

# Respiratory Symptoms due to Vascular Ring in Children

GM ZHENG, XH WU, LF TANG

## Abstract

**Aim:** To highlight the clinical features, signs and diagnosis of vascular ring. **Methods:** A total of 33 patients (22 boys and 11 girls) diagnosed from January 2010 to July 2014 were enrolled. The types of vascular ring, basic demographic data, clinical symptoms, imaging and associated other malformations were analysed. **Results:** Among these patients, pulmonary artery sling was found in 17, right aortic arch in 9, double aortic arch in 5, and aberrant right subclavian artery in 3 (one with pulmonary artery sling). The median age (min-max) at onset and diagnosis were 1.8 (0.0-8.4) and 6.9 (0.1-149.0) months, respectively. Patients with pulmonary artery sling had higher incidence of stridor and dyspnea than patients with right aortic arch ( $P=0.028$  and  $P=0.036$ , respectively). All patients combined with other anomalies, including airway anomalies in 31 (93.94%) and cardiovascular anomalies in 23 (69.70%). The diagnostic accuracy of computed tomography with contrast/angiography, magnetic resonance imaging and cardiac catheterisation angiography were high (up to 100%) and lower with X-ray and endoscopy. **Conclusion:** Vascular ring should be considered in infants and young children with recurrent or chronic respiratory complaints and other anomalies. Computed tomography with contrast/angiography or magnetic resonance imaging should be performed to confirm the diagnosis.

**Key words** Children; Diagnosis; Pulmonary; Vascular ring

## Introduction

Vascular ring is a set of aortic arch malformations that are the result of abnormal development of the embryologic aortic arches. The abnormal development of the fourth and sixth paired aortic arches forms anatomically complete or incomplete vascular ring around the trachea, esophagus, or both during fetal life.<sup>1,2</sup> The first report named "vascular

ring" was published by Gross in the New England Journal of Medicine in 1945.<sup>3</sup> It was classified into double aortic arch (DAA), right aortic arch (RAA) with left ligamentum, pulmonary artery sling (PAS), and innominate artery compression by the International Congenital Heart Surgery Nomenclature and Database Committee.<sup>4</sup> The vascular ring can cause various respiratory and/or esophageal symptoms especially in infants and young children because of compression of the trachea and/or esophagus. However, a few patients with vascular ring do not present symptoms until adolescence or adulthood, or even entire life.<sup>5</sup> The common clinical features were respiratory symptoms, including cough, stridor, wheezing, recurrent respiratory tract infections, dyspnoea, respiratory distress, and even respiratory arrest.<sup>6-10</sup> The oesophageal symptoms have occurred in a few cases, including dysphagia, slow feeding, reflux, vomiting, choking and failure to thrive.<sup>7,8,11</sup> These various clinical manifestations mainly depend on the different types and severity of vascular rings.<sup>5</sup> Other

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symptoms associated with other cardiovascular anomalies and tracheal anomalies have also been reported.<sup>1,5,8,12</sup> As most of these patients presented with respiratory symptoms, but not cardiovascular symptoms,<sup>1</sup> it is difficult to diagnose in infants and young children if the medical staff do not pay attention or are unfamiliar with this rare condition. Misdiagnosis and missed diagnosis have been reported frequently.

In this study, we analysed retrospectively the clinical features, imaging and associated anomalies of 33 paediatric patients with respiratory symptoms due to vascular rings in order to highlight the clinical features and diagnosis of this rare condition.

## Patients and Methods

### Patients

A total of 33 patients with vascular ring diagnosed in our unit from January 2010 to July 2014 were retrospectively reviewed and analysed. They were 22 boys and 11 girls aged from 3 days to 12 years with a median (range) age of 6.9 (0.1-149.0) months at the time of diagnosis. Their basic demographic data, type of abnormalities, clinical symptoms and signs, imaging, endoscopic findings, and associated other malformations were recorded for further analysis.

Consent was obtained from the parents and the study was proved by the Ethical Committee of the Children's Hospital of Zhejiang University School of Medicine.

### Statistical Analysis

Statistical analyses were conducted using SPSS software (version 11.5). The Fischer's Exact test was used to measure enumeration data among the groups. The data with skewed distributions were presented as median (min-max) analysed by nonparametric test (Kruskal-Wallis test). Significant differences were regarded if a P value  $\leq 0.05$ .

## Results

Among these 33 patients, the ratio of male to female was 2 to 1. The median age at clinical feature onset was 1.8 (0.0-8.4) months. PAS was predominant type (Figure 1), which was found in 17 patients, followed by RAA with aberrant left subclavian artery in 9, DAA in 5 (Figures 2a-2b), and aberrant right subclavian artery (ARSA) in 3 (one with PAS as well) (Figures 2c-2e). The differences of gender

and age among children with different types of vascular ring were not significant, as showed in Table 1.

In this series, all the patients were admitted with the respiratory symptoms. Cough was the most common symptom, which was complained in 28 patients. Moreover, recurrent cough was complained in 23 patients and chronic cough in 4. Stridor and wheezing were the other common symptoms and noted in 24 patients, respectively. Serious symptoms including dyspnoea and cyanosis were also common with the same incidence of 39.39%. All patients with DAA presented with cough, stridor and wheezing. Two patients had a history of "asthma" without significant improvement after receiving the standardised treatment of asthma. Two patients (one PAS and one DAA) were admitted to hospital because of "laryngitis" with acute laryngeal obstruction. Two patients with RAA and aberrant left subclavian artery had additional complaint of dysphagia as well (Table 1).

While analysing clinical features among the different types of vascular ring, we noted that there was significant difference of stridor among the four types ( $P=0.001$ ), and patients with PAS had a significantly higher rate of stridor than that of patients with RAA (88.24% vs. 44.44%,  $P=0.028$ ). Also, there was a marginal difference of dyspnoea among the four types ( $P=0.077$ ), and dyspnoea in patients with PAS was more common than that in the patients with RAA (58.82% vs. 11.11%,  $P=0.036$ ). No significant difference of cough, recurrent cough, chronic cough, or cyanosis was found among the four different types of vascular ring, as shown in Table 1.

Among these patients, other malformations, mainly airway or cardiovascular anomalies, were found in all patients. Airway anomalies were presented in 31 patients (93.94%), including tracheal or main bronchial stenosis in 28 (84.85%), tracheal bronchus in 4, laryngomalacia in 3, tracheomalacia in 2, bridging bronchus in 1 and bronchus atresia in one. The tracheal stenosis in 28 patients occurred almost around the tracheal bifurcation level (22/28, 78.57%). The malformations of lung included circumscribed emphysema in 4, pulmonary hypoplasia in 3, pulmonary sequestration and pulmonary cysts in one, respectively. The concurrent rate of different type of airway anomalies had no significant difference among the four types, except for the pulmonary hypoplasia ( $P=0.022$ ). It was notable that tracheal bronchus, tracheomalacia and bronchus atresia were found in PAS patients only, but not found in others, as shown in Table 2.

Other cardiovascular anomalies presented in 23 patients (69.70%), which mainly included the ventricular septal

**Table 1** The basic demographic data and respiratory symptoms according to type of vascular ring

	Total	PAS	RAA	DAA	ARSA	$\chi^2$	P value	Multiple comparison <sup>†</sup>
Number (%)	33	17 (51.52)	9 (27.27)	5 (15.15)	3 (9.09)			
Male/female	22/11	14/3	6/3	2/3	1/2	5.068	0.128	N
Age at onset (M)	1.8 (0.0-8.4)	1.6 (0.0-8.4)	0.9 (0.0-8.0)	3.1 (0.1-7.8)	1.0 (0.0-7.9)	1.443	0.695	N
Age at diagnosis (M)	6.9 (0.1-149.0)	5.6 (0.7-56.0)	9.0 (0.7-149.0)	8.1 (0.1-19.0)	8.0 (2.7-61.0)	2.268	0.519	N
Cough (%)	28 (84.85)	13 (76.47)	8 (88.89)	5 (100.00)	2 (66.67)	2.143	0.584	N
Recurrent cough (%)	23 (69.70)	11 (64.71)	6 (66.67)	4 (80.00)	2 (66.67)	0.651	1.000	N
Chronic cough (%)	4 (12.12)	4 (23.53)	0	0	0	3.009	0.412	N
Stridor (%)	24 (72.73)	15 (88.24)	4 (44.44)	5 (100.00)	0	12.876	0.001	PAS vs. RAA (0.028)
Wheeze (%)	24 (72.73)	13 (76.47)	5 (55.56)	5 (100.00)	1 (33.33)	4.954	0.154	N
Dyspnoea (%)	13 (39.39)	10 (58.82)	1 (11.11)	1 (20.00)	1 (33.33)	6.399	0.077	PAS vs. RAA (0.036)
Cyanosis (%)	13 (39.39)	9 (52.94)	2 (22.22)	1 (20.00)	1 (33.33)	3.121	0.377	N

M, month; PAS, pulmonary artery sling; RAA, right aortic arch; DAA, double aortic arch; ARSA, aberrant right subclavian artery; <sup>†</sup>P<0.05.

**Table 2** The associated malformations according to type of vascular ring

	Total (%)	PAS	RAA	DAA	ARSA	$\chi^2$	P value	Multiple comparison <sup>†</sup>
Number	33	17	9	5	3			
Airway								
Stenosis	28 (84.85)	13 (76.47)	8 (88.89)	5 (100.00)	2 (66.67)	2.143	0.593	N
Tracheal bronchus	4 (12.12)	4 (23.53)	0	0	0	3.009	0.415	N
Laryngomalacia	3 (9.09)	0	2 (22.22)	1 (20.00)	0	4.842	0.143	N
Tracheomalacia	2 (6.06)	2 (11.76)	0	0	0	1.790	0.729	N
Bridging bronchus	1(3.03)	1(5.88)	0	0	0	2.329	1.000	N
Bronchus atresia	1 (3.03)	1 (5.88)	0	0	0	2.329	1.000	N
Emphysema	4 (12.12)	3 (17.64)	0	0	1 (33.33)	3.318	0.302	N
Pulmonary hypoplasia	3 (9.09)	1 (5.88)	0	0	2 (66.67)	7.365	0.022	N
Others	2 (6.06)	1 (5.88)	1 (11.11)	0	0	1.554	1.000	N
Total (%)	31 (93.94)	17 (100.00)	8 (88.89)	5 (100.00)	2 (66.67)	5.024	0.099	N
Cardiovascular								
VSD	13 (39.39)	6 (35.29)	4 (44.44)	1 (20.00)	2 (66.67)	1.965	0.682	N
ASD	12 (36.36)	10 (58.82)	1 (11.11)	0	1 (33.33)	8.607	0.021	PAS vs. RAA (0.036)
PDA	9 (27.27)	2 (11.76)	5 (55.56)	1 (20.00)	1 (33.33)	5.821	0.095	PAS vs. RAA (0.028)
Other	6 (18.18)	3 (17.64)	2 (22.22)	0	1 (33.33)	1.876	0.698	N
Total (%)	23 (69.70)	14 (82.35)	6 (66.67)	1 (20.00)	3 (100.00)	7.249	0.050	PAS vs. DAA (0.021)
Other	4 (12.12)	1 (5.88)	2 (22.22)	0	1 (33.33)	3.528	0.220	N

VSD, ventricular septal defect; ASD, atrial septal defect; PDA, patent ductus arteriosus; PAS, pulmonary artery sling; RAA, right aortic arch; DAA, double aortic arch; ARSA, aberrant right subclavian artery; <sup>†</sup>P<0.05.

defect (VSD) in 13, atrial septal defect (ASD) in 12 and patent ductus arteriosus (PDA) in 9. The other cardiovascular malformation included persistent left superior vena cava, single left coronary artery, tetralogy of Fallot and pulmonary artery atresia. We found that the concurrent rate of cardiovascular anomalies had a significant difference among the four types ( $P=0.050$ ). It was higher in patients with ARSA or PAS, but lower in patients with DAA, with a significant difference between patients with PAS and DAA (82.35% vs. 20.00%,  $P=0.021$ ). 58.82% of patients with PAS had ASD, which were higher than that in RAA (58.82 vs. 11.11%,  $P=0.036$ ). It was notable that 23 (69.70%) patients had both airway and cardiovascular anomalies. Other anomalies were found in 4 of 33 patients, including talipes equinus, congenital syndactyly, congenital choanal atresia, and renal cyst.

The age at diagnosis ranged from 3 days to 12.4 years with a median age of 6.9 (0.1-149.0) months, which was about 5.1 months later after the first presentation (Table 1). Only 4 (12.12%) patients were diagnosed in the neonatal period while 23 (69.70%) were diagnosed within the first year of life. Only 7 (21.21%) patients were diagnosed at first time of hospital admission. A patient with RAA and aberrant left subclavian artery has been misdiagnosed as asthma until the age of 12.4 years.

Among these patients, chest X-ray was performed for all patients due to their respiratory symptoms. Besides bronchitis or pneumonia, airway compression was speculated in 4 patients as localised emphysema and tracheal stenosis. Bronchoscopy was performed in 10 patients (all PAS patients), tracheal or bronchial stenosis were found in all patients, tracheomalacia in 2, and atresia of right main bronchus in one. Fibrelaryngoscopy was performed in 3 patients with obvious stridor, and it showed laryngomalacia and subglottic stenosis. Slightly compression of oesophagus was found in 2 of 3 patients by oesophagography. However, no confirmations were obtained by the above 4 diagnostic methods, only some signs secondary to vascular ring and other combined abnormalities were found (Table 3).

The computed tomography (CT) was performed for 31 patients, only 10 (32.26%) were diagnosed as vascular ring and 8 (25.81%) were suspected. The echocardiography was also performed in 31 patients and only 11 (35.48%) were diagnosed. Magnetic resonance imaging (MRI) and cardiac catheterisation angiography were performed in 7 patients, respectively. The diagnosis of all these patients with different types of vascular ring were confirmed by the above two methods, including one patient who had suspected DAA during the fetal period by fetal echocardiography and was

confirmed by MRI after birth. The diagnosis of vascular ring was confirmed in all 23 patients who had undergone the 3-dimensional volume-rendered CT with contrast/angiography (CTC/A), including 8 of them suspected by the CT. The diagnostic rate of the 3-dimensional CTC/A (100.00%) for vascular ring and was higher than those of the CT (32.26%) or echocardiography (35.48%) ( $P<0.001$ , respectively).

## Discussion

Since the first case of vascular ring reported in 1945,<sup>3</sup> patients with initial missed diagnosis or misdiagnosis were commonly reported. In our series of 33 cases, we noted that the male dominates female with a ratio of 2:1. It was consistent with Woods' report,<sup>13</sup> but significantly different from Bakker (female preponderance) or Phelan's (without difference) reports.<sup>7,12</sup> Whether this difference is associated with the racial or demographic difference required further studies.

Among the 4 types of vascular ring, we found that the most common type was PAS, followed by RAA, DAA and ARSA in our series. This was different from several previous studies,<sup>1,8,13,14</sup> which reported that the most common types of vascular ring were DAA, ARSA or RAA. This difference may be associated with the fact that most patients in our series were diagnosed in the department of pulmonology, but not department of cardiology. We had excluded the other

**Table 3** Imaging modalities of vascular rings

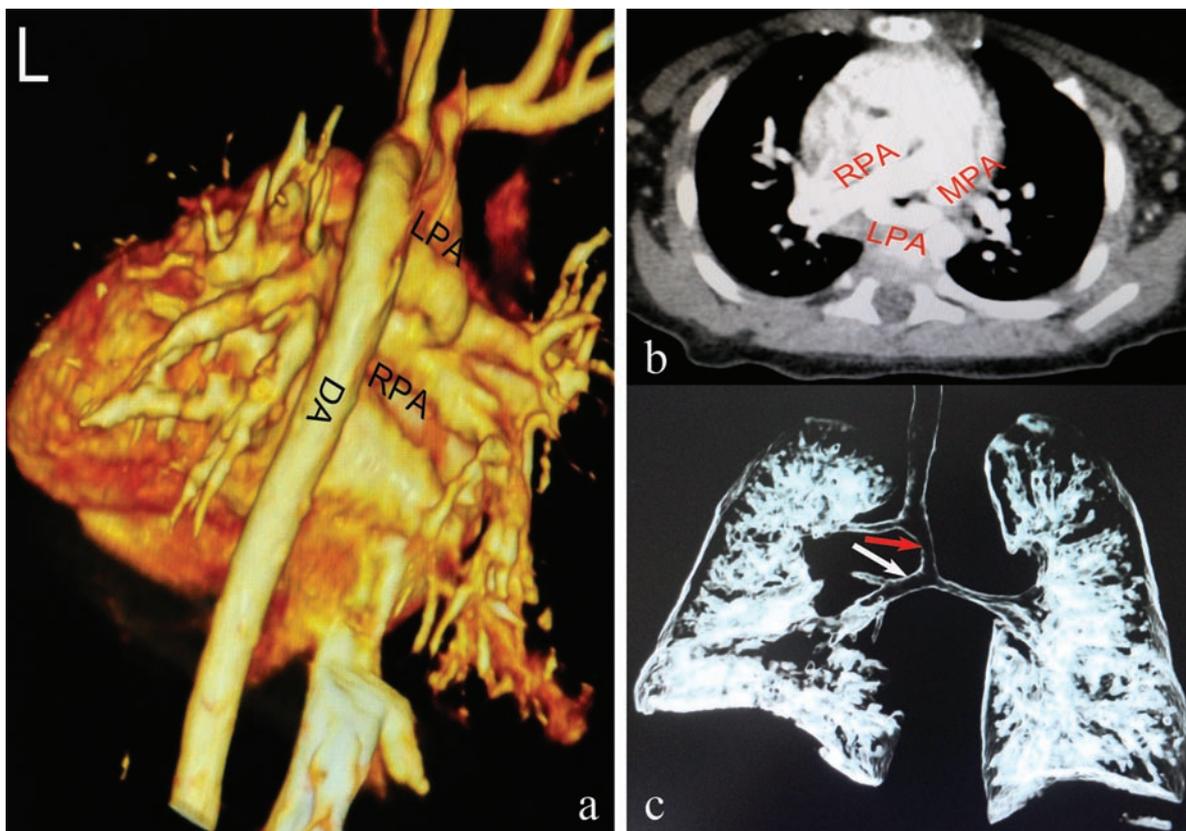
	Performed	Suspicion (%)	Confirmation (%)
X-ray	33	4 (11.76)	
Bronchoscopy	10	10 (100.00)	
Fibrelaryngoscopy	3	3 (100.00)	
Oesophagography	3	2 (66.67)	
Computed tomography	31	8 (25.81)	10 (32.26)
Echocardiography	31	2 (6.45)	11 (35.48)
Cardiac catheterisation angiography	7	7 (100.00)	
Magnetic resonance imaging	7		7 (100.00)
Computed tomography with contrast/angiography	23		23 (100.00)

9 patients with vascular ring who were admitted to hospital without airway symptoms. It may be also associated with limited sample size, patient source, race and demography.

Although vascular ring is a rare cause of extrinsic tracheal compression, it was the most frequent cause of the airway compression due to the cardiovascular disease in children.<sup>15</sup> In this study, all patients were admitted with clinical respiratory symptoms. This was similar to Humphrey's report, which also showed that respiratory symptoms and signs presented in 94% of patients with vascular ring.<sup>1</sup> In this series, cough was the most common presenting symptom and it was consistent with Gaafar's report.<sup>6</sup> Moreover, dyspnoea and cyanosis were also noted in 39.39% of patients, respectively. These suggested that in a young child with recurrent or chronic cough, wheezing, stridor, dyspnoea and/or cyanosis, vascular ring should be

considered in the differential diagnosis. It was notable that patients with PAS had higher incidence of stridor and dyspnoea. This may be associated with more common tracheal anomalies, other cardiovascular anomalies, or more serious airway compression in patients with PAS.

In this study, the airway anomalies were found in 93.94% of patients, which was higher than previous reports (about 40.0%).<sup>5</sup> Tracheal stenosis was the most common, which was noted in 84.85% of patients, followed by tracheal bronchus, laryngomalacia or tracheomalacia. We noted a higher incidence of tracheal stenosis with a rate of 76.47% in patients with PAS, but still lower than Chen's report (100%).<sup>16</sup> The rate of tracheal bronchus in our series was 23.53%, which was similar with the above report (22%).<sup>16</sup> In addition, PAS patients combined with complete tracheal cartilage ring and oesophageal lung were also reported.<sup>7,16-19</sup>



**Figure 1** Imaging of a 4M-22D-old boy with PAS and tracheal malformations. (a) Posterior view of PAS by 3D-reconstruction CTC. LPA originates from the posterior of the RPA and passes leftward around the right bronchus. (b) Axial CTC shows the standard view for diagnosing the vascular ring formed by PAS. (c) 3D-reconstruction of airway shows the presence of the left main bronchial stenosis (grey arrow) and bridging bronchus (white arrow). PAS, pulmonary artery sling; CTC, computed tomography with contrast; LPA, left pulmonary artery; RPA, right pulmonary artery; MPA, main pulmonary artery; DA descending aorta.



**Figure 2** Imaging of DAA, ARSA and associated tracheal malformations. (a) Posterior view of 3D-reconstruction CTC shows a DAA with the left and right arches joining posteriorly. The left and right arches give rise to the left and right common carotid and subclavian arteries, respectively. (b) Anterior view shows the right-sided aortic arch and DAA arising from the descending aorta. (c) Posterior view shows the right-sided aortic arch and aberrant left subclavian artery arising from the descending aorta. (d) 3D reconstruction of airway shows the ARSA associated with severe stenosis of left main bronchus and pulmonary hypoplasia. (e) 3D reconstruction of airway shows the DAA associated with tracheal stenosis (arrow). DAA, double aortic arch; ARSA, aberrant right subclavian artery; CTC, computed tomography with contrast; DA, descending aorta; AA, ascending aorta; RAA, right aortic arch; LAA, left aortic arch; LSCA, left subclavian artery; LCCA, left common carotid artery; RSCA, right subclavian artery; RCCA, right common carotid artery.

Browne even reported that 40%-50% patients with PAS were combined with complete tracheal cartilage ring.<sup>17</sup> However, it was not found in anyone of our series. The reason of this difference is unclear.

The rate of cardiovascular anomalies in our series was 69.70%, which was also higher than previous studies (29%-63%).<sup>1,5,8,12</sup> The most common was VSD (39.39%), followed by ASD (36.36%), and PDA (27.27%). Moreover, we noted that patients with PAS had a higher rate of associated cardiac malformations while patients with DAA seldom had cardiac malformations, which was consistent with Kellenberger's view.<sup>2</sup> It was reported that RAA was often associated with congenital heart disease (especially tetralogy of Fallot) with an incidence of approximately 50%.<sup>13,17</sup> However, the only one patient with tetralogy of Fallot was the patient with RAA in our series. The cause of this difference was unclear. Higher incidence and variable anomalies implied that careful physical and imaging examination should be performed for every patient diagnosed with vascular ring.

It was reported that the vascular ring accounts for about 1% of congenital cardiovascular anomalies.<sup>7</sup> In our hospital, more than 5 000 patients with congenital cardiovascular anomalies and about 35 000 patients with respiratory symptoms were admission during this period, but only 42 patients were diagnosed as vascular ring. The overall incidences of vascular ring in patients with congenital cardiovascular anomalies or respiratory symptoms were about 8.4‰ and 1.2‰, respectively.

The median age at onset of our patients was 1.8 months, which was earlier than 2.6 months reported by Suh et al.<sup>5</sup> However, the median age of diagnosis was 5.1 months later after the age of clinical feature onset in our series, which was longer than 4.4 months reported by Suh.<sup>5</sup> Moreover, misdiagnosis as "asthma" or "laryngitis" was noted in our series. These implied that some patients had misdiagnosis or missed diagnosis till now due to the patients with slight symptom and/or paediatrician's lack of the knowledge of the vascular ring.

In patients with recurrent or chronic respiratory symptoms, chest X-ray as non-invasive imaging examination should be performed initially. Bronchial compression with localised pulmonary emphysema and tracheal stenosis may be a clue of vascular ring. Also, bronchoscopy or fibrelaryngoscopy may be performed to exclude the airway abnormalities as recurrent or chronic respiratory symptoms. Compressed airway and some other combined airway abnormalities may be found in patients with vascular ring. Also, barium oesophagography may provide the imaging of compressed oesophagus in patients with dysphagia.<sup>12,13</sup>

These findings may serve as clues to vascular ring, but cannot confirm the diagnosis. It is very important that further investigations apart from barium study should be undertaken.

Although echocardiogram had diagnosed only about one third of patients with vascular ring in this study and other reports,<sup>9,12</sup> it is a non-ionising radiation, non-invasive and helpful tool for evaluating additional cardiac anomalies as a complementary procedure.<sup>1</sup> Echocardiography by experienced experts may serve as a critical screening examination especially in basic hospitals without CTC/A, MRI, or angiography.

Historically, cardiac catheterisation angiography, an invasive method, was regarded as the gold standard in the diagnosis of vascular ring.<sup>20</sup> In recent reports, CTC/A and MRI have been used frequently for the definite diagnosis of vascular ring.<sup>8,11,12</sup> Similar to our study, Fleenor reported that 49 patients with vascular ring initially diagnosed by MRI were all confirmed at surgery, and suggested MRI as a gold standard for diagnosing vascular ring.<sup>21</sup> However, several studies suggested that MRI has several disadvantages compared with CT in some aspects, such as poorer spatial resolution, deep sedation of children, limited evaluation of airway and lung, even taking longer time and higher medical expense.<sup>21-23</sup> The CTC/A can characterise the exact nature of the vascular ring, assess extrinsic mass effect on the trachea, and assist in surgical planning by a combination of axial, 2D reformatted and 3D reconstructed images.<sup>22</sup> Moreover, as our series, the diagnosis rate of the 3D reconstructed CTC/A was much higher than that of the CT.

In summary, vascular ring is a rare cause of common respiratory symptoms. It should be considered in infants and young children with recurrent or chronic respiratory complaints and other anomalies. The CTC/A and MRI should be performed to confirm the diagnosis.

## Conflict of interest

There are no competing interests.

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