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FULL PAPER

A prospective evaluation of contrast and radiation dose and image quality in cardiac CT in children with complex congenital heart disease using low-concentration iodinated contrast agent and low tube voltage and current

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Objective: To assess image quality, contrast dose and radiation dose in cardiac CT in children with congenital heart disease (CHD) using low-concentration iodinated contrast agent and low tube voltage and current in comparison with standard dose protocol.

Methods: 110 patients with CHD were randomized to 1 of the 2 scan protocols: Group A ($n = 45$) with 120 mA tube current and contrast agent of 270 mgI/ml in concentration (Visipaque™; GE Healthcare Ireland, Co., Cork, UK); and Group B ($n = 65$) with the conventional 160 mA and 370 mgI/ml concentration contrast (Iopamiro®; Shanghai Bracco Sine Pharmaceutical Corp Ltd, Shanghai, China). Both groups used 80 kVp tube voltage and were reconstructed with 70% adaptive statistical iterative reconstruction algorithm. The CT value and noise in aortic arch were measured and the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated. A five-point scale was used to subjectively evaluate image quality. Contrast and radiation dose were recorded.

Results: There was no difference in age and weight between the two groups (all $p > 0.05$). The iodine load

and radiation dose in Group A were statistically lower (3976 ± 747 mgI vs 5763 ± 1018 mgI in iodine load and 0.60 ± 0.08 mSv vs 0.77 ± 0.10 mSv in effective dose; $p < 0.001$). However, image noise, CT value, CNR, SNR and subjective image quality for the two groups were similar (all $p > 0.05$), and with good agreement between the two observers. Comparing the surgery results, the diagnostic accuracy for extracardiac and intracardiac defects for Group A was 96% and 92%, respectively, while the corresponding numbers for Group B were 95% and 93%.

Conclusion: Compared with the standard dose protocol, the use of low tube voltage (80 kVp), low tube current (120 mA) and low-concentration iodinated contrast agent (270 mgI/ml) enables a reduction of 30% in iodine load and 22% in radiation dose while maintaining compatible image quality and diagnostic accuracy.

Advances in knowledge: The new cardiac CT scanning protocol can largely reduce the adverse effects of radiation and contrast media to children. Meanwhile, it also can be used effectively to examine complex CHD.

INTRODUCTION

Congenital heart disease (CHD) is the most common type of congenital malformation. It has a great negative effect on the growth and development of children and early diagnosis is crucial for treatment and prognosis. Echocardiography, cardiac MR and CT are the primary modalities used for evaluating CHD. Echocardiography can provide information of cardiac anatomy, assess haemodynamics and is more suitable for late follow-up. But, it has

limitations in acoustic window, spatial resolution and the diagnosis of extracardiac defects.^{1,2} Although MRI has some advantages such as being ionization-free and giving a high resolution for soft tissues, it is time consuming and needs prolonged sedation, which is not suitable for infants with severe clinical symptoms. CT, with its high spatial resolution and good temporal resolution, can provide good anatomical details. But, there are concerns about the effects of radiation dose on paediatric patients who have higher

radiosensitivity.³ In addition, iodinated contrast media (CM) are commonly used in diagnosing CHD, but have a potential risk of leading to acute renal failure.⁴ In recent years, efforts have increased to reduce both radiation dose and contrast dose while maintaining image quality in many aspects of paediatric imaging.^{5–7} The purpose of our study was to assess the feasibility of reducing both contrast and radiation dose while maintaining image quality in the process of cardiac CT scanning in children with CHD by using a low-concentration iodinated contrast agent and low tube voltage and tube current.

METHODS AND MATERIALS

Study groups and CT scanning

This prospective study was approved by our institutional review board. In this prospective study, from January to March 2016, 110 consecutive patients (54 males and 56 females; $5\text{ kg} < \text{weight} < 10\text{ kg}$) with CHD were randomly assigned to 1 of the 2 cardiac CT groups: Group A [lower dose group, $n = 45$; 20 males and 25 females; mean age: 8.20 ± 4.37 months (standard deviation); mean weight: $7.36 \pm 1.38\text{ kg}$ (standard deviation); mean body mass index (BMI): $16.73 \pm 2.61\text{ kg m}^{-2}$ (standard deviation)]; and Group B [standard dose group, $n = 65$; 34 males and 31 females; mean age: 8.57 ± 4.68 months (standard deviation); mean weight: $7.79 \pm 1.38\text{ kg}$ (standard deviation); mean BMI: $17.31 \pm 5.04\text{ kg m}^{-2}$ (standard deviation)].

The inclusion criteria were children with CHD who were scheduled for cardiac CT for further information (cardiovascular anatomy which included the coronary artery). The exclusion criteria were hypersensitivity to iodine CM and an impaired renal function defined as glomerular filtration rate $< 60\text{ ml min}^{-1}/1.73\text{ m}^2$. All studies were performed on a multidetector CT scanner (Discovery HD 750; GE Healthcare, Waukesha, WI) using the prospective electrocardiogram (ECG)-triggering technique. Group A used a low-dose protocol with 120 mA tube current and a low concentration (270 mgI/ml) of contrast agent (Visipaque™, GE Healthcare); Group B used a standard scan protocol with 160 mA tube current and a standard concentration (370 mgI/ml) of contrast agent (Iopamiro®, Bracco). The tube voltage was 80 kVp in both groups. The scan parameters for prospective scanning were the same as that of our previous study.⁸ The detailed parameters were as follows: prospectively ECG-triggered step-and-shoot axial scanning and a collimation of $64 \times 0.625\text{ mm}$ with a scan field of view of 25 cm and gantry rotation time of 0.35 s. The data acquisition window was 380 ms with padding technique. The centre of the data acquisition window was set at 35–45% of the R–R interval when

heart rate was over 75 bpm and at 65–85% of the R–R interval when heart rate was lower than 75 bpm. The scanning direction was craniocaudal in most cases and extended from the level of the thoracic inlet to the diaphragm. The CM was administered with a power injector (Mallinckrodt, Liebel-Flarsheim Company LLC, Cincinnati, OH) through an antecubital vein. The dose of CM was 2 ml kg^{-1} . The range of the injection rate of the CM was 0.8–2.0 cc/s. All scans were reconstructed using 70% adaptive statistical iterative reconstruction (ASIR) algorithm at 0.625-mm image slice thickness.

Radiation doses estimation

The volumetric CT dose index (in milligray) and dose-length product (DLP) (in milligray centimetre) were automatically recorded by the software of the CT scanner. And the effective dose (ED) (in millisievert) was calculated using age-appropriate dose conversion factors k : $\text{ED} = k \cdot \text{DLP}$ (Table 1).⁹

Quantitative analysis of the images

Quantitative analysis was performed on a post-processing workstation (General Electric Medical Systems-AW 4.6; GE Healthcare, Waukesha, WI, USA) by a single investigator. For images in Group A and Group B, the mean CT value (Hounsfield units) and standard deviation for the aorta were obtained by placing a circular region of interest (ROI) in the ascending aorta. CT values and their standard deviations of the thymus and fat were also measured at the same level of the ascending aorta. All measurements were performed using an ROI of $0.8\text{--}1.0\text{ cm}^2$ in size. Three measurements were recorded at the same slice to get an average value. The standard deviation measurement in fat was used to represent image noise. ROI measurements were used to calculate the contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR) for the aorta as follows: $\text{CNR} = (\text{mean CT values of aorta} - \text{mean CT values of thymus})/(\text{standard deviation of fat})$ and $\text{SNR} = \text{mean CT values of aorta}/\text{standard deviation of aorta}$.

Subjective evaluation of image quality

Two radiologists (with 30 and 27 years' experience in paediatric CT imaging) independently and blindly assessed the image quality of images in both Groups A and B using a five-point grade scale scoring system (Table 2).

Surgical results

64 children were operated on ($n = 26$ in Group A and $n = 38$ in Group B) and the findings of these patients with pre-operative cardiac CT were compared with surgical results.

Table 1. Chest age-specific conversion factors for dose-length product-based CT dosimetry

Age group	Conversion factors k ($\text{mSv mGy}^{-1}\text{cm}^{-1}$)
Newborn to 3 months	0.039
From 4 months to 2 years and 11 months	0.026
From 3 years to 7 years and 11 months	0.018
From 8 years to 14 years and 11 months	0.013
≥ 15 years	0.014

Table 2. Five-point scales

Score	Description
1	Not assessable, bad image quality with severe image noise and artefacts; cannot demonstrate coronary arteries, pulmonary veins, aortopulmonary collaterals or other small details
2	Poor, major noise and image artefacts that hamper a complete evaluation; poor demonstration of coronary arteries or other small details
3	Sufficient, some noise and artefacts but permit acceptable image evaluation; fair demonstration of coronary arteries or other small details
4	Good, minor image noise and artefacts permit confidence image evaluation; good demonstration of coronary arteries or other small details
5	Excellent, excellent image quality with minimal image noise and without artefacts; excellent demonstration of coronary arteries or other small details

Statistical methods

Analyses were performed by using statistical software SPSS® v. 19.0 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL). Continuous variables were expressed as mean $\pm$ standard deviation. The differences in patient age, weight and BMI, total iodine load and effective radiation dose, and quantitative images parameters (including CT value, image noise, SNR, CNR and degree of enhancement) were tested between the two cohorts (Groups A and B) using an independent-samples *t*-test. For the qualitative image analysis, the five-point score averaged from the two observers was compared between the two protocols (Groups A and B) by using

the Mann–Whitney *U*-test. The *p*-value was obtained for each comparison and a value <0.05 was considered to be of statistical significance. Interobserver agreement in subjective image quality assessment was expressed by kappa coefficient. A value of 0.8 or above indicates excellent agreement, 0.6–0.8 good agreement, 0.4–0.6 fair agreement and <0.4 poor agreement.

RESULTS

Patient demographics, iodine load and radiation dose of CT scan

There were 18 cases of cyanotic CHD and 27 cases of acyanotic CHD in Group A, while 22 cases of cyanotic CHD and 43 cases of acyanotic CHD in Group B. The acyanotic CHD included complete atrioventricular canal, pulmonary stenosis, ventricular septal defect or atrial septal defect or patent ductus arteriosus, right aortic arch with aberrant subclavian artery and aortic valve stenosis. The cyanotic CHD included tetralogy of Fallot, pulmonary atresia with ventricular septal defect, pulmonary atresia with intact ventricular septum, coarctation of the aorta, total anomalous pulmonary venous connection, double-outlet right ventricle, transposition of the great artery, partial anomalous pulmonary venous connection and single ventricle. The information of the total 110 patients is outlined in Table 3.

There was no significant difference in age, weight, BMI and heart rate between the two groups (all $p > 0.05$). The protocol used in Group A had a lower iodine load than that in Group B, and there was a significant difference between them (3976 ± 747 mgI in Group A vs 5763 ± 1018 mgI in Group B; $p < 0.001$). The volumetric CT dose index, DLP and ED values in Group A (1.35 mGy, 15.29 ± 1.91 mGycm and 0.60 ± 0.07 mSv, respectively) were also lower than those in Group B (1.81 mGy,

Table 3. Patient information in Group A and Group B

Cardiac defects	Group A(cases)	Group B(cases)
Tetralogy of Fallot	11	12
Single ventricle	1	1
Pulmonary atresia with ventricular septal defect	2	2
Pulmonary atresia with intact ventricular septum	1	2
Double-outlet right ventricle	0	2
Transposition of the great arteries	0	2
Total anomalous pulmonary venous connection	2	0
Partial anomalous pulmonary venous connection	1	1
Complete atrioventricular canal	2	1
Right aortic arch with aberrant subclavian artery	1	0
Coarctation of the aorta	0	1
Aortic valve stenosis	1	1
Atrial septal defect/ventricular septal defect	17	27
Patent ductus arteriosus	3	4
Pulmonary stenosis	3	9
Total	45	65

20.11 ± 2.13 mGy cm and 0.77 ± 0.10 mSv, respectively) (all $p < 0.001$) (Table 4).

Quantitative analysis of images

The mean aortic arch CT values of Group A and Group B had no significant difference (429.4 ± 110.1 HU vs 466.8 ± 91.62 HU; $p > 0.05$). The image noises, CNR and SNR values for Group A (16.24 ± 1.41 HU, 21.84 ± 7.04 and 26.64 ± 7.35 , respectively) and Group B (16.67 ± 1.59 HU, 23.12 ± 5.92 and 28.28 ± 6.15) were also similar (all $p > 0.05$) (Table 5).

Subjective evaluation of image quality

Image quality scores by the two observers were 4.60 ± 0.20 and 4.60 ± 0.19 in Group A and 4.64 ± 0.19 and 4.65 ± 0.20 in Group B with good consistency between the two observers (kappa value of 0.74 in Group A and 0.76 in Group B). Also, the mean image quality score for the two observers was 4.60 ± 0.20 in Group A and 4.64 ± 0.19 in Group B with no statistical difference ($p > 0.05$) (Table 5) (Figures 1 and 2).

Diagnostic accuracy

Comparing the surgery results ($n = 26$ in Group A and $n = 38$ in Group B), the diagnostic accuracy for extracardiac and intracardiac defects for Group A was 96% and 92%, respectively, while the corresponding numbers for Group B were 95% and 93%.

DISCUSSION

Although CT, with its higher spatial and temporal resolution, is increasingly being used clinically in children with CHD, ionizing radiation exposure is still a major concerning issue in paediatric cardiac CT procedures. However, the use of prospective ECG-triggering scanning technique can reduce the radiation exposure in the process of CT examination.^{4,10} The retrospective ECG-gating technique requires application of ionized X-ray radiation during the entire cardiac cycle, while the prospective ECG-triggering technique requires application of ionized X-ray radiation only during a certain predefined period of the cardiac cycle. So, the latter can greatly reduce radiation dose while ensuring the diagnostic image quality.^{11,12} At the same time, low tube voltage is often used in CT angiography for small objects to

fully take advantage of the higher CNR enabled by X-ray photons with low energies. In our study, all patients underwent cardiac CT using prospective ECG-triggering mode with 80-kVp tube voltage to realize submillisievert in ED. In addition, a lower tube current was used to produce over 20% reduction in ED for Group A (0.60 ± 0.08 mSv in Group A and 0.77 ± 0.10 mSv in Group B).

With the conventional scan and reconstruction algorithm using filtered back-projection (FBP), reducing radiation dose will inevitably increase image noise and then result in a lower SNR, CNR and image quality.^{13,14} Moreover, FBP has limitations in three-dimensional cone-beam geometry, data completeness and low photon environments.¹⁵ This limitation can be overcome by carefully limiting the lower boundary of the reduced X-ray dosage to ensure acceptable image quality and by using iterative reconstruction (IR) techniques.¹⁶ IR techniques are mainly used to improve CT image quality by reducing quantum noise and artefacts. Several studies have demonstrated the ability of IR in improving image quality under low-dose conditions and improving the diagnostic accuracy of coronary CT angiography, in comparison with the standard FBP reconstruction algorithm.^{17–19} In addition, a research reported that the combination of low-concentration CM and a low tube voltage technique together with IR is a feasible method, providing sufficient contrast enhancement and image quality on CT aortography in adults.²⁰ In our study, scan data in both Group A and Group B were reconstructed using 70% ASIR algorithm; so, even though there was no additional advantage for Group A from reconstruction, the image noise impact with the lower X-ray dose in Group A was minimized by using ASIR. There was no difference in image noise and objective image quality score between the two groups, and all images were acceptable for clinical diagnosis.

The use of iodinated CM may increase the risk of acute renal failure. Using low-concentration CM to reduce the total iodine load is certainly a solution to reduce this risk. The decreased attenuation of using lower concentration CM may be compensated by using lower tube voltage. As mentioned before, low-concentration CM combined with IR algorithm, low tube

Table 4. Patient demographics, iodine load and radiation dose of CT scan

Parameters	Group A	Group B	<i>p</i> -value	
Number	45	65		
Age (months)	8.20 ± 4.37	8.57 ± 4.68	0.677	>0.05
Weight (kg)	7.36 ± 1.38	7.79 ± 1.38	0.116	>0.05
BMI	16.73 ± 2.61	17.31 ± 5.04	0.480	>0.05
Heart rate (bpm)	115.4 ± 2.10	119.9 ± 1.75	0.1007	>0.05
Iodine load (mgI)	3976 ± 747	5763 ± 1018		<0.001
DLP (mGy·cm)	15.29 ± 1.91	20.11 ± 2.13		<0.001
CTDI _{vol} (mGy)	1.35	1.81		<0.001
ED (mSv)	0.60 ± 0.08	0.77 ± 0.10		<0.001

BMI, body mass index; CTDI_{vol}, volumetric CT dose index; DLP, dose-length product; ED, effective dose.

Table 5. Quantitative and subjective analyses in different groups

Parameters	Group A	Group B	<i>p</i> -value	
CT value (HU)	429.4 ± 110.1	466.8 ± 91.62	0.055	>0.05
Noise	16.24 ± 1.41	16.67 ± 1.59	0.149	>0.05
CNR	21.84 ± 7.04	23.12 ± 5.92	0.306	>0.05
SNR	26.64 ± 7.35	28.28 ± 6.15	0.206	>0.05
Score (Observer 1)	4.60 ± 0.20		0.791	>0.05
Score (Observer 2)	4.61 ± 0.19			
Score (Observer 1)		4.64 ± 0.20	0.752	>0.05
Score (Observer 2)		4.65 ± 0.20		
Score (average)	4.60 ± 0.20	4.64 ± 0.19	0.139	>0.05

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

voltage and tube current technique is a feasible method for reducing both radiation dosage and iodine load. In our study, we demonstrated a 30% iodine load reduction with the use of a lower concentration iodine contrast agent (3976 ± 747 mgI vs 5763 ± 1018 mgI) and low tube voltage. Although the use of 270-mg iodine/ml CM provided lower enhancement than the 370-mg iodine/ml CM, there was no significant difference between the contrast enhancements of the two groups ($p > 0.05$). This result suggested that when using low-concentration CM, a low tube voltage helped to improve vascular attenuation. Another possible explanation could be that a lower concentrated CM might be advantageous in that as injection pressures proved to be lower with lower concentration, CM distribution within the blood may be accelerated.^{21,22} In addition, the lower concentration CM has lower peak pressures; so it benefits patients whose i.v. access is

small.²³ The standard deviation of the attenuation values in the two groups was considered somewhat broad, but still within the range of previous published data.^{20–22} This is an indication that attenuation values were quite variable, which might have a relationship with the variable body weight and other factors (e.g. cardiac output, heart rate).

The new CT cardiac scanning protocol provided clear views of the coronary arteries, resulting in 96% and 92% diagnostic accuracy for extracardiac and intracardiac defects, respectively, to demonstrate its added clinical application value in diagnosing children with CHD.

Our study has several limitations. First, the patient population in this study was limited to children with ages of 1 year and younger.

Figure 1. Transverse CT views of a 64-row CT scan: (a, b): the four-chamber heart level and aortic arch level of a 7-month-old female [weight 6 Kg, body mass index (BMI) 13.77, iodine load 4440 mgI, 80 kVp, 160 mA]; (c, d) the four-chamber heart level and aortic arch level of a 10-month-old male (weight 6 Kg, BMI 15.61, iodine load 3240 mgI, 80 kVp, 120 mA).

Figure 2. (a) A 6-month-old male in Group A: the left coronary artery is clearly shown. (b) A 22-month-old female in Group B: we can also clearly see the left and right coronary arteries.

In the future study, we will enrol older paediatric patients. Second, the evaluation of this study was still largely focused on image quality. Third, owing to the hardware limitation, we only used 80 kVp for imaging. For the patient size included in our study, a lower tube voltage may be more advantageous and further study using 70-kVp tube voltage is desirable.

CONCLUSION

In conclusion, compared with the standard dose protocol, the use of low-concentration iodinated contrast (270 mgI/ml) in

combination with 80-kVp tube voltage, low tube current (120 mA) and ASIR enables 30% reduction in iodine load and 22% reduction in radiation dose while maintaining compatible image quality and diagnostic accuracy in cardiac CT scans for children with CHD.

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