injection duration is too short, the bolus will be not enough to maintain adequate enhancement during the volume data acquisition, which will lead to inhomogeneous enhancements between the proximal and distal portions of the coronary artery. In our study, the injection duration was 9.70 ± 1.44 s in group A, 7.85 ± 1.18 s in group B, and 6.14 ± 0.75 s in group C. And the results showed no significant difference in the enhancement values between the proximal and distal portions of RCA in groups A and B, indicating that the injection duration was adequate. However, the enhancement values of the proximal and distal portions of the RCA were significantly different in group C, demonstrating it was difficult to maintain consistent contrast enhancement in the whole coronary artery. In consideration of partial volume effects, measurements were not taken in the distal portions of LAD and LCX because the diameter of these vessels was ≤ 1.5 mm in most patients.

With a lower CM volume and shorter injection duration, exact determination of CM arrival time is crucial to synchronize CT image acquisition for optimal coronary enhancement Determination of CM arrival time is typically done using either the test bolus (TB) technique or automatic bolus-tracking (BT) technique. However, the TB has been abandoned because it requires the use of a small volume (10 - 20 ml) of CM, which is incompatible with the goal of reducing the CM volume used in CCTA. The automatic BT is based on real-time monitoring of the main bolus during injection with the acquisition of a series of dynamic low-dose monitoring scans at the midlevel of heart, where the CM can be visually observed passing through the RA, RV, and pulmonary circulation and finally reaching the LA and LV at the "first pass". Tatsugami et al. reported that the use of a two-threshold setting in the AA could reduce inter-patient variability using the automatic trigger mode of BT in 320-detector row CTCA [17]. Nevertheless, when the two thresholds are set in the AA, the patient only has approximately 3 s to complete the movement of taking a breath and holding it, which is difficult to achieve, especially for some elderly patients. In our study, we selected two ROIs in the LV and the DA with threshold values of 100 and 280 HU, respectively. When the CM arrived at the LA, the first threshold (100 HU) was triggered to instruct the patient to take a breath and hold it. After approximately 5.5 s, the enhancement value in the DA reached 280 HU (second threshold); the diagnostic scan was performed automatically while the patient was holding his/her breath. The mean BHT was 8.22 ± 0.69 s in group A, 8.23 ± 0.73 s in group B, and 8.27 ± 0.80s in group C. Compared with the traditional methods in which the patient is instructed to begin the breath hold at 14 s after the initiation of intravenous CM injection, this method shortens the BHT, especially for some patients with reduced pulmonary circulation. It also avoids the respiratory motion artifacts.

5. Conclusion

In conclusion, a total of at least 0.6 ml/kg with a 350 mg I/ml concentration of CM at 5.5 ml/s injection rate are required to achieve sufficient and credible evaluation of the coronary artery in 320-detector row CCTA. Increasing the injection rate can compensate for the lower coronary arterial enhancement caused by the minimized CM volume to some extent.

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