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Full Length Research Paper

Diagnosis of complicated congenital heart diseases in neonates and infants using 64-slice spiral CT

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Although Ultrasonic Cardiography (UCG) is effective, non-invasive, and the most commonly used examination method for Congenital Heart Disease (CHD), other modern medical imaging modalities such as Computed Tomography (CT) are needed to further clarify the disease before surgical intervention. To explore the clinical value of CT in diagnosis of complicated CHD in neonates and infants compared with UCG, 103 neonates and infants with clinically diagnosed complicated CHD underwent cardiac CT angiography (CTA) with a 64-slice CT scanner. UCG and surgical operations were performed in all patients, and 22 patients received Diagnostic Cardiac Catheterization (DCC). The accuracy rate of CTA was higher than that of UCG in detecting deformities of complicated CHD. CTA was as accurate as UCG in revealing intracardiac deformities but superior to UCG in identifying extracardiac deformities. Combining UCG with CTA could improve the definite diagnostic rate of deformities to 99.53%. In the 22 patients who received DCC, CTA was as accurate as DCC in revealing cardiac deformities. CTA with a 64-slice CT is a credible technique for diagnosis of complicated CHD in neonates and infants. After initial assessment with UCG, CTA can be used to replace DCC for further accurate clarifications.

Key words: Congenital heart disease, 64-slice CT, ultrasonic cardiography, diagnostic imaging.

INTRODUCTION

Although Ultrasonic Cardiography (UCG) is effective, non-invasive, and the most commonly used examination method for Congenital Heart Disease (CHD), other modern medical imaging modalities such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are sometimes needed to further clarify the disease before surgical intervention (Curtis and Stuart, 2005). Clarification is needed because complicated CHDs may be usually associated with developmental anomalies of the Aortic Artery (AA), Pulmonary Artery (PA) and/or Coronary Artery (CA). It is a standard clinical practice for diagnostic Cardiac Catheterization (DCC), which has a small but recognized risk, to be performed as an invasive method if UCG fails to provide a confident evaluation of the lesions. However, non-invasive cardiac imaging using multi-slice CT (MSCT) or MRI has evolved rapidly (Ley et al., 2007). Because of its limitations (e.g., requiring a long time for the scan and low-resolution image quality), MRI is not suitable for children with complicated CHD, whose condition is often unstable. With the development of MSCT (especially 64-slice CT or more advanced CT), CT angiography (CTA) became more acceptable to referring physicians and patients (Mertens et al., 2008; Nikolaou et al., 2004). However, it is not known how the new approach compares with UCG and DCC in diagnosing complicated CHD in neonates and infants. In this study, cardiac CTA with 64-slice CT was performed on neonates and infants with complicated CHD to assess its value in diagnosing complicated CHD.

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MATERIALS AND METHODS

Clinical data

The protocol for this study was approved by our institutional ethics committee on clinical research. Before CT examination, the potential risks of radiation exposure and contrast medium injection were explained to the parents. Written informed consent was obtained from all parents.

From April 2007 to March 2010, CTA was performed in 103 neonates and infants who were clinically diagnosed with complicated CHD (72 males, 31 females; age: 4 days to 43 months, the average age 324.92 days; weight: 2.8 to 15 kg, the average body weight 7.64 kg). CHD was considered when a child experienced cyanosis, growth retardation, cardiac failure, pathological noise at auscultation. UCG was routinely performed. If complicated CHDs such as right-to-left shunt are detected, CT examination is required. DCC was employed in 22 patients, all of whom were infants (17 males, 5 females; age: 125 days to 43 months, the average age 550.91 days; weight: 6.5 to 13 kg, the average body weight 9.74 kg).

CT examination

CT scans were taken using a Somaton Sensation Cardiac 64 (Siemens AG, Forchheim, Germany) in all patients. A 50 mg/kg dose of chloral hydrate was taken orally as a sedative before the scan for breathing control. Omnipaque (350 mg/ml; Iohexol, GE Healthcare, Ireland) in a dose of 1.2 ml/kg was injected through a peripheral vein (a 24-gauge intravenous catheter was placed in the dorsal aspect of the right hand) at a rate of 1.5 ml/s, followed by the same volume of normal saline at the same injection rate. Bolus tracking was used in the arterial phase to inspect contrast enhancement in the descending aorta at the level of the carina, a point that is always easily identified on the plain image. After the contrast enhancement reached 80 HU, a 9-s post-threshold delay was applied before the scan.

The scans covered an area from the upper margin of the shoulder to the lower end of the liver. The parameters of the scans included a 0.33 s rotation time, 1.2 spiral distance, 0.6 mm collimation, 0.6 mm slice thickness, 80～100 kV voltage, and 80–100 mAs tube-current. The pitch of the acquisition was 1.2.

Image post-processing

After the scan, a 1 mm reconstruction increment, 0.6 mm reconstruction distance, and Kernel B25f reconstruction manner were used. All reconstructed images were loaded into the CT work station (Syngo Multi Modality Workplace). Multiple Planar Reformation (MPR), Volume Rendering (VR), and Maximum Intensity Projection (MIP) analyses were performed for all patients. The radiological findings were interpreted by two senior radiologists (Yang and Gong (2008).

Outcome measures

All malformations of the heart and major blood vessels confirmed by surgery and detected by UCG, CTA, and DCC, including intracardiac deformities and extracardiac anomalies, were recorded. The false positive and false negative diagnoses from UCG, CTA, and DCC were noted, and the diagnostic accuracy rates for UCG, CTA, and DCC as well as the sensitivity and specificity of CTA and UCG were calculated.

Statistical analysis

Statistical analysis was performed using commercially available software (SPSS 11.5 for Windows; SPSS, Inc.). Comparisons were performed with Chi-Square tests using *n*-1 degrees of freedom to test for any significant differences with regard to the diagnostic accuracy rate between CTA and UCG and the deformity rates of complicated CHD detection for CTA and DCC. Similarly, comparisons of the sensitivity and specificity of CTA and UCG were performed using Chi-Square tests. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 423 malformations in 103 patients were confirmed by surgery, as shown in Table 1. The accuracy rates of CTA and UCG in detecting deformities of complicated CHD were 97.16 and 83.22%, respectively. CTA was superior to UCG in detecting deformities of complicated CHD (χ^2 = 46.502, p = 0.000). Combining CTA with UCG could improve the definite diagnostic rate to 99.53% (421/423). The number of false positive and false negative diagnoses resulting from CTA and UCG is also shown in Table 1. The sensitivity of CTA (97.40%) was superior to that of UCG (85.34%) (χ^2=38.995, p=0.000), and the specificity of CTA (99.76%) was superior to that of UCG (97.57%) (χ^2=7.426, p=0.006).

A total of 163 intracardiac deformities and 260 extracardiac anomalies were surgically confirmed in 103 patients. The intracardiac deformities visualized included various diseases such as ventricular septal defect (VSD) (Figure 1), Atrial Septal Defect (ASD) (Figure 2), Complete Endocardial Cushion Defect (CECD), single ventricle, hypoplastic left heart, right ventricular hypertrophy, and dexiocardia. A total of 260 extracardiac anomalies, including transposition of the great arteries (TGA) (Figure 3), double-outlet ventricle (Figures 4 to 6), truncus arteriosus, aortic striding, Anomalous Pulmonary Venous Connection (APVC), pulmonary venous stenosis, pulmonary artery stenosis, pulmonary artery atresia (Figure 7), aortic coarctation, anomalous aortic origin or pulmonary artery origin (such as aberrant subclavian artery, double aortic arches, dextroaortic arch, pulmonary artery sling), Patent Ductus Arteriosus (PDA), and abnormal coronary artery, were detected.

A total of 154 of 163 (94.48%) intracardiac deformities were demonstrated by CTA, whereas 160 of 163 (98.16%) were demonstrated by UCG (χ^2 = 3.115, p=0.078). The false negative patients included eight ASD and one CECD patients with CT and two right ventricular hypertrophy and one dexiocardia patients with UCG. In addition, dexiocardia was misdiagnosed in a patient assessed with CT.

Extracardiac anomalies were visualized in 257 of 260 lesions with CTA (98.85%) and 192 of 260 (73.85%) with UCG (χ^2 = 68.917, p = 0.000). False negative diagnoses using CTA occurred in two aortic striding and one perpetuation of left superior vena cava patients; with UCG, false negatives occurred in 68 lesions of varying types. In addition, nine anomalies were misdiagnosed with UCG.

A total of 100 malformations from 22 patients examined with DCC were confirmed by surgery, as shown in Table

Table 1. Comparison of CTA and UCG in the diagnosis of cardiovascular malformations.

Cardiovascular malformations	Number confirmed	UCG			CTA		
		Number diagnosed	False positive	False negative	Number diagnosed	False positive	False negative
VSD	72	72	0	0	72	0	0
ASD	54	54	0	0	46	0	8
CECD	2	2	0	0	1	0	1
Single ventricle	2	2	0	0	2	0	0
Hypoplastic left heart	2	2	0	0	2	0	0
Right ventricular hypertrophy	28	26	0	2	28	0	0
dexiocardia	3	2	0	1	4	1	0
TGA	6	5	0	1	6	0	0
double-outlet ventricle	11	10	0	1	11	0	0
Truncus arteriosus	9	10	1	0	9	0	0
Aortic striding	28	27	0	1	26	0	2
APVC	4	3	1	2	4	0	0
Pulmonary venous stenosis	5	1	0	4	5	0	0
Absence of superior vena cava	1	1	0	0	1	0	0
Left superior vena cava	11	4	1	8	10	0	1
Pulmonary artery dilation	25	24	0	1	25	0	0
Pulmonary artery atresia	15	12	1	4	15	0	0
Pulmonary artery stenosis	34	37	5	2	34	0	0
Aortic coarctation	16	16	0	0	16	0	0
Interrupted aortic arch	1	1	0	0	1	0	0
Pulmonary artery sling	1	0	0	1	1	0	0
Aberrant subclavian artery	11	0	0	11	11	0	0
Double aortic arches	2	0	0	2	2	0	0
Dextroaortic arch	15	10	0	5	15	0	0
PDA	29	25	0	4	29	0	0
Aortopulmonary window	1	0	0	1	1	0	0
Aortopulmonary collaterals	29	15	0	14	29	0	0
Abnormal coronary artery	6	0	0	6	6	0	0
Total	423	361	9	71	412	1	12

Abbreviations: CTA=CT angiography, UCG=ultrasonic cardiography, VSD=ventricular septal defect, ASD=atrial septal defect, CECD=complete endocardial cushion defect, TGA=transposition of the great arteries, APVC=anomalous pulmonary venous connection, PDA=patent ductus arteriosus.

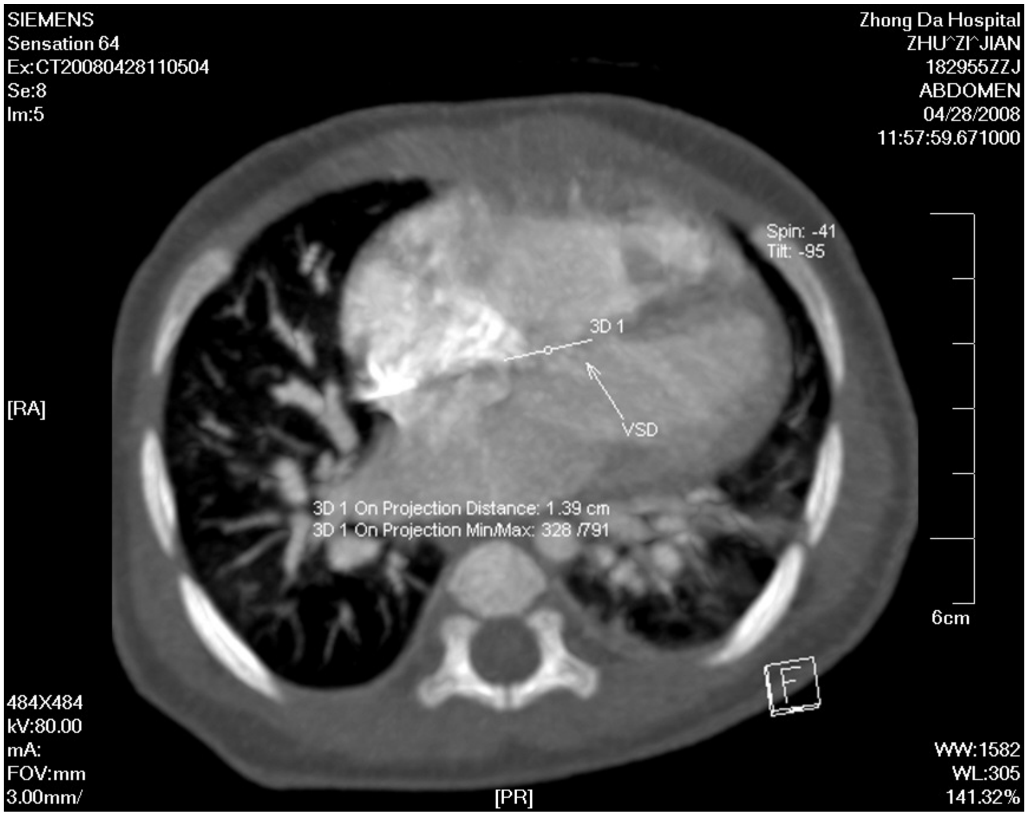

Figure 1. MIP of four cavities heart shows VSD (arrow).

2. DCC found 99 cardiac deformities and missed 1 right ventricular hypertrophy case. CTA found 98 cardiac deformities, missed 3 ASD cases, and misdiagnosed 1 dexiocardia case. The accuracy rates of DCC and CTA were 99.0 and 97.0%, respectively. CTA was as accurate as DCC with respect to revealing cardiac deformities (χ^2=1.020, p=0.312).

DISCUSSION

The 64-slice CT adopts a folium isotropy detector and utilizes a faster scan speed than earlier MSCT techniques due to its shorter rotation time of 0.33 s. Meanwhile, it adopts an advanced brainpower sieve, tube-current auto-modulate, and auto-setup techniques. The scan radiation dose is reduced dramatically, so it is much safer for use in children (especially neonates and infants) (Nikolaou et al., 2004; Paul and Abada, 2007). In this study, a weight-based low-dose CT protocol (80-100 kV) was used with automatic tube current modulation software (CAREDose4D, Siemens Medical Solutions). The pitch of the acquisition was 1.2. Meanwhile the time taken to complete the entire chest scan was only about 3.0 s, and the faster scan speed decreased false movement images (e.g., those due to respiration and the heartbeat). Therefore, a 64-slice CT can be used in neonates and infants, and we believe the CT examinations are necessary in our patients of the study, although, we knew the children would take some dose radiation exposure during the examination of CT. All neonates and infants, including those with the clinically unstable conditions, underwent successful inspection because the patients did not need to hold their breath during the examination process.

The setup of the scan delay time is very important after contrast medium injection (Dawson, 2004). In the arterial phase, bolus tracking was used to inspect the contrast enhancement in the descending aorta. After the enhancement reached 80 HU, a 9-s post-threshold delay was applied before the scan. All images in the 103 patients demonstrated a satisfactory enhancement effect. In order to visualize accurately the anatomical structure of the vasculature and heart in neonates and infants, we chose an effective slice thickness of 0.6 mm, a reconstruction increment of 1.0 mm, and a reconstruction distance of 0.6 mm. As a result, the examination process of CTA was smooth. The images of the anatomical structure were acquired in a satisfactory manner, and no complications related to the examination (e.g., renal impairment) occurred.

With the maturity of CTA technique, the 3-D post-processed images from 64-slice CT can wholly and directly depict the heart’s structure, as well as its

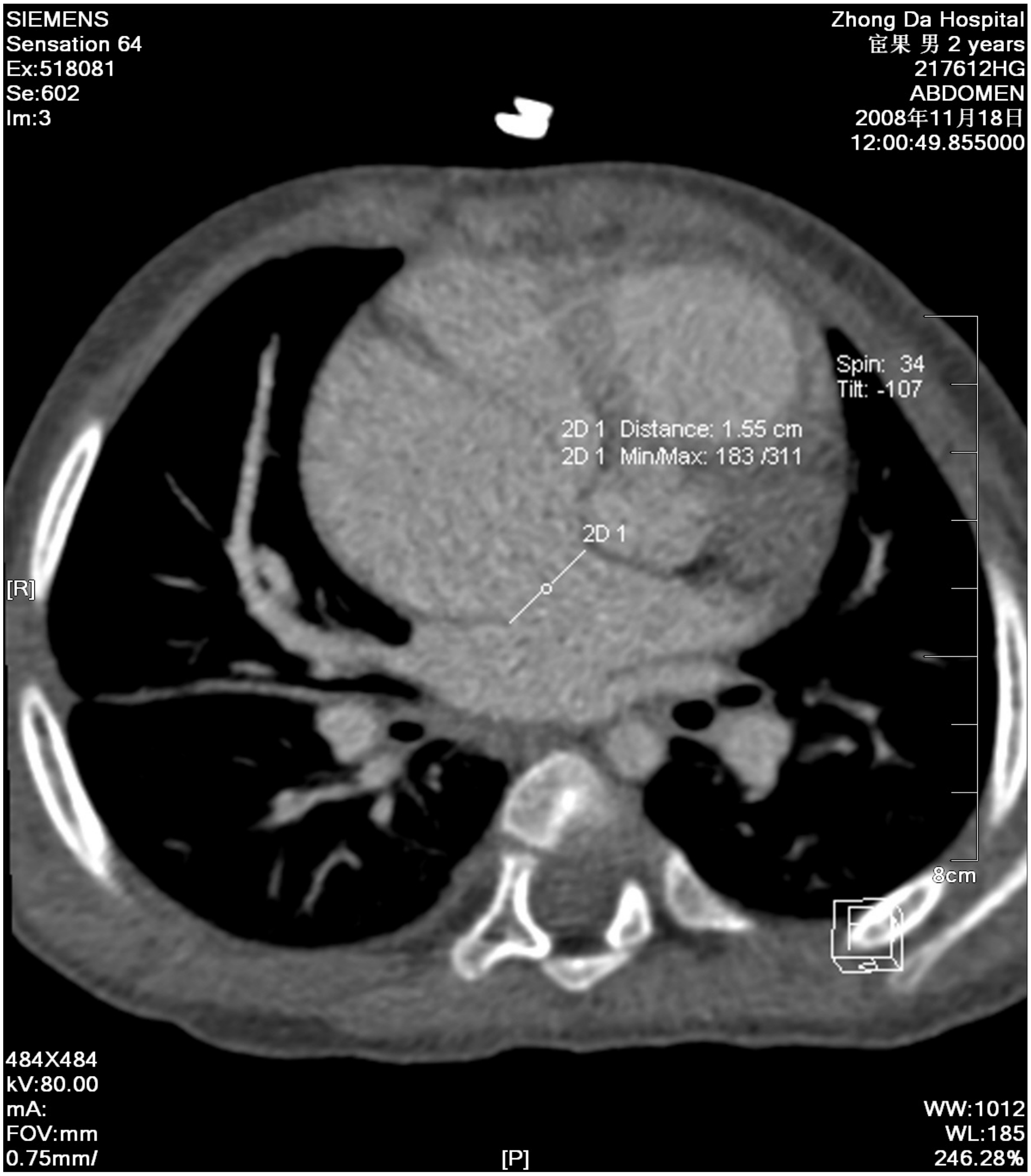

Figure 2. MIP of four cavities heart shows ASD.

relationship with the vasculature. In this study, MPR, MIP, and VR (Cook and Raman, 2007; Hayabuchi et al., 2010; Yang et al., 2008) analyses were performed in all cases to reconstruct the images. Although, the MPR, MIP, and VR analyses required the time of a radiologist, they provided direct images for the clinicians.

MPR can clearly display the heart's structure, and the AA and PA can be visualized sufficiently. However, MPR has some limitations in displaying the CA. MIP is suitable for direct observation of the structure of the heart and its relationship with the vasculature. It can reveal important structures from different directions and angles and directly display abnormalities. Especially with regard to visualization of the AA, PA, and CA, clipped MIP has significant advantages. For example, VSD (Figure 1), ASD (Figure 2), and double-outlet right ventricle (Figure 6) cases could be diagnosed clearly. VR can wholly display the AA, PA, and CA. Images obtained with this modality were entirely consistent with those obtained during operation and were praised by clinicians abroad. In this study, extracardiac anomalies, including TGA and PDA (Figure 3), double-outlet ventricle (Figures 4 to 5), truncus arteriosus, aortic striding, APVC, pulmonary venous stenosis, pulmonary artery stenosis, pulmonary

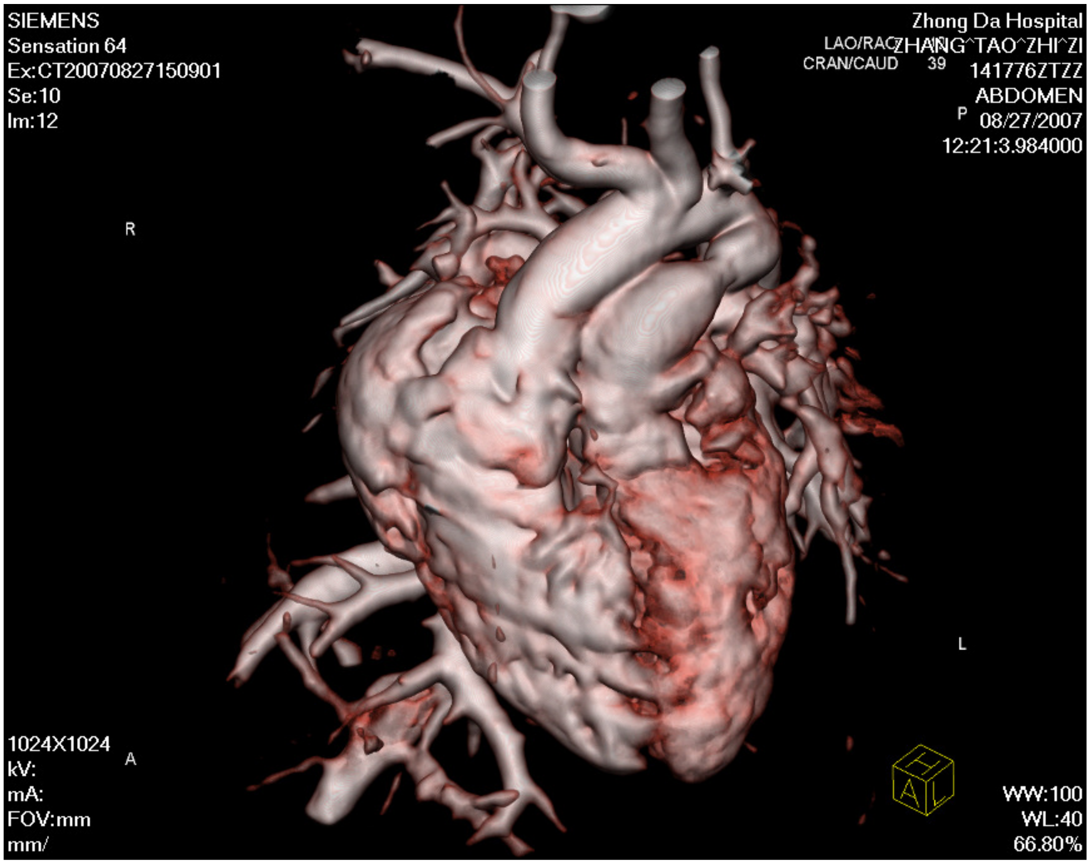

Figure 3. VR shows TGA and PDA.

Table 2. Comparison of CTA and DCC in the diagnosis of cardiovascular malformations.

Cardiovascular malformations	Number confirmed	DCC			CTA		
		Number diagnosed	False positive	False negative	Number diagnosed	False positive	False negative
VSD	18	18	0	0	18	0	0
ASD	11	11	0	0	8	0	3
CECD	1	1	0	0	1	0	0
Hypoplastic left heart	2	2	0	0	2	0	0
Right ventricular hypertrophy	4	3	0	1	4	0	0
Dexiocardia	1	1	0	0	2	1	0
TGA	4	4	0	0	4	0	0
Double-outlet ventricle	5	5	0	0	5	0	0
Truncus arteriosus	3	3	0	0	3	0	0
Aortic striding	3	3	0	0	3	0	0
APVC	1	1	0	0	1	0	0
Left superior vena cava	4	4	0	0	4	0	0
Pulmonary artery dilation	1	1	0	0	1	0	0
Pulmonary artery atresia	8	8	0	0	8	0	0
Pulmonary artery stenosis	6	6	0	0	6	0	0
Aortic coarctation	2	2	0	0	2	0	0
Interrupted aortic arch	1	1	0	0	1	0	0
Dextroaortic arch	3	3	0	0	3	0	0
PDA	7	7	0	0	7	0	0

Table 2. Contd.

Aortopulmonary collaterals	12	12	0	0	12	0	0
Abnormal coronary artery	3	3	0	0	3	0	0
Total	100	99	0	1	98	1	3

Abbreviations: CTA=CT angiography, DCC=diagnostic cardiac catheterization, VSD=ventricular septal defect, ASD=atrial septal defect, CECD=complete endocardial cushion defect, TGA=transposition of the great arteries, APVC=anomalous pulmonary venous connection, PDA=patent ductus arteriosus.

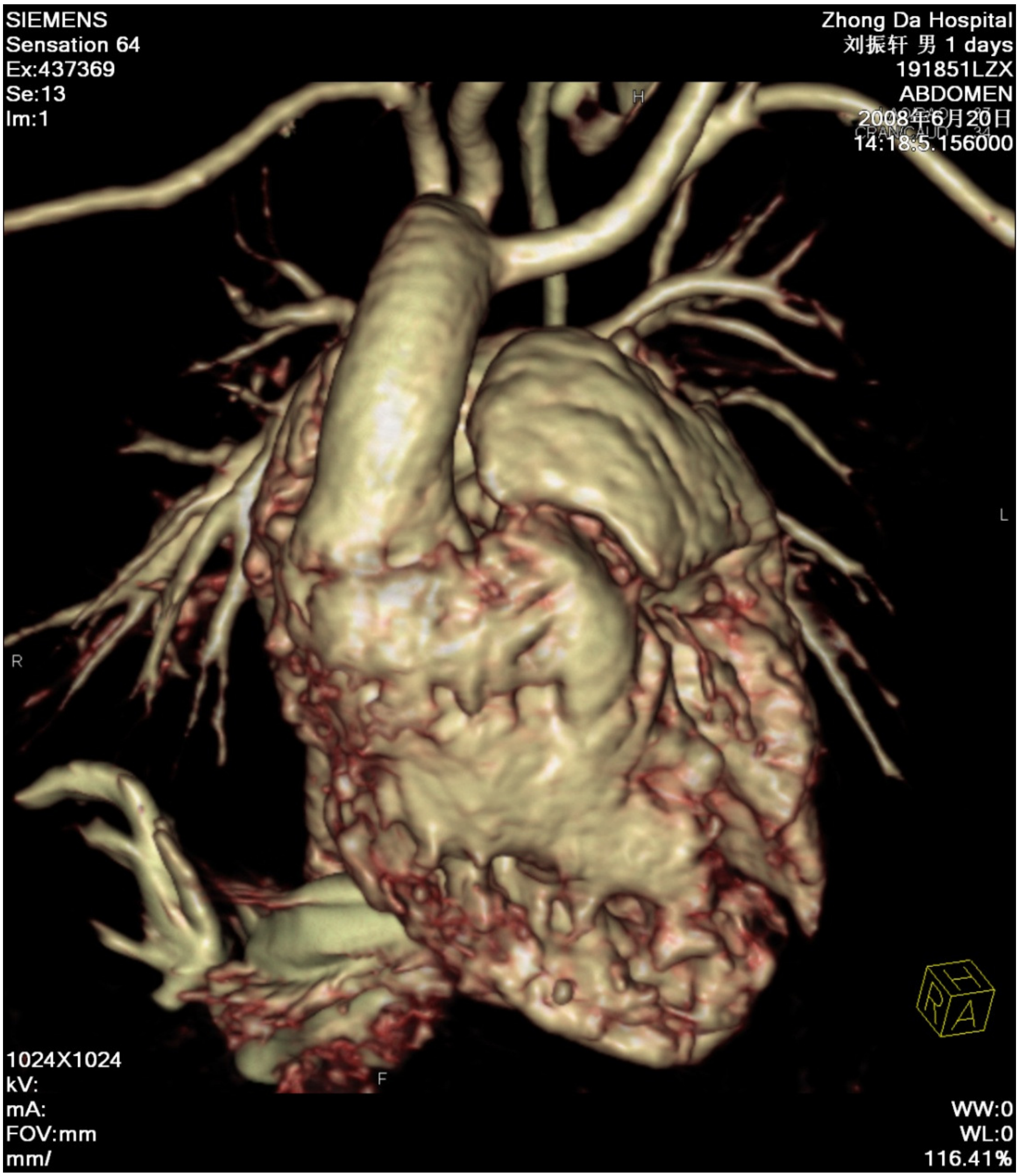

Figure 4. VR shows right ventricle emits AA and PA synchronously.

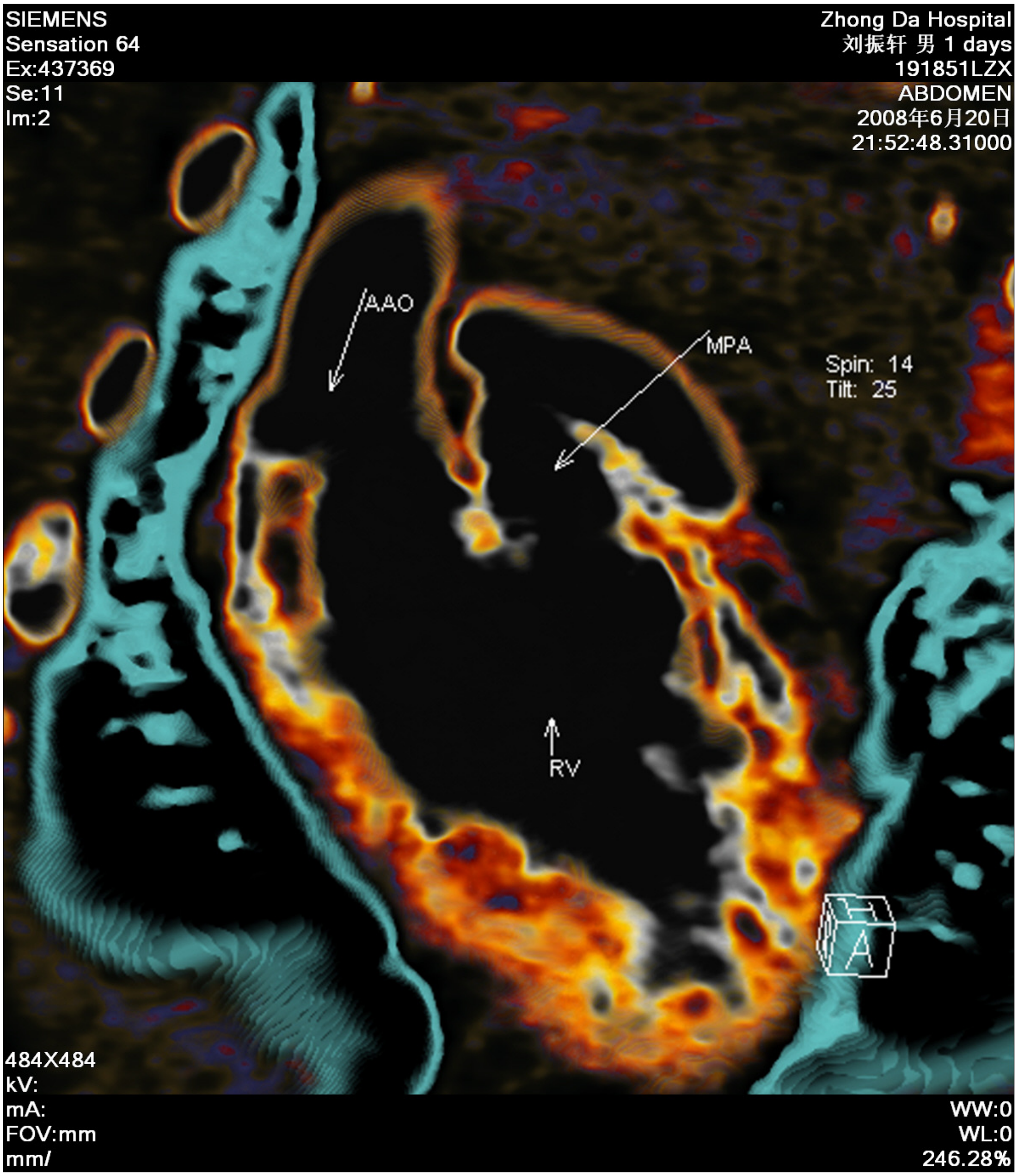

Figure 5. VR incision of patient seen in Figure 4 shows double-outlet right ventricle.

artery atresia (Figure 7), aortic coarctation, anomalous aortic origin or pulmonary artery origin, and abnormal coronary artery, were displayed in sufficient detail. However, they had some limitations with respect to displaying the heart's structure.

In summary, every post-processing method that uses 64-slice CT images has advantages and disadvantages. The information revealed by each modality can complement the information found in others. Therefore, post-processing methods need to be combined to display all of the abnormalities in complicated CHD. Because of its evaluation of AA, PA, and CA anomalies and the major aortopulmonary collateral arteries (Sun et al., 2008), CTA is extremely valuable for planning operative procedures in patients with complicated CHD.

UCG is a routine examination for diagnosing CHD. It has advantages in the diagnosis of heart malformation and provides real-time, dynamic, and multiple cross-section 2D imaging. Due to the impact of the sonic window, however, UCG cannot display large vessels outside of the heart and the coronary artery, which restricts UCG's usefulness in diagnosing complicated CHD (Klewer et al., 2002). With the development of MSCT (especially 64-slice CT), CTA has become

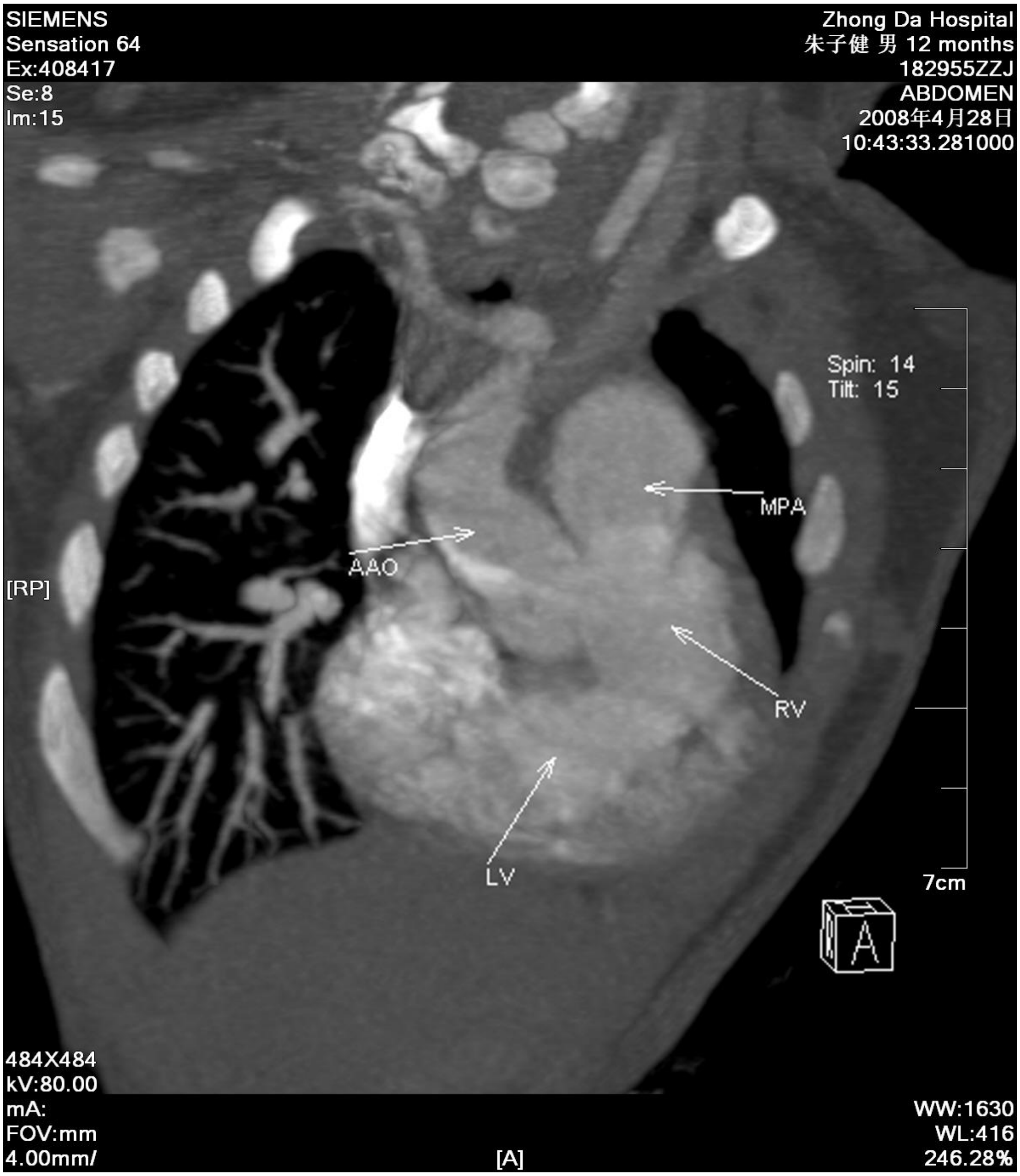

Figure 6. MIP shows right ventricle emits AA and PA synchronously.

available as a means for diagnosing complicated CHD. In this study, the accuracy rate of CTA was superior to that of UCG in detecting deformities of complicated CHD; the sensitivity and specificity of CTA were also superior to those of UCG. CTA was as accurate as UCG in revealing intracardiac deformities, but superior to UCG when identifying extracardiac deformities. Thus, CTA compensated for UCG's inability to diagnosis extracardiac deformities. The combination of CTA with UCG improved the definite diagnostic rate to 99.53%.

DCC has long been the gold standard for evaluating cardiac anatomy and function. Moreover, it is the only method that can be used to determine pulmonary vascular pressure and oxygen saturation. Because DCC is an invasive method, however, the procedure is more likely to induce complications like blood vessel injury, thrombogenesis, and arrhythmia. Additionally, the complexity of the operation restricts body positions, and the overlap of the heart and large vessels combined with the relatively high doses of ionizing radiation limits its application in small infants. Therefore, DCC is usually performed if UCG fails to provide a confident evaluation of existing lesions. The previous literature on 40-detector-row CT in complicated CHD in neonates assessed the

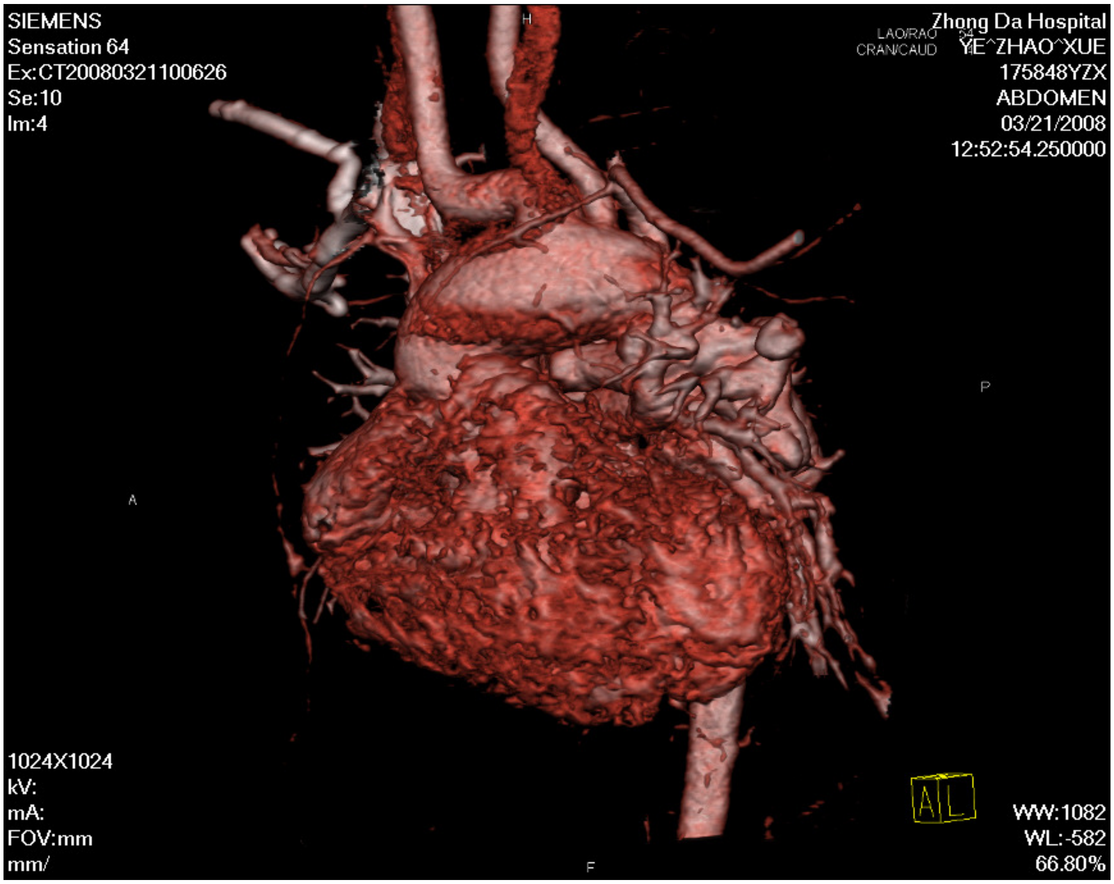

Figure 7. VR shows left ventricle emits AA and right ventricle does not emit PA.

feasibility of replacing cardiac catheterization with a multidisciplinary congenital heart disease team (Lee et al., 2006). Our study provides further evidence of the utility of CTA for replacing DCC in infants. A total of 22 infants received DCC, and 99 out of 100 cardiac deformities were found. CTA found 98 out of 100 cardiac deformities, demonstrating that it is as accurate as DCC in revealing cardiac deformities. No neonates received DCC because we considered it unethical to perform additional DCC in this population group (body weight range: 3 to 3.4 kg at delivery).

Although MRI has been recently used in adult CHD, it is much more expensive and time-consuming than CTA. MRI appears to be an ideal technique for children (especially neonates and infants) because it carries the substantial advantage of having no radiation burden. However, it suffers from various limitations. Its major limitation is the need for prolonged sedation and close monitoring, especially in neonates and infants with complicated CHD whose condition is often unstable (Bailliard et al., 2008). Therefore, MRI only used in unusual cases in our institute, and we did not compare with MRI in this study.

There are several limitations of CTA in diagnosing complicated CHD. The most disadvantage of CTA in diagnosing complicated CHD is that it cannot provide information regarding hemodynamics or blood oxygen content (Ley et al., 2007). Although 64-slice CT has a rapid scan speed, the image quality is still influenced to some extent by heart rate and respiration. In this study, eight patients with a septum defect less than 5 mm in size were misdiagnosed using CTA. Further improvements in temporal resolution should reduce this issue in the future. It is well known that children are more sensitive to radiation than adults. In addition, because they have a longer life span from the point of the scan, there is greater potential for the development of radiation-induced malignancies. Thus, the long-term effects of radiation exposure in children, especially neonates and infants, present another issue. Hopefully, technical improvements and low-radiation exposure scanning protocol in this study will not cause severe problems in these patients.

Conclusions

The 64-slice CT which is a minimally invasive examination with fast scanning and clear visualization of cardiovascular deformities is suitable for neonates and infants. CTA is a credible technique for diagnosing complicated CHD in neonates and infants. The combination of 2D and 3D images available from CTA not only shows the structure of the heart but also demonstrates AA, PA, and CA anomalies. CTA is thus extremely valuable when planning operative procedures for patients with complicated CHD. CTA compensates for UCG's shortcomings in diagnosing extracardiac deformities, and the combination of UCG and CTA improves the definite diagnostic rate. After initial assessment with UCG, CTA can replace DCC for further anatomical clarification in neonates and infants.

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