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Original Article

The diagnostic value of dynamic volume computed tomography angiography in children with anomalous origin of the left coronary artery from the pulmonary artery

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Abstract: There have been almost no reports on the technique of dynamic volume computed tomography angiography (DVCTA) in children with anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA). Twelve children with ALCAPA, aged 5 months to 15 years, were enrolled in this retrospective study to explore the clinical value of DVCTA in the diagnosis of ALCAPA in children. All patients underwent low-dose prospective ECG-gated 320-slice DVCTA and transthoracic echocardiography. Two radiologists evaluated the image quality of the DVCTA and recorded the radiation dose at the same time. The accuracy of DVCTA in the diagnosis of ALCAPA was 100%, with the left coronary artery (LCA) opening in the left wall of the pulmonary artery in 4 cases (33.3%), the right wall in 2 cases (16.7%), and the posterior wall in 6 cases (50.0%). All children completed 320-slice DVCTA at a single timepoint; all of the images were diagnosable, and the subjective score was 3.3±0.6, with good consistency between the evaluations performed by the two radiologists (k=0.79). From the echocardiographs of these cases, 4 cases (33.3%) of ALCAPA were diagnosed correctly, 4 cases (33.3%) were misdiagnosed as LCA-pulmonary artery fistula, and 4 cases (33.3%) were missed, including a small LCA that was not displayed in 2 cases. The average CT radiation dose was 0.83±0.57 mSv. Low-dose DVCTA clearly showed the origin, course, and collateral vessels of ALCAPA and could be used reliably for noninvasive diagnosis of ALCAPA in children.

Keywords: Computed tomography, ALCAPA, children, coronary anomalies

Introduction

Anomalous origin of the coronary artery from the pulmonary artery (ACAPA) is a life-threatening congenital heart disease. There are four types of ACAPA: origin of the left coronary artery from the pulmonary artery (ALCAPA), origin of the right coronary artery from the pulmonary artery (ARCAPA), origin of an accessory coronary artery from the pulmonary artery, and origin of the entire coronary circulation from the pulmonary artery [1]. ALCAPA, despite being more common than the others, is still an extremely rare congenital disability, accounting for 0.25% to 0.46% of all cases of congenital heart disease [2, 3]. ACAPA is easily misdiagnosed or missed because the clinical manifestations are mostly unspecific cardiac insufficiency, and the children's symptoms are insidious. In addition to the extremely poor prognosis, the mortality rate of patients without surgical treatment is extremely high. Up to 9 of 10 children with ALCAPA are expected to die within the first year of life if no surgical intervention is performed. Therefore, accurate diagnosis and prompt treatment are essential [4, 5].

Echocardiography is the initial diagnostic modality for ACAPA. However, ACAPA is easily misdiagnosed or missed because of the limitation of the sonographic window and operational experience in the observation of coronary artery

disease. A false sign can appear when the ostium of the left coronary artery (LCA) is close to the left sinus of Valsalva [6, 7]. Cardiovascular angiography is a conventional modality for the diagnosis of ACAPA, but this invasive examination is very risky for children.

In recent years, with the emergence of ECG gating technology, computed tomography angiography (CTA) has been used for noninvasive and accurate diagnosis of coronary artery disease. CTA has technical challenges in diagnosing coronary artery disease because of infants' rapid heart rate, their inability to hold their breath, and the small structure of their coronary arteries. This study intends to analyze the clinical data of 12 children with ALCAPA retrospectively and explore the clinical diagnostic value of 320-slice dynamic volume computed tomography angiography (DVCTA) in the diagnosis of young children with ACAPA.

Materials and methods

Case selection

We performed a retrospective single-center study of ACAPA cases confirmed by surgery from June 2010 to January 2020. A confirmed case was defined as an abnormal origin of the coronary artery from the pulmonary artery during the operation. All family members were informed of the specifics and risks of 320-slice DVCTA and signed informed consent.

DVCTA image acquisition

All subjects underwent 320-slice dynamic volume CT in a Toshiba Aquilion ONE scanner with a detector width of 16 cm and a rack rotation time of 0.35 s. An iodine allergy test was performed on all children before the examination. A 10% chloral hydrate solution (0.5-1.0 ml/kg) was administered orally to children who could not cooperate. At the same time, the children's vital signs were carefully monitored, and the scans were performed only after safety was confirmed. Each child lay flat, and his or her hands were lifted. The scanning range was from the upper limit of the thorax to 5 cm below the diaphragmatic surface of the left ventricle. The target scanning parameters were as follows: target ECG-gated scanning, with the target set at 55% of the phase of the R-R interval; a tube voltage of 80 kV; automated tube current modulation technology; detectors at 0.5 mm ×320 rows; a simulated heart rate of 60 bpm; a scanning time of 0.35 s; an X-ray tube rotation speed of 0.35 s/r. A dual-head power injector was used to inject nonionic iodinated contrast (ioversol 320 mg I/ml, kg +2 ml body weight) through a peripheral vein at a flow rate of (kg/10) ml/s followed by a 10-20 ml physiological saline chaser injected at the same time. The Sure Start contrast medium tracking technique was used, whereby the CT scan was manually triggered when a contrast threshold of 200-350 Hounsfield units (HU) was achieved in the left atrium and left ventricle on the monitoring sequence. Radiation dose parameters were recorded (volume CT dose index [CTDIvol] in mGy, dose-length product [DLP] in mGy·cm and effective dose [ED] in mSv). According to the infant-specific values of κ (0.039 for infants less than 3 months, 0.026 for infants between 4 months and 35 months and 0.018 for infants between 36 months and 95 months), the method for calculating the effective radiation dose was to multiply recorded DLP by κ [8].

Image interpretation

The infants' original images were imported into an external workstation (Vitrea workstation) for postprocessing reconstruction. The images with optimal phase are usually accomplished using volume rendering, maximum intensity projection, and multiple planar reconstructions, fully displaying the coronary artery, superior and inferior vena cava, heart, aorta, and pulmonary artery and vein. The images were diagnosed and analyzed by two experienced cardiac radiologists. The image quality was evaluated using a five-grade scoring system without the diagnostic results of the infants: Grade 5: excellent anatomical structures and excellent image quality; Grade 4: good anatomical structures and all structures interpretable; Grade 3: general anatomical structures, and the anatomical relationships required clinically could be defined with confidence; Grade 2: poor image quality or anatomical details and incomplete demonstration of anatomical structures; Grade 1: no useful information obtained. Examinations graded 3 or higher met the needs for clinical diagnostic purposes [9].

Statistical analysis

The consistency of subjective scores was compared by two radiologists using the κ test. A κ

Table 1. General situation of children with ALCAPA

Case	Sex	Age	DVCTA				Echocardiogram	Operation
			Origin site on PA (CT)	Course	Collateral vessels	Complications		
1	M	5 months	posterior wall	normal	LCA and RCA not enlarged	present[a]	misdiagnosed	confirmed
2	M	9 months	right wall	normal	LCA and RCA not enlarged	present[a]	missed	confirmed
3	F	14 months	right wall	normal	RCA dilation and tortuous	present[a]	confirmed	confirmed
4	F	10 months	left wall	normal	LCA and RCA not enlarged	present[a]	confirmed	confirmed
5	F	23 months	posterior wall	normal	LCA dilation	present[a]	confirmed	confirmed
6	F	10 years	left wall	normal	rich	present[a]	confirmed	confirmed
7	M	5 months	posterior wall	normal	LCA and RCA not enlarged	present[a]	missed	confirmed
8	F	8 months	posterior wall	normal	LCA and RCA not enlarged	present[a]	missed	confirmed
9	F	1 month	left wall	normal	LCA and RCA not enlarged	present[b]	missed	confirmed
10	M	6 months	posterior wall	normal	LCA and RCA not enlarged	present[a]	missed	confirmed
11	M	13 years	left wall	normal	rich	present[a]	misdiagnosed	confirmed
12	F	15 years	posterior wall	normal	LCA dilation	present[a]	misdiagnosed	confirmed

Notes: M: male; F: female; PA: pulmonary artery; LCA: left coronary artery; RCA: right coronary artery; a: enlargement of the left ventricle and formation of a ventricular aneurysm; b: pulmonary arterial hypertension.

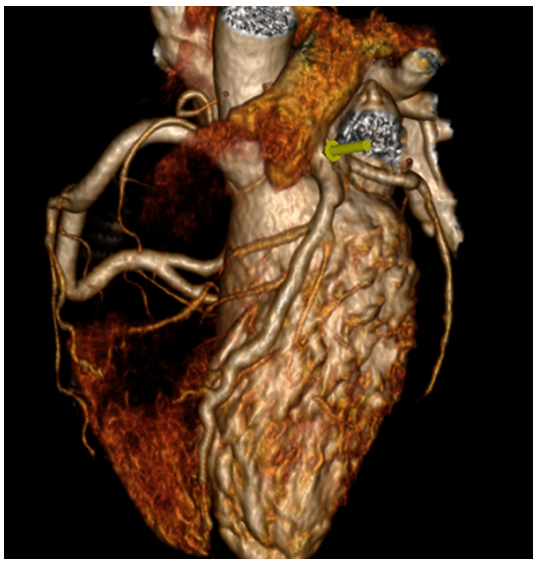

Figure 1. Images obtained in patient 6, a 10-year-old girl with a cough. The scan was performed at 80 kVp and 114 mAs after injection of 30 mL of iodinated contrast medium (320 mg I/mL) at 1.9 mL/s, and the mean heart rate during the scan was 72/min. Volume-rendered imaging was performed to define the LCA originating from the left lateral aspect of the pulmonary artery.

value of 0.21-0.40 indicates poor consistency, 0.41-0.60 indicates moderate consistency, and 0.61-0.80 indicates good consistency. The accuracy of ALCAPA diagnosis by DVCTA was calculated with surgical results as the diagnostic criteria.

Results

Demographic and clinical characteristics

Twelve cases of ACAPA were included in this study, and their 320-slice DVCTA images and related clinical data (**Table 1**) were analyzed. The subjects comprised 5 males and 7 females; the youngest was 5 months old, and the oldest was 15 years old. These young children were admitted with a heart murmur or cardiac dysfunction, and 2 cases were complicated with purpura. All children underwent echocardiography before 320-slice DVCTA.

Interobserver consistency of CT visual quantitative evaluation

All children completed 320-slice DVCTA at a single timepoint, and there were no obvious adverse reactions. The images from all patients met the requirements for clinical diagnostic purposes, with an average image score of 3.30±0.6, and the image quality evaluation of the two radiologists showed good consistency (K=0.79). The average CT radiation dose was 0.83±0.57 mSv.

DVCTA imaging findings

The DVCTA images clearly showed the specific location of the abnormal origin of the LCA in the pulmonary artery, and the diagnostic accuracy of ALCAPA was 100%. The specific location of the origin was as follows: 4 patients (33.3%, **Figure 1**) had a left-sided ostium of the pulmonary trunk, 2 patients (16.7%, **Figure 2**) had a right-sided ostium, and 6 patients (50.0%, **Figure 3**) had a posterior ostium. Among them, the courses of the main trunk and branches were normal in all patients.

The RCA was distorted and the lumen dilated to varying degrees in 5 cases, with enlarged coronary collateral vessels including the right conus

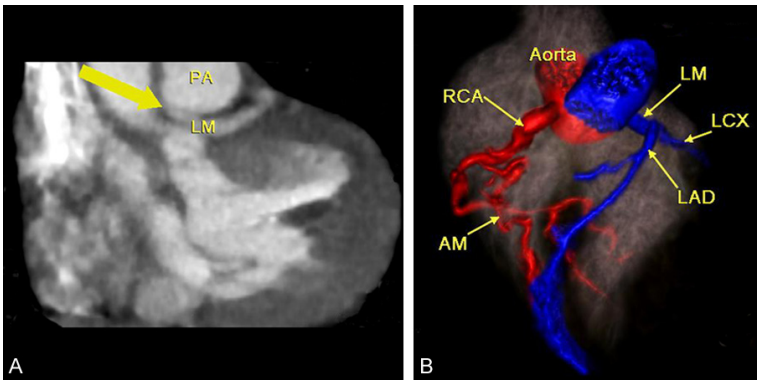

Figure 2. Images obtained in infant 3, a 14-month-old, 9.5-kg girl with heart failure. 12 mL of contrast at 320 mg I/mL was injected at a rate of 1 mL/s, and 10 mL of saline was injected at a rate of 1.0 mL/s. An anomalous LCA arising from the right lateral aspect of the pulmonary artery (A) was visible in coronal MPR. Volume-rendered coronary tree images (B) showed an extended and tortuous RCA.

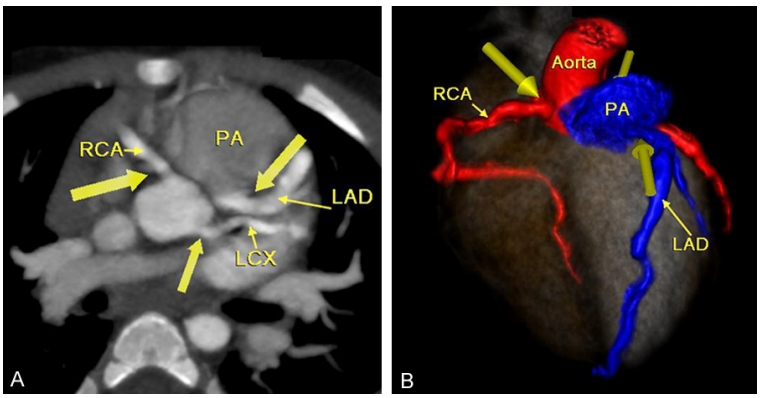

Figure 3. Images obtained in patient 5, a 23-month-old, 11-kg girl with a cardiac murmur. 13 mL of contrast at 320 mg I/mL was injected at a rate of 1.1 mL/s, and 10 mL of saline was injected at a rate of 1.1 mL/s. The axial image (55% phase of the RR interval) clearly demonstrated that the LCA originated from the posterior aspect of the pulmonary artery (A), while the left circumflex artery originated from the left sinus of Valsalva. Volume-rendered coronary tree images (B) showed an extended LCA.

artery and the right marginal branch. No enlarged collateral vessels or dilation appeared in the other 7 cases.

All 12 cases showed enlargement of the left ventricle to different degrees and ventricular aneurysm formation at the apex. One patient had pulmonary arterial hypertension, 7 patients had significant expansion of the left ventricle, and 4 patients had pulmonary inflammation.

Comparison with transthoracic echocardiography

Four cases (33.3%) of ALCAPA were diagnosed correctly, with retrograde blood flow in the LCA. In 1 of these patients (8.3%), the anomalous vessel arose from the left lateral aspect of the pulmonary artery trunk; in 1 patient (8.3%), it arose from the right lateral aspect; in 2 patients, it arose (16.7%) from the posterior aspect. The other 4 cases (33.3%) were misdiagnosed as LCA-pulmonary artery fistula. Four cases (33.3%) were missed because the retrograde blood flow was too fine to be seen. All cases had dilatation of the left ventricle to different degrees, and 4 cases had weakened motion of the left ventricle wall. All of them were found to have abundant coronary blood flow signals in the interventricular septum myocardium.

Discussion

Pathology and clinical treatment of ACAPA

In ACAPA, LCA, RCA, or their branches abnormally originate from the pulmonary valve sinus or pulmonary trunk, while the distribution and course of the coronary arteries are normal and are among the most severe congenital coronary artery malformations. The most common ACAPA is ALCAPA, which Bland, White, and Garland first described in 1933. Therefore, it is also known as Bland-White-Garland syndrome, a rare and extremely severe extracardiac vascular malformation [10, 11]. ARCAPA has been reported only in isolated case reports [12]. ACAPA is usually a single malformation, which may be accompanied by ventricular septum defects (VSDs), atrial septum defects (ASDs), patent ductus arteriosus (PDA), coarctation of the aorta, or other heart anomalies [13]. In this study, 7 patients with isolated LCA originating from the pulmonary artery had enlargement of the left ventricle to different degrees and formation of ventricular aneurysms at the apex.

The severity of symptoms was determined by the pressure changes in the systemic circula-

tion and pulmonary circulation as well as the time and the number of collateral vessels established between coronary arteries. In the early stage of the neonatal period, mild myocardial hypoxia may occur due to the high pulmonary artery pressure and the abnormal origin of the coronary artery supplied by the pulmonary artery. In the later stage, the pulmonary artery pressure continued to decrease due to physiological occlusion of the ductus arteriosus. The coronary artery blood supply of the infants mainly relied on collateral circulation from the contralateral coronary artery. Therefore, severe myocardial ischemia often occurs at this stage, resulting from decreased coronary perfusion pressure caused by insufficient collateral circulation compensation and coronary artery dilation [14]. Cardiac enlargement, cardiac dysfunction, formation of ventricular aneurysm, calcification of endocardium and papillary intima, and mitral regurgitation caused by mitral papillary muscle ischemia may present simultaneously. In this study, a case of ALCAPA was diagnosed at 6 months, with a long duration of myocardial ischemia. Calcification of the endocardium and papillary intima was observed, the left ventricle was significantly enlarged, and a ventricular aneurysm at the apex of the left ventricle was formed.

The collateral circulation between the left and right coronary arteries is divided into an infant type and an adult type [15]. The infant type has few or no intracoronary collaterals and a reduced myocardial blood supply, and cardiac enlargement and cardiac dysfunction are usually present in the early stage. In contrast, well-established collateral vessels are classified as the adult type, but patients with this type of circulation are prone to fatal arrhythmias. In this study, well-established collateral vessels were found in 4 cases and no collateral vessels in 8 cases. Early restorative surgical treatment for a dual-coronary-artery circulation system restored myocardial perfusion and normal systolic function of the left ventricle, thus improving the survival rate.

Imaging evaluation methods for ALCAPA and their advantages and disadvantages

ALCAPA is easy to miss or even misdiagnose due to the lack of specificity of its clinical, electrocardiographic, and biochemical features. Thus, the accurate diagnosis of ALCAPA is of great importance. The diagnostic process must rely on imaging examinations, including chest X-ray, echocardiography, magnetic resonance imaging (MRI), CT, and coronary angiography. Chest X-rays can show only the changes in the shape of the heart and pulmonary circulation. Echocardiography can detect the retrograde flow of the LCA to make a qualitative diagnosis and show concomitant lesions. However, echocardiography is susceptible to the acoustic window and relies on the operator's experience and skills to some extent [6, 16]. A study by Wang et al. suggests that ACAPA cannot be diagnosed when echocardiography fails to detect the openings of the coronary artery [17]. In this study, 4 cases (33.3%) were misdiagnosed and 2 cases (33.3%) were missed on echocardiography. MRI was limited with a longer examination time and lower spatial resolution, and it also required general anesthesia [18]. Coronary angiography is the conventional modality for the definite diagnosis of ACAPA, as it can fully display the coronary artery and its collateral circulation and reveal whether the artery has an abnormal origin. Thus, it provides important information for surgery [19, 20]. However, angiography is an invasive examination and can easily induce arrhythmia during surgery, aggravating heart failure and even leading to death. In addition, it may not show abnormal coronary arteries due to pressure changes between the aorta and pulmonary artery.

Advantages of DVCTA in the diagnosis of ACAPA

The limitations of CT in infant coronary artery imaging include the small size of the coronary artery, which requires high spatial and temporal resolution, the fast heart rate of the subjects, which is difficult to control at an ideal level with drugs, and the inability of infants to hold their breath during ECG-gated scanning. Additionally, radiation doses must be controlled at lower levels for infants compared with adults, as infants are more sensitive to radiation. In recent years, various CTAs have been used to diagnose coronary artery diseases and recognized as the imaging modality of choice suitable for fast and accurate diagnosis of coronary abnormalities in infants and children [21, 22]. The direct CTA sign of ACAPA is that the coro-

nary artery originates from the pulmonary artery sinus or above the sinus. The indirect signs are compensatory dilatation of the contralateral coronary artery, formation of collateral vessels and ventricular aneurysm, ventricular enlargement, and so on. The formation of collateral vessels is especially common. In this study, 4 cases of ALCAPA showed dilatation of the LCA and formation of collateral vessels.

The advantages of 320-slice DVCTA in the diagnosis of infant ALCAPA are mainly shown in the following aspects

First, a 320-slice dynamic volume CT scanner has a 160-mm-wide detector covering the entire chest of the infant and takes only 0.35 s to rotate once. Therefore, it completely overcomes the influence of heartbeat, respiration, and other factors on image quality. It also completely avoids the phenomenon of inconsistency over the course of the scan, as is found in traditional multislice spiral CT contrast-enhanced scanning, and it eliminates the scanning motion artifacts caused by the moving bed, which greatly improves the examination success rate and the image quality. In this study, all subjects completed the 320-slice DVCTA successfully at a single timepoint, and the image quality was sufficient for diagnostic purposes.

Second, the radiation dose of CT is affected by many factors, such as detector, rack, scanning mode, and software control. Volume scanning with 320-slice CT greatly reduces exposure time by eliminating the need to take overlapping scans and reconstruct images from overlapping datasets, as was necessary in the previous multislice spiral CT techniques. In this study, a target prospective ECG-gated technique was used to achieve a whole cardiac scan in one cardiac cycle by using sector acquisition with extremely high temporal resolution. The target scanning mode was used to trigger the single-sector volume scanning by ECG gating according to an external simulated heart rate. The time resolution of the target scanning mode was 180 ms, much lower than the 350 ms volume. The target scanning mode needs only 180 ms to obtain the original data. Dynamic imaging of the heart for 180-350 ms is obtained by post-scanning reconstruction. Afterward, high-quality images are selected from the period with minimum artifacts from the heartbeat and respiratory motion. The average CT radiation dose in this study was approximately 0.83±0.57 mSv, which was lower than the radiation dose produced by the retrospective ECG-gated scanning method reported in the literature (1.11-1.62 mSv) [21]. The feasibility of diagnosing ALCAPA at a low radiation dose was preliminarily confirmed.

Third, without increasing the total amount of contrast medium, the right atrium and ventricle, the pulmonary artery and vein, the left atrium and ventricle, the ascending aorta, and even the coronary artery could be shown with a single examination. In this way, 320-slice DVCTA provides “one-stop” access to comprehensive imaging information in cardiovascular diseases. In this study, the total amount of contrast medium was approximately 8.0-10.0 mL.

Fourth, the comprehensive application of various postprocessing techniques of 320-slice CT can display ALCAPA more comprehensively and achieve almost the same effect as digital subtraction angiography (DSA). 320-slice CT can also be used to observe the coronary artery from multiple angles, clearly showing the abnormal origin, course, and collateral circulation of the coronary artery. Simultaneously, 320-slice CT can identify atrioventricular, macrovascular, and lung lesions to provide sufficient evidence for the final diagnosis and serve as a preoperative examination method for ALCAPA. Multiplanar reconstruction (MPR) images can be used to observe the abnormal origin of the coronary artery. It can accurately measure the diameter of the coronary artery, the diameter of collateral vessels, the size of the ventricular cavity, and the thickness of the ventricular wall and identify concomitant malformations. The maximum density projection (MIP) images of thin layers are more suitable for observing small collateral vessels. Volume rendering technique (VRT) images allow comprehensive, stereoscopic, intuitive observation of the origin and course of the coronary artery and its overall positional relationship with the aorta and heart, which plays an important role in the formulation of the surgery program [23, 24].

Fifth, age or duration of symptoms does not affect the diagnosis effectiveness of DVCTA, and its diagnostic accuracy rate was higher

compared with that of echocardiography in younger children.

Limitation and deficiencies of DVCTA in the diagnosis of ACAPA

DVCTA has high accuracy in the qualitative diagnosis of ALCAPA. Nevertheless, it has limitations in showing small collateral vessels, revealing the direction of collateral blood flow, and enabling calculation of the flow rate. On the one hand, as the age grows, the diameter of the coronary artery and the collateral vessels would increase with each passing year. Larger blood vessels make it easier to observe the origin of the coronary arteries and blood perfusion in the pulmonary artery. On the other hand, from a theoretical point of view, the clinical symptoms of the ALCAPA in neonates were not easy to catch. With the gradual decrease of pulmonary artery pressure, the child gradually developed symptoms of myocardial ischemia. This series of factors would improve the accuracy of ultrasound diagnosis. To better confirm our conclusions, if stratified by age, there may be a difference in diagnostic efficacy between DVCTA and echocardiography. Echocardiography is comparatively accurate in the determination of the heart cavity malformation (atrial septum, interventricular septum, heart valves), but poor in the display of extracardiac vascular malformations [25]. What's more, it is difficult to evaluate the conditions of coronary artery and its collateral vessels due to the influence of acoustic window and intrapulmonary gas interference. However, in our study, because the number of ALCAPA cases was limited, it is difficult to objectively give clear conclusions. Overall, the limitations of this retrospective analysis are as follows. First, the data in this study were from a single center, and relatively few cases were collected, which may limit the representativeness of the data. Second, it is necessary to further improve the technical scanning program to obtain higher quality images while minimizing the radiation dose.

Conclusion

DVCTA is a "one-stop", single-scan examination with a low radiation dose, low total usage of contrast medium, and a wide range of adaptation. Through the comprehensive application of various postprocessing techniques, DVCTA can directly and accurately display the ostium, course, and related indirect signs of ALCAPA, such as compensatory dilatation of the contralateral coronary artery, the formation of collateral vessels, and ventricular enlargement. Therefore, DVCTA is a reliable method to obtain thorough knowledge of the imaging manifestations of coronary origin anomalies for early diagnosis of ACAPA, which is imperative for precise diagnosis and subsequent treatment planning.

Disclosure of conflict of interest

None.

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