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Computed Tomography Coronary Angiography for Evaluation of Children With Kawasaki Disease

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Objective: We sought to assess the feasibility of computed tomography coronary angiography (CTCA) on a 128-slice, dual source scanner in children with acute and convalescent phase Kawasaki disease (KD).

Materials and Methods: A prospective study of 49 children with KD (12 at presentation and 37 in the convalescent phase) was conducted between November 2013 and April 2015. CTCA was performed with either prospective ($n = 37$) or retrospective ($n = 12$) electrocardiographic gating. A radiologist blinded to clinical profile and echocardiogram evaluated each scan.

Results: Median age (36 boys and 13 girls) was 7 years. Median dose-length product value and median effective CT radiation dose was 32 mGy cm (interquartile range [IQR]: 21–74) and 0.54 mSv (IQR: 0.77–3.2) for all scans, and 27 mGy cm (IQR: 18.5–33.75) and 0.48 mSv (IQR: 0.18–1.17) for prospectively triggered scans ($n = 37$). Fourteen subjects (30 coronary segments) showed abnormalities by CTCA including aneurysms ($n = 27$) and stenoses ($n = 3$). In the acute phase ($n = 12$), aneurysms were detected in 5 children (18 segments).

Conclusion: CTCA allows comprehensive evaluation of coronary arteries in children with KD.

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Introduction

Echocardiography has hitherto been the imaging modality of choice for assessment of coronary artery aneurysms in children with Kawasaki disease (KD), both during the acute phase and on follow-up.¹ It has several inherent advantages in that it is easily available, is relatively inexpensive and can be repeated as often as required. However, it is highly operator dependent and requires skill, patience and experience in interpreting the images, especially in infants and young children.² Further, one can only visualize proximal segments of coronary arteries and changes in the vessel wall are difficult to assess.^{3,4} Moreover, the acoustic window for adequate examination becomes limited as the child grows. Catheter angiography, though considered a gold standard for evaluation of luminal abnormalities, is not a valid option in young children in KD as it is invasive, requires general anesthesia, (GA) has a significant radiation exposure and cannot be repeated as often as required.^{2,5} Magnetic resonance coronary angiography is technically very challenging to perform and interpret in young children.⁶ Moreover, acquisition times are often prolonged (up to 90 minutes) and require GA.⁶

With advances in technology, computed tomography coronary angiography (CTCA) can be developed as a low-radiation imaging paradigm for children with KD.^{7–10} Advantages over echocardiography include the ability to visualize middle and distal coronary segments with little or no interobserver variability.³ Unlike catheter angiography, CTCA is noninvasive and clearly delineates intramural abnormalities. Besides, the measurements of coronary artery abnormalities (CAA) on catheter angiography correlate well with CTCA.¹¹

In the present study, we evaluated the feasibility of CTCA for assessment of CAA in children with KD in both the acute and convalescent phases of the disease.

Material and Methods

A prospective study comprising 49 children with KD was conducted between November 2013 and April 2015 at the Department of Radiodiagnosis and Imaging and the Department of Pediatrics, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India. Our Institute is a federally funded, not-for-profit tertiary level hospital in northwest India.

The study protocol was approved by the Institute Ethics Committee and the Departmental Publication Review Board. Written consent was obtained from the parents before performing the procedure.

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Patient Selection

A total of 12 children with newly diagnosed KD who either had an echocardiographic abnormality or had clinically severe disease were evaluated by CTCA. Furthermore, 37 children with KD on follow-up were selected for evaluation by CTCA. The median time from KD onset to imaging was 1.5 years (interquartile range [IQR]: 0.42–3.3).

Patient Preparation

CTCA was performed without sedation or anesthesia in children greater than 5 years. CTCA was done under short anesthesia (ketamine and midazolam) for children less than 5 years. GA was administered to 1 infant in the study. Oral metoprolol (2 mg/kg body weight) was administered to all children 30 minutes prior to CTCA. The aim was not only to achieve a low but also a stable heart rate.

Contrast Injection Protocol

Nonionic contrast (Omnipaque 350, GE Healthcare, Ireland) 2–4 mL/kg was injected at a rate of 4 mL/s (through 20G cannula) for children greater than 5 years, and 1.5–2.5 mL/s for infants and children less than 5 years, in the right antecubital vein. This was followed by a saline push with a dual head power injector. The acquisition was carried out using the bolus tracking technique with the circular region of interest set at the level of the descending thoracic aorta with threshold attenuation value of 100 HU.

CTCA Technique

CTCA was carried out on a second generation dual-source CT 128-slice scanner (SOMATOM Definition Flash, Siemens, Erlangen, Germany) with the following parameters: temporal resolution—75 milliseconds, gantry rotation time—0.28 seconds, slice thickness—0.6 mm. The scan was conducted in a craniocaudal direction from just below the carina to the diaphragm. At the beginning of the study, we used retrospective-triggered electrocardiogram (ECG)-synchronized CT scanning for data acquisition as we had the

apprehension that prospective gating might be inappropriate for the anticipated high heart rates in small children. We soon realized that it was feasible to carry out the same procedure with prospective-triggered ECG-synchronized CT scanning. The latter scanning protocol was carried out in 37 patients, and this enabled us to achieve low radiation exposures without compromising image quality. Adaptive prospective ECG-gating with full tube current was performed between 30% and 80% R-R interval (to obtain both systolic and diastolic images).

Scanning parameters were customized to ensure minimal radiation exposure (Table 1). The dose parameters of peak kilovoltage (kVp), milli-ampere second (mAs), and volume CT dose index were adjusted according to body size-adapted protocols that include body weight and cross-sectional area. Automatic Care kV was switched off and adjusted to 80 kVp in all children except for 4 subjects for whom it was reduced further to 70 kVp. These modifications, along with care-dose 4D tube current modulation, enabled us to reduce further the effective radiation dose. The lowest kVp and mAs values that ensured optimal image quality with minimum possible radiation exposure were selected. The mAs values ranged between 48 and 220. Effective CT radiation dose estimates were calculated by multiplying dose-length product (DLP) value and an appropriate conversion factor provided by the CT manufacturer (0.026, 0.018, and 0.014 for ≤ 1 year, 5–10 years, and > 10 years, respectively).

Postprocessing

Postprocessing was done on a dedicated Syngo.via workstation (Siemens, Germany) for reconstruction of the coronary arteries. Curved multiplanar reconstructions, maximum intensity projections, and volume rendered images were reviewed by the lead author (M.S.) who was blinded to details of clinical profile and echocardiography findings. A second radiologist (P.G.) correlated CTCA data with clinical data.

Assessment of Coronary Arteries

Coronary arteries were evaluated using the 13 segment model proposed by the American Heart Association (AHA).¹² Side

TABLE 1
Scan acquisition protocol

CTCA parameters	Details
Scan area	Floor of carina to base of heart
Data acquisition technique	Bolus tracking technique (region of interest in the ascending aorta with preset of 100 HU)
Scan delay	5 s after achievement of 100 HU
Kilo-voltage	80 kV
Tube current	Automatic exposure control system-based tube current modulation (Care-DOSE; Siemens Medical Solutions)
ECG gating	Adaptive prospective ECG-gating with full tube current between 30% and 80% R-R interval (to obtain both systolic and diastolic images)
Detector collimation	2 × 64 × 0.6 mm
Slice acquisition	2 × 128 × 0.6 mm by means of a z-flying focal spot
Gantry rotation time	280 ms
Temporal resolution	75 ms
Reconstructed slice thickness	0.75 mm with a reconstruction increment of 0.5 mm
Image window	Soft-tissue convolution kernel (B26f)
Image postprocessing	Syngovia (Siemens Medical Solutions). Images constructed in multiplanar, maximum intensity projection and volume rendering along with axial data set.
Contrast injection protocol	Dual head pressure injector with saline flush (saline flush for 5 s at same flow rate of contrast)
Calculation of contrast volume	Flow rate × (scan time + scan delay) *Fixed at 5 s
Contrast flow rates	24G cannula: 1.5 mL/s (2–4 mL/kg) 22G cannula: 2.5–3 mL/s (2–4 mL/kg) 20G cannula: 4 mL/s (2–4 mL/kg)
Beta-blocker	5 mg/kg oral 30 min prior to scanning. Intent was to stabilize rather can reduce heart rate.

TABLE 2
Effective CT radiation exposure according to age and type of ECG-triggering

Sl. no.	Age group	ECG-triggering			
		Retrospective		Prospective	
		Median radiation dose		Median radiation dose	
		DLP mGy.cm	Eff dose mSv	DLP mGy.cm	Eff dose mSv
1	0-1	-	-	10*	0.25*
2	1-5	112*	2.8*	20 (IQR: 20-40.5)	0.5 (IQR: 0.28-0.59)
3	6-9	100 (IQR: 74-144)	1.8 (IQR: 1.33-2.61)	29.5 (IQR: 25.15-38.5)	0.53 (IQR: 0.45-0.54)
4	10-12	142 (IQR: 102.2-185.5)	1.58 (IQR: 1.31-1.51)	32.5 (IQR: 17.75-66.75)	0.47 (IQR: 0.25-0.94)

* Single patient.

branches were included in the analysis wherever these were visualized.

Coronary artery imaging was graded on a 4-point scale for each coronary artery segment as follows: 1, excellent (no artifacts); 2, good (minor artifacts); 3, adequate (moderate artifacts); and 4, poor (severe artifacts impairing accurate evaluation). Clinically assessable images were those with scores of ≥ 3 .

Aneurysms were assessed in terms of number, shape, size, location, and presence of intraluminal thrombi. Aneurysmal dilatation was defined by an internal diameter ≥ 1.5 times that of an adjacent segment. Aneurysms were measured perpendicular to the long axis of the vessel at the site showing the greatest internal diameter. Aneurysms were defined as saccular if they had nearly equal axial and lateral diameters, and fusiform if they showed symmetric dilatation with gradual proximal and distal tapering. Categorization of aneurysms was as follows: small (< 5 mm), medium (5 mm to ≤ 8 mm), or giant (> 8 mm). The degree of luminal stenosis was graded as follows: no stenosis, mild stenosis ($< 50\%$), moderate stenosis (50%-69%), and severe stenosis (70%-99%).

Data Analysis

Scanning parameters (kVp, mAs, and DLP) were recorded. Heart rate at which data were acquired was recorded along with ECG tracing. Findings on echocardiography were correlated with abnormalities detected on CTCA in terms of number, shape, size, location, and presence of intraluminal thrombi.

Results

Demographic Characteristics

A total of 637 coronary artery segments were assessed in 49 subjects (36 boys and 13 girls). The median age of our cohort was 7 years (IQR: 5-9, range: 5 months-12 years).

Radiation Dose

Median DLP value was 32 mGy cm (IQR: 21-74) and median effective CT radiation dose was 0.42 mSv (IQR: 0.29-1.03) for all scans. In the prospective ECG-gated group ($n = 37$), median DLP was 27 mGy cm (IQR: 18.5-33.75) and median effective CT radiation dose was 0.37 mSv (IQR: 0.25-0.48). A CT dose less than 1 mSv was achieved in 36 of 37 children who underwent prospectively triggered CTCA. In the retrospective ECG-gated group ($n = 12$), the median effective CT radiation dose was 1.48 mSv (IQR: 1.09-1.98) (Table 2).

CAA on CTCA

All coronary segments were assessable by CTCA with no artifact ($n = 39$) and minor artifact ($n = 10$). Fourteen of the 49 subjects (28.6%) (29 coronary segments) showed abnormalities including aneurysms (27 segments) and stenoses (3 segments). Partial thrombosis was seen in 1 aneurysm. None of the segments showed calcification. Of the 27 aneurysms, 14 were small and 11 were medium. Two subjects had giant aneurysms. There were 5 saccular and 22 fusiform aneurysms. The mean diameter of aneurysms was 4.3 mm (range: 2.2-9 mm).

Echocardiography Findings at Presentation

Twelve children had both CTCA and echocardiography performed at the time of initial diagnosis. CTCA at presentation revealed abnormalities in 5 of 12 children (Table 3, Figs 1 and 2). The echocardiogram was abnormal in 5 patients (aneurysms). Aneurysms were detected in 2 segments, both involving left anterior descending (LAD)1, however, they were later not confirmed on CTCA. CTCA detected aneurysms in 5 segments, (LAD1 [$n = 2$], right coronary artery [RCA]1 [$n = 1$], RCA3 [$n = 2$]) not detected at echocardiography. Even in subjects for whom echocardiography detected an abnormality, the number of segments reported to be abnormal was less with echocardiography ($n = 7$) as compared to CTCA ($n = 18$). The segments in which

TABLE 3
Distribution of CAA on CTCA

Aneurysms	
RCA	8
RCA1	4
RCA2	1
RCA3	3
LCA	2
LCX	4
LCX1	3
LCX2	1
LCX3	0
LAD	9
LAD1	9
LAD2	0
LAD3	0
OM1	2
D1	1
Stenosis	
LCX1	2
D1	2

D1, first diagonal branch of LAD; LCX, left circumflex artery; OM1, first obtuse marginal branch of LCX.

FIG 1. Aneurysms of distal RCA and proximal LAD. Maximum intensity projection (A and C) and volume rendered (B and D) CTCA images in a 3-year-old boy at presentation of KD using prospective ECG-gated triggering (80 kVp, 34 mAs, DLP 13 mGy cm, effective dose 0.18 mSv, heart rate 104 beats per minute) shows 2 saccular aneurysms each in distal RCA (arrows, A and B) and proximal LAD (arrows, C and D). CTCA, CT coronary angiography; DLP, dose-length product; ECG, electrocardiogram; LAD, left anterior descending; RCA, right coronary artery. (Color version of figure is available online.)

echocardiography failed to detect abnormalities included RCA1 ($n = 2$), RCA2 ($n = 1$), RCA3 ($n = 3$), left Circumflex artery (LCX)1 ($n = 2$), LCA ($n = 2$), and D1 ($n = 1$).

Echocardiography Findings in Convalescence

The median interval from clinical presentation to CTCA was 1.5 years (IQR: 0.42–3.3). The mean interval between last echocardiography and CTCA was 1.7 years (IQR: 0.47–3.5). Comparison between echocardiography and CTCA was not performed in convalescent phase due to the long and rather heterogeneous lag between acquisitions of 2 modalities.

Of 9 children who showed abnormalities on CTCA, only 4 had documented abnormalities by echocardiography (Table 4, Fig. 3). Of 15 patients with abnormalities on echocardiography, CTCA abnormalities were detected in 9. This could be because of resolution of the abnormality during the intervening period as CTCA in these patients was performed later in the disease course.

Abnormalities on CTCA were reported in 5 children in whom echocardiography was reported as normal.

Discussion

In our study, the use of CTCA allowed detection of CAA in children with KD both during the initial and convalescent phases of the illness. CTCA was particularly helpful in imaging distal lesions that could not be assessed by echocardiography. CTCA has not been widely adopted for the assessment of children with KD because of the high radiation exposures with which this investigation has hitherto been associated.¹³ However, with advances in technology and refinement of radiation protocols it is now possible to carry out this investigation with minimal radiation exposure, at any heart rate, with free breathing and short (or no) anesthesia.^{14–17}

Dose-saving strategies in CTCA include child-size bowtie filter and scanning field of view, body size-adapted protocols including low tube voltage techniques; ECG-controlled and attenuation-based tube current modulations, and prospectively ECG-triggered sequential scanning. Lowering the kVp values (to 80) results in a significant dose reduction with acceptable image quality.¹⁸ In a recent study Kim et al had applied 80 kVp (besides attenuation-based and ECG-controlled tube current modulations, and prospectively

FIG 2. Aneurysms of RCA, LAD, D1, and LCX. Curved reformatted, maximum intensity projection axial and volume rendered CTCA images in an 5-year-old boy of KD at presentation using prospective ECG-gated triggering (80 kVp, 39 mAs, DLP 24 mGy cm, effective dose 0.33 mSv, heart rate 78 beats per minute) shows aneurysmally dilated RCA (long arrows), LAD and its D1 branch (thick arrows), and LCX (small arrow). CTCA, CT coronary angiography; D1, diagonal artery; DLP, dose-length product; ECG, electrocardiogram; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery. (Color version of figure is available online.)

ECG-triggered sequential scanning), for CTCA in children with KD.¹⁰ CT dose parameters (volume CT dose index is 15.3 ± 12.0 mGy; DLP, 229.0 ± 198.0 mGy cm; effective dose, 2.6 ± 2.6 mSv) were lower than those in previously reported studies.⁶ However, details of other scanning parameters were not reported in this study. Similarly, Duan et al¹⁹ performed all their scans at 80 kVp and reported images of sufficient quality in all patients with a mean effective dose of 0.36 ± 0.06 mSv. In our study clinically assessable images were

achieved in all children with the application of 80 kVp in 46 and 70 kVp in 3, without compromising image quality.

Prospective ECG-gating allows acquisition of data and thus X-ray output in a specific phase of the cardiac cycle, thereby reducing the radiation dose. In the study by Duan et al,¹⁹ the mean effective dose was reported to be 0.36 ± 0.06 mSv in 19 children who underwent prospective ECG-triggered dual source CT. Similarly, in a study by Kim et al⁶ on 5 patients with KD under the age

TABLE 4
Echocardiography (ECHO) and CT coronary angiography (CTCA) findings in acute phase of Kawasaki disease ($n = 12$)

S.No	Age (y)/sex	Echocardiography findings	CT coronary angiography findings
1	8/M	Normal	RCA1-fusiform aneurysm (5.3 mm) RCA3-saccular aneurysm (3.1 mm) LAD1-saccular aneurysm (8.6 mm)
2	3/M	Normal	LAD1-fusiform aneurysm (3.9 mm) RCA3-fusiform aneurysm (4.3 mm)
3	11/M	Proximal LAD fusiform aneurysm (6 mm) Rest of the coronary segments reported normal	LAD1-fusiform aneurysm (6.8 mm) LCX1- fusiform aneurysm (4.1 mm) RCA1-fusiform aneurysm (6.6 mm) RCA2-fusiform aneurysm (3.3 mm)
4*	10/M	Normal	Normal
5*	9/M	Normal	Normal
6	9/M	Normal	Normal
7#	2/F	Proximal LAD fusiform aneurysm (3 mm) Rest of the coronary segments reported normal	Normal
8	5/M	Proximal LAD fusiform aneurysm (7.2 mm) Proximal RCA fusiform aneurysm (7.1 mm) Rest of the coronary segments reported normal	LAD1- fusiform aneurysm (7.1 mm) LCA-fusiform aneurysm (3.7 mm) LCX1-fusiform aneurysm (3.9 mm) RCA1- fusiform aneurysm (4.4 mm) D1-fusiform aneurysm (2.2 mm)
9	7/M	Normal	Normal
10	12/M	Normal	Normal
11#	4/M	Proximal LAD saccular aneurysm (4.3 mm) Rest of the coronary segments reported normal	Normal
12	0.7/M	Proximal LAD fusiform aneurysm (7 mm) Proximal RCA fusiform aneurysm (6.4 mm) Rest of the coronary segments reported normal	LAD1-fusiform aneurysm (9 mm) LCA-saccular aneurysm (4 mm) RCA1-fusiform aneurysm (6.4 mm) RCA3-saccular aneurysm (2.7 mm)

D1, first diagonal branch of LAD; F, Female; M, male; LCA, left main coronary artery; LCX, left circumflex artery; OM1, first obtuse marginal branch of LCX.

* Technical problem.

Mistaken call by echocardiography.

FIG 3. Aneurysm of proximal LAD and LCX. CTCA images (prospective ECG-gating, 80 kVp, 75 mAs, DLP 54 mGy cm, effective dose 0.75 mSv, heart rate 55 beats per minute) of a 6-year-old boy with KD of 4 years duration who had dilated proximal LAD on echocardiography. Volume rendered (A and B) and curved reformatted (C) shows fusiform aneurysms of proximal LAD and LCX (arrows). CTCA, CT coronary angiography; DLP, dose-length product; ECG, electrocardiogram; LAD, left anterior descending; LCX, left circumflex artery. (Color version of figure is available online.)

of 2 years who underwent prospective ECG-triggered sequential CT scanning, the radiation dose was only 0.6 ± 0.5 mSv (range: 0.2–1.3 mSv). Huang et al.²⁰ reported that diagnostic quality images were possible in all cases with diagnostic accuracy up to 95.9%. Lee et al compared nongated, retrospectively gated and prospectively gated CTCA in 64-slice and 256-slice CT scanners. They concluded that the prospectively gated CTCA protocol allows one to balance radiation exposure and image quality for infant CTCA.²¹ We evaluated 37 patients with the prospective method with an effective dose comparable to recently published case series. Clinically assessable images were achieved in all children.

In KD, any segment of coronary arteries and their major branches can be involved, although the majority of aneurysms occur in proximal segments. On echocardiography, it is difficult to evaluate middle and distal segments of coronary arteries, particularly in older children.^{22,23} Besides, CTCA is superior to echocardiography in the assessment of coronary stenoses and calcifications.⁴

We have used oral metoprolol in all our patients prior to scanning. This was done to achieve a stable heart rate during the procedure. In our experience it is the variability in the heart rate, rather than the rate itself, that compromises data acquisition and image quality in CTCA. We were able to obtain good quality images even at heart rates as high as 130/min. None of our patients required a repeat study and all coronary arterial segments were assessable.

We recognize several strengths and weaknesses of our study. We have been able to achieve radiation exposures as low as 0.18 mSv through innovative techniques that have not been previously described. However, this remains a single center experience, and the number of subjects in the study is small. Our findings need to be replicated on a larger cohort, and in other centers, before definitive conclusions can be drawn. Nonetheless, our results emphasize the great potential of CTCA in the assessment of coronary arteries in children with KD in acute as well as convalescent phases of the disease. The other major limitation was lack of comparison of CTCA with echocardiography. This was due to the inclusion of large number of children in the convalescent phase of KD and heterogeneous time interval between acquisitions of data by 2 modalities. Furthermore, the clinical significance of detection of a greater number of CAA in a child is not clear at present.

In conclusion the recently introduced radiation-sparing strategies, particularly prospective ECG-triggering, allow CTCA to be

consistently performed at low radiation dose. It is likely that this technique will be increasingly used for assessment of coronary arteries in children with KD.

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