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Cardiovascular Image

Application of 270 mgI/mL Iodinated Contrast Media in Dual-Source Computed Tomography Coronary Artery Imaging

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Background: This study aimed to explore the application of 270 mg I/mL iodinated contrast agent with a tube voltage of 100 kV scanning in coronary computed tomography angiography (CCTA).

Methods: This CCTA study was a prospective observational study. The two radiologists were blinded to both patient information and image date arrangement. One-hundred twenty patients (body mass index < 25.0 kg/m^2) were randomly divided into three groups based on contrast agent concentrations of 370, 320, and 270 mg I/mL, scanning at an injection rate of 5 ml/s. Then, the coronary artery branches of the three groups were compared, and the display rate, mean computed tomography (CT) value, signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), image noise, and radiation dose were analyzed.

Results: The artery display rates of the four main branches of coronaries in the three groups were all 100%, and the difference in the display rates of the remaining small branches in the three groups exhibited no statistical significance ($p > 0.05$). A comparison of the mean CT value of the coronary artery of three groups in the ascending aorta, descending aorta, left main, left ventricular wall, right coronary artery, left anterior descending, and left circumflex showed a statistically significant difference ($p < 0.05$). A comparison of the SNR, CNR, image noise, and radiation dose showed no statistically significant difference ($p > 0.05$).

Conclusions: Using a tube voltage of 100 kV combined with 270 mg I/mL iodinated contrast media in CCTA examination can achieve the "double low dose" effect while ensuring image quality.

Key Words: Contrast agent • Contrast to noise ratio • Coronary angiography • Signal noise ratio

INTRODUCTION

Multi-slice spiral computed tomography (CT) has high temporal and spatial resolution and can achieve a multi-angle display of the coronary artery and its branches. This method is safe, reliable, and relatively noninvasive, similar to the coronary artery disease (CAD) noninvasive screening method, which has been widely used in clinical practice.[1,2] The main existing problems are the toxic side effects of radiation dose and contrast agent.[3,4] Recent studies have described the use of contrast material with iodine content (300 mg I/mL) for coronary CT angiography (CCTA).[5] However, the effects of lower iodine concentration contrast material (270 mg I/mL) on the vessel visibility of CCTA have not been sufficiently evaluated. Therefore, this research involved the use of a 270 mg I/mL isotonic iodine contrast agent with tube voltage of 100 kV CCTA for patients with normal body mass index (BMI). The performance of this agent was compared with that of the 370 and 320 mg I/mL contrast material, which are two kinds of low osmolar contrast agents, to explore the clinical value of

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low concentrations of contrast agent combined with low tube voltage technique for double low dose of CCTA examination.

This prospective study aimed to compare the image quality of CCTA using dual souce CT with three contrast agents. The attenuation obtained in the coronary and great arteries, as well as the subjective degree of enhancement in the coronary arterial segments, was evaluated.

METHODS

Objects and grouping

Subjects of this study comprised 120 patients clinically suspected to have coronary heart disease from June 2012 to December 2012. These patients underwent CCTA. Among the 120 patients, 66 were male, and 54 were female. The patients were from 49 to 76 years of age, with a mean age of 56.1 ± 11.30. Inclusion criteria included body mass index (BMI, weight kg/height m^2) of less than 25, as well as no apparent heart enlargement upon imaging or clinical signs of heart failure. Exclusion criteria were high risk of allergy to iodine contrast agent and bypass surgery. The 120 cases were randomly divided into three groups, with 40 cases in each group, using iodine contrast agents of 370, 320, and 270 mg I/mL (hereinafter referred to as the 370, 320, and 270 groups, respectively). This study was conducted in accordance with the declaration of Helsinki, and with approval from the Ethics Committee of Kunming Medical University. Written informed consent was obtained from all participants.

CTA examination

A Siemens second-generation dual source CT with 64 multi-slices (Somatom Definition, Siemens Healthcare, Forchheim, Germany) was employed, and prospective electrocardiography (ECG) triggering sequence scanning was adopted. The tube voltage was 100 kV. Upon opening the vendor technique (CARE Dose4D), the CARE kV was set to Semi, the reference voltage was 120 kV, the current was 400 mAs, collimation was 128 × 0.6 mm, field of view (FOV) was 150 mm × 150 mm to 180 mm × 180 mm. According to the heart rate, the pitch was automatically set (range of 0.2 to 0.5), the scan ranged from 1 cm below the carina of the trachea to the diaphragmatic surface of the heart, and the actual scan length (Scan lengths, LEN) was determined by a computer.

A double-tube injector (Stellant D, Medrad, Indianola, PA, USA) was used to inject the contrast agent to the antecubital vein with a flow rate of 5 ml/s. The three groups of contrast agent were iopromide 370 mg I/mL (Ultravist, 370 mg I/mL iopromide, Bayer, Wayne, NJ, USA), ioversol 320 mg I/ml (Ioversol, 320 mg I/mL ioversol, JiangSu HengRui Medicine CO., LTD, China), and iodixanol 270 mg I/mL (Iodixanol, 270 mg I/mL Iodixanol, GE Healthcare AS, USA). The dose ranged from 55 mL to 65 mL. Saline was subsequently added at 30 mL to 40 mL. By applying the contrast agent tracer method (bolus tracking), the region of interest (ROI) was set at the aortic root level to detect the CT value. The scan was set to start 5 seconds after the CT number of ROI reached 100 HU.

Processing and analysis after image

The best coronary phase (minimum motion artifact image) was selected for image processing using sinogram-affirmed iterative reconstruction-3. The data were transmitted to the workstation (Syngo MMWP, version 2008A; Siemens Medical Solutions), and image analysis was performed using circulation and 3D software. The multi-planar reconstruction, maximum intensity projection, and volume rendering were mainly applied to obtain the multi-slice coronary artery image range for observation.

Evaluation of coronary artery branch display

Coronary artery branches are defined as follows:[6] The left coronary artery system included the left anterior descending (LAD) and circumflex (CX) branches issued by the left main coronary artery. The anterior descending branch is divided into three sections: LAD1 from the initiation of the anterior descending branch to the origin of first diagonal branch or septal branch; LAD2 from the origin of the first diagonal branch to corner of the heart septal surface part of the anterior descending branch; and LAD3 from the heart septal surface part of the anterior descending branch. The anterior descending branch mainly includes the septal (S) and diagonal branches (D). The circumflex branch is divided into two sections: CX1 is from the initiation of the circumflex branch to the origin of the first obtuse marginal (OM) branch, whereas CX2 arises from the origin of the first OM branch and its distal part running in the atrioventricular groove. The main branch of the circumflex is the OM branch and left atrial branch. The right coronary artery (RCA) was divided into three segments: RCA1, RCA2, and RCA3. RCA1 is from the ostium of the RCA to origin of the first right ventricular branch, RCA2 is from the origin of the first right ventricular branch (RVB) to the origin of the margin branch, and RCA3 from the origin of the margin branch to the origin of the posterior descending artery. The branches of the RCA include the right atrial branch, cone branch, right ventricular branch (RVA), acute marginal branch, posterior descending artery, posterior branch of the left ventricle, and branch of atrioventricular node (AVNB).

Evaluation of image quality

The mean CT value of each ROI was directly measured in the originally obtained axial images. The measurement of the large vascular and ventricular sections included the ascending aorta (AAO), descending aorta (DAO), left ventricular (LV), and left ventricular wall (left ventricular wall, LVW). Measurement of the coronary artery included the following four main branches: the RCA, left main (LM), LAD, and left circumflex (LCX), with the image noise as the standard deviation of the mean CT value of the root of the aorta (near the ostial of the left main coronary artery).

Measurement of signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR)

Approximately 2 mm^2 ROI was placed in nine parts of the coronary arteries, including the left main coronary artery, proximal segment of anterior descending branch, distal segment of the anterior descending branch (beyond the ostial of the second pair of diagonal branches), proximal segment of the first pair of diagonal branches, proximal segment of the circumflex branch, distal segment of the circumflex branch (beyond the ostial of second obtuse marginal branch), proximal segment of the first obtuse marginal branch, proximal segment of the RCA, and distal segment of the RCA (in the front of the ostial of posterior descending branch).[7] The calculation formula[8] was: SNR = CTlumen/image noise, CNR = (CT_{lumen} − $CT_{connective\ tissue}$)/image noise, where CT_{lumen} is the mean CT value of each part of coronary ROI, $CT_{connective\ tissue}$ is the mean CT value of approximately 2 mm^2 ROI of the tissue around the blood vessel (which was placed in the adipose tissue surrounding the coronary artery at the level of the ostial of the left main coronary artery).

Analysis of radiation dose

The statistics of radiation dose used in this research was the radiation dose of coronary CTA, excluding the setting radiation dose. Volume CT dose index (CTDIvol) and dose length produce (dose length produce, DLP) are given by the computer. The effective radiation dose (effective dose, ED) followed the formula ED = K × DLP, where K is the conversion factor. The adopted mean chest value was 0.014 mSv/(mGy cm) according to the European CT Quality Standard Guide.[9]

Statistic analysis

SPSS 16.0 statistical software package was used to compare the age, heart rate, BMI and scanning length (LEN) using the multi-sample non-parametric Kruskal-Wallis test. The coronary artery branch display rate of three groups using a Chi-square test was also ascertained. To compare the image noise, the mean CT value, CNR, SNR, CTDIvol, DLP, and ED of three groups were determined using single-factor analysis of variance, with $p < 0.05$ considered as statistically significant.

RESULTS

General information

The multi-sample non-parametric Kruskal-Wallis test was used to compare the age, heart rate, BMI, LEN, and coronary artery branch display rate of the three groups. The difference was not statistically significant (Table 1, $p > 0.05$).

Display rate of each coronary artery branch

Three groups were treated with different concentrations of contrast agent, and the display rate of the three main branches of the coronary arteries all reached 100%, whereas the display rare of the remaining small branches showed no statistically significant difference ($p > 0.05$, Table 2 and Figure 1).

Table 1. The comparison of age, heart rate, BMI and LEN in three groups ($\bar{x}$ ± s, n = 40)

	370 group	320 group	270 group	Chi-Square	p value
Age(yrs)	58.90	58.65	58.35	1.732	0.180
Heart rate (beats/min)	77.40	76.35	75.55	2.824	0.132
BMI (kg/m^2)	22.70	22.30	22.10	5.420	0.198
LEN (cm)	15.15	15.28	15.38	0.622	0.212

BMI, body mass index; LEN, lengths.

Evaluation of image quality

The mean CT value, image noise, SNR, and CNR were compared using F test (Tables 3 and 4). A comparison of the coronary image noise, SNR, and CNR at different concentrations of agent for the three groups exhibited no significant difference ($p > 0.05$). A comparison of the mean CT value in AAO, DAO, LM, RCA, LAD, LM, and LCX of different concentrations of agents in three groups showed a significant difference ($p < 0.05$). A comparison of the three groups' coronaries revealed that the mean CT value in LVW had no significant difference ($p > 0.05$).

Comparison of radiation dose

Three groups of coronary arteries were scanned under the same conditions. An F test was used to compare the CTDIvol, DLP, and ED. The CTDIvol, DLP, and ED values of the three groups showed no statistically significant difference ($p > 0.05$, Table 5).

DISCUSSION

With the rapid development of CT technology, CCTA is becoming more widely used. Thus, radiation dose risk has become a clinical focus. However, several methods have recently been introduced to reduce the radiation dose. Among these methods, the lower tube voltage and tube current scanning method are the most widely used. According to reports,[3,10-12] CCTA imaging at 100/80 kV tube voltage in non-obese patients significantly reduces radiation dose and ensures high image quality. However, at low tube voltage,[13] based on the photoelectric effect, the iodine in the contrast agent may increase the absorption efficiency on X-ray, which increases the CT value. A decrease in tube voltage will cause the coronary CT value to rise exponentially. In our study, all groups of cases used 100 kV tube voltage and 5 ml/s injection rate scanning. The mean CT values of the 370 and 320 groups reached 400 HU to 750 HU, and those of the 270 group reached 300 HU to 350 HU. The difference was statistically significant. In other parts and organs, a higher degree of contrast enhanced vessel re-

Table 2. The display rate percentage of the coronary artery branches of the three groups patients (%, n = 40)

	370 group	320 group	270 group	p value
LM	100	100	100	–
LAD1	100	100	100	–
LAD2	100	100	100	–
LAD3	100	100	100	–
S1	20	20	15	0.074
S2	0	0	0	–
S3	0	0	0	–
D1	100	100	100	–
D2	60	50	70	0.084
D3	30	20	30	0.090
CX1	100	100	100	–
CX2	100	100	100	–
LAB	10	5	5	0.065
OM1	100	100	100	–
OM2	30	40	35	0.067
OM3	5	10	10	0.054
RCA1	100	100	100	–
RCA2	100	100	100	–
RCA3	100	100	100	–
CB	15	10	15	0.089
RAB	55	60	65	0.120
RVB1	100	100	100	–
RVB2	20	30	20	0.080
AM	45	55	55	0.067
PDA1	100	100	100	–
PDA2	30	20	30	0.090
AVNB	80	90	85	0.094
PLVB1	100	100	100	–
PLVB2	50	50	55	0.056

AM, acute marginal branch; AVNB, atrioventricular node; CB, cone branch; CX, circumflex; LAB, left atrial branch; LAD, left anterior descending; LM, left main; OM, obtuse marginal; PDA, posterior descending artery; PLVB, posterior branch of the left ventricle; RAB, right atrial branch; RCA, right coronary artery; RVB, right ventricular branch.

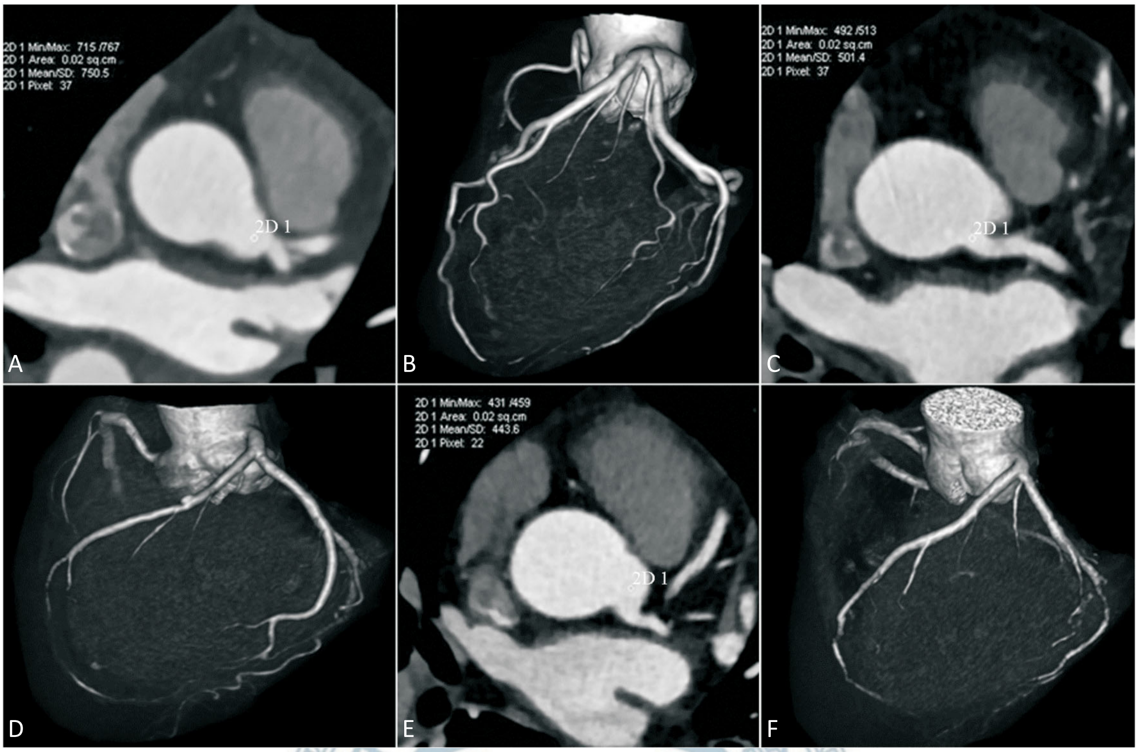

Figure 1. *The mean CT values of transverse images of left coronary artery in three kinds of injection scheme were compared and evaluated. (A-B) The contrast agent 370 mgI/mL, the transverse figure showed the mean computed tomgraphy (CT) value at the ostial of the left main coronary was 750.5 HU, and volume rendering (VR) showed septal branch (S), diagonal branch (D)1, 2, obtuse marginal branch (OM) 1, 2 clear. (C-D) The contrast agent 320 mgI/mL, the transverse figure showed the mean CT value at the ostial of the left main coronary was 501.4 HU, and VR showed S, D1, D2, OM1, OM2 clear. (E-F) The contrast agent 270 mgI/mL, the transverse figure showed the mean CT value at the ostial of the left main coronary was 443.6 HU, and VR showed S, D1, D2 VR, OM1, OM2 clear.*

Table 3. Comparison of image noise, SNR and CNR of three groups ($\bar{x}$ ± s, n = 40)

Index	370 group	320 group	270 group	p value
Image noise (HU)	17.71 ± 3.21	16.26 ± 3.14	16.06 ± 3.02	0.20
SNR	27.42 ± 4.21	27.68 ± 4.09	26.12 ± 4.13	0.43
CNR	21.7 ± 4.4	20.1 ± 5.2	21.2 ± 5.7	0.32

CNR ,contrast-to-noise ratio; SNR, signal-to-noise ratio.

Table 4. Comparison of mean CT value of coronary artery of three groups ($\bar{x}$ ± s, n = 40, HU)

Parameter	370 group	320 group	270 group	F value	p value
LM	706.64 ± 53.27	465.56 ± 50.85	393.65 ± 50.86	2.410	0.026
LAD	696.56 ± 54.23	467.65 ± 47.65	392.43 ± 49.54	5.570	0.017
LCX	700.43 ± 56.65	465.45 ± 48.65	390.45 ± 48.45	3.221	0.013
RCA	710.32 ± 45.65	466.76 ± 45.65	390.65 ± 50.34	3.432	0.044
LV	734.43 ± 45.56	486.57 ± 47.67	418.65 ± 56.65	2.312	0.033
LVW	119.78 ± 14.56	114.43 ± 13.34	112.43 ± 13.31	3.231	0.654
AAO	728.43 ± 45.67	474.43 ± 45.65	406.65 ± 56.45	1.432	0.032
DAO	715.54 ± 56.34	666.65 ± 56.54	404.45 ± 54.65	3.432	0.021

AAO, ascending aorta; DAO, descending aorta; LAD, left anterior descending; LCX, left circumflex; LM, left main; LV, left ventricular; LVW, left ventricular wall; RCA, right coronary artery.

Table 5. Comparison of $CTDI_{vol}$ and ED of three groups ($\bar{x} \pm s$, n = 40)

Index	370 group	320 group	270 group	p value
$CTDI_{vol}$ (mGy)	26.24 ± 2.43	26.74 ± 2.13	26.54 ± 2.23	0.55
DLP (mGy × cm)	512.85 ± 97.14	527.86 ± 82.14	515.86 ± 88.57	0.45
ED (mSv)	7.18 ± 1.36	7.39 ± 1.15	7.25 ± 1.24	0.65

$CTDI_{vol}$, CT dose index; ED, effective dose.

sults in more evident vasculature and tissues, as well as sharper and clearer blood vessel edges. However, in the case of the coronary artery running in the coronary ditch and interventricular groove and surrounded by fat wrapping, the density contrast of fat and vascular strength were satisfactory.

At the same time, the CT value of atherosclerotic and fibrous plaques formed at the coronary vascular wall was approximately 20 HU to 90 HU. If the mean CT value of the coronary artery is extremely high, the density D-value increases with the vascular wall plaque, which directly affects the accuracy of the detection of coronary atherosclerotic plaques and the degree of stenosis. Small vascular stenosis can be seriously underestimated. According to Nikolaou et al., when the mean CT value of the coronary reaches 300 HU to 350 HU, the requirements of clinical diagnosis can be met within the most optimal range.[14] The degree of vascular enhancement was positively related to the unit volume of iodine content.[15] At a certain contrast agent injection rate, a higher contrast agent concentration results in higher iodine content per unit time and a higher degree of vascular enhancement. However, when low concentrations of contrast agent (such as 270) could display the coronary artery and its branches, further increasing the contrast agent concentration had a negligible effect. With the 100 kV scanning protocol, although the image noise increased in the 270 group, the contrast noise ratio likewise increased such that image noise was evidently improved using SAFIRE reconstruction.[16] In this study, the results of the three groups of image noise was similar to that of Fei et al.[17] when using 120 kV scanning. According to Karaca's study,[18] CNR > 8 resulted in better image quality, 4 < CNR < 8 resulted in good image quality, and CNR < 4 resulted in poor image quality. All three groups of CNR could meet the requirements.

Higher iodine load is known to bring more potential harm to patients. The potential hazard has certain relevance associated with contrast agent concentration and dose rate. Ensuring the enhancement effect to reduce the contrast agent concentration has become an important concern.[19] Contrast agents are classified as hypertonic, relatively hypotonic, and isotonic.[20] If the contrast agent osmotic pressure is higher than the plasma osmotic pressure, the contrast agent running in the blood vessels may cause an increase in plasma osmotic pressure, which can cause the oxygen carrying capacity and deformation capability of the red blood cells to decrease. To maintain the normal function of tissues and organs, heart rate compensation increases, whereas vascular endothelial cells may shrink, thus increasing the possibility of thrombosis forming in the distal peripheral vascular area. Finally, the entrance of interstitial fluid promotes vascular expansion, which causes pain, heat, and discomfort in patients, thus hindering them from cooperating during the check-up.[21] Meanwhile, increasing the heart preload of the patient causes a change in heart rate, which may affect the image quality of coronary angiography. In this study, 370 and 320 mg I/mL are relatively low osmolar contrast agents with osmotic pressure of 695 mOsm/kg H_2O to 780 mOsm/kg H_2O, whereas 270 mg I/mL is an ISO osmolar contrast agent with osmotic pressure of 290 mOsm/kg H_2O isotonic (with normal body fluids). According to a previous report,[22] a relatively low osmolar contrast agent can be classified as "high isotonic". An isotonic contrast agent is more conducive to the reduction of the occurrence of contrast-induced nephropathy than low osmolar contrast agents. This study used an isotonic osmolar contrast agent for CCTA without affecting the vascular enhancement degree while reducing the concentration of the contrast agent and minimizing the irritation effect on blood vessels. These findings are of important significance in improving the safety and comfort degree of patients.

LIMITATIONS

This research had some limitations. First, 270 mg I/mL iodine contrast agent was clinically applied only within a short period of time. The optimal dosage of the contrast agent and drug delivery speed used in dual source CCTA imaging require further study with large samples and multiple injection schemes. A digital subtraction angiography control study is also required.

CONCLUSIONS

In sum, dual CT low tube voltage (100 kV) combined with 270 mg I/mL iodinated contrast coronary artery imaging not only guarantees image quality, but also re- duces radiation dose and iodine content to achieve the “double low dose”, which has positive clinical application value. If other individual conditions, such as BMI, heart size, breast size if female patients, cardiothoracic ratio, heart function, and heart rate, can be comprehensively evaluated, individualized scan schemes can be established. Such schemes can use Flash mode, 80 kV or 70 kV with the appropriate injection rate while reducing the amount of contrast agent and further reducing the dose.

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