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Symptom persistence after vascular ring repair in children ☆

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ABSTRACT

Purpose: Vascular rings are often diagnosed after evaluation for swallowing and breathing difficulties. Data regarding symptoms following vascular ring repair is sparse. We sought to determine whether symptoms persist using chart review and a survey.
Methods: Sixty-three patients underwent open vascular ring repair from July 2007 to May 2018. Data regarding vascular anatomy, demographics, pre- and postoperative symptoms, and chromosomal abnormalities were collected. Freedom from reoperation, 30-day mortality, and complications were assessed. Patient families were contacted for a symptom focused survey.
Results: The median age of surgical intervention was 14.4 months (IQR 5.8–34.7 months) for single aortic arches with an aberrant subclavian artery (SAA), and 5.3 months (IQR 1.3–10.1 months) for double aortic arches (DAA) (Table). Prior to surgery, all but two SAA were symptomatic. There was no operative mortality. Three patients required re-exploration for chylothorax, and three required late aortopexy. At last follow-up, 45% (18/40) SAA and 65% (15/23) DAA had post-operative symptoms. Fourteen patient families completed the symptom survey (10 SAA, 4 DAA). Five SAA had breathing and swallowing symptoms, and 3 SAA and 3 DAA had breathing difficulties.
Conclusions: Open vascular ring repair remains a safe repair. However, further investigation of the persistent symptoms in these patients is merited.
Study Type / Level of Evidence: Retrospective Comparative Study, Level III

The differential diagnosis for breathing and swallowing difficulties in children is broad. The diagnosis of a vascular ring is often made after extensive investigation. The most common form of vascular ring is a single aortic arch (SAA) known as a Neuhauser anomaly. A Neuhauser anomaly consists of a right aortic arch, aberrant left subclavian artery and a left ligamentum arteriosum. The mirror image SAA or a left aortic arch, aberrant right subclavian artery, and a right ligamentum arteriosum occurs far less frequently. The second most common vascular ring is a double aortic arch (DAA) with one dominant and usually one atretic arch (Fig. 1). The majority of patients with vascular rings present with respiratory symptoms as an indication for repair. The remainder present with swallowing difficulties [1–6]. Children often present with symptoms in the first few months of life and require surgery within the first year of life [1, 2, 7].

Surgical repair of a vascular ring is thought to provide relief of respiratory and swallowing symptoms, yet few studies have reported on the resolution of symptoms after surgery. The majority of papers have follow-up between six months and two years [3, 4, 8, 9]. The longest study followed patients to a median of 11 years. However, this report was over a four-decade period (1978-2014) [10]. In addition, the role of subclavian reimplantation as part of vascular ring repair has been evolving. As most studies did not follow their patients beyond two years, we sought to determine whether vascular ring repair is successful in relieving preoperative breathing and swallowing symptoms in our contemporary series.

1. Methods

1.1. Study sample

With IRB approval, we retrospectively reviewed 63 consecutive patients who underwent isolated repair of a vascular ring via thoracotomy from July 2007 to May 2018 at our institution. Data were collected regarding demographics, genetic abnormalities or syndromes, vascular ring anatomy, perioperative morbidity, operative mortality, as well as operative technique. Vascular ring anatomy was based on operative reports and preoperative imaging. Respiratory and swallowing symptoms were obtained from the preoperative notes, operative reports and the most recent and relevant outpatient clinic visit documented in the electronic record.

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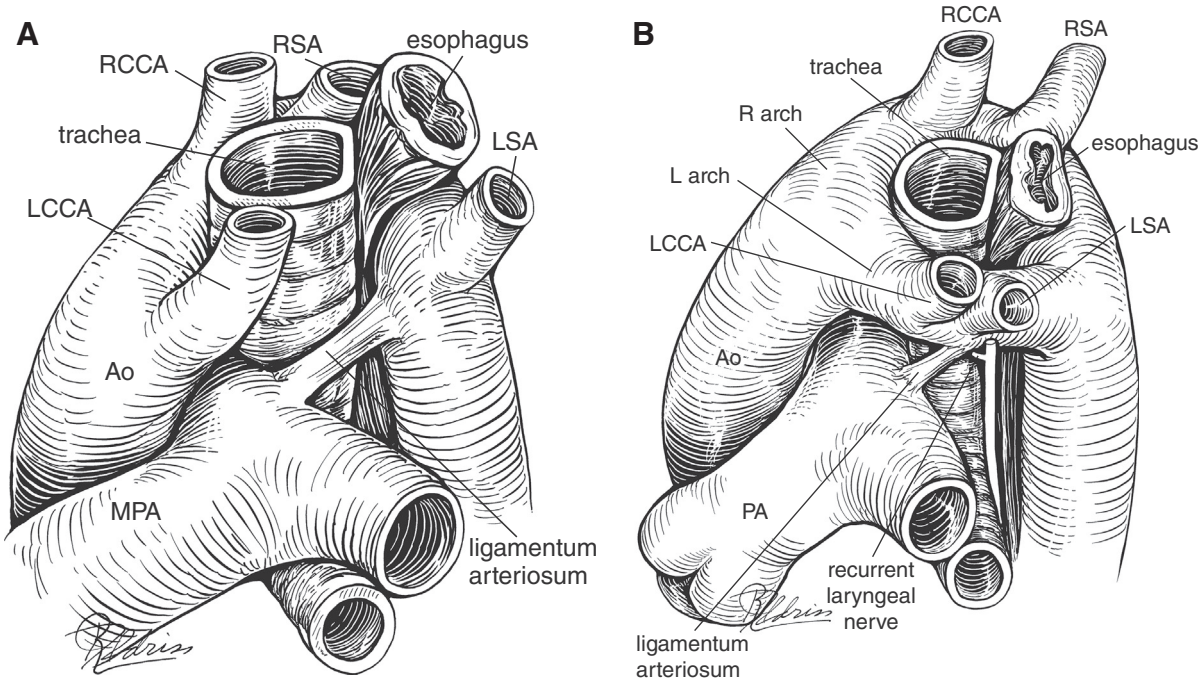

Fig. 1. Representative images of vascular rings – A: Single aortic arch. B: Double Aortic Arch. Reproduced with permission from Backer CL, Mavroudis C. Vascular rings and pulmonary artery sling. In: Mavroudis C, Backer Cl. *Pediatric Cardiac Surgery, Philadelphia*: Wiley; 2003; 234-255. [7]

1.2. Survey

As our patients are young, their families were contacted by phone and offered a symptom focused survey to determine if there was resolution of breathing and swallowing symptoms after surgery (Supplementals 1–2). Each family received two phone calls and a voicemail if possible. All families who completed the survey consented to study participation. The respiratory portion of the survey consisted of 7 questions modified from the Self Evaluation of Breathing Questionnaire [11]. The PEDI-EAT 10 was used to assess for swallowing symptoms and had 10 questions [12].

1.3. Surgical technique

Vascular ring repair was performed through a thoracotomy contralateral to the dominant arch in all patients. The ligamentum arteriosum was divided in all SAA and DAA as well as the non-dominant arch segment for DAA. Depending on surgeon preference and anatomic considerations, SAA patients underwent resection of the Kommerell's diverticulum and reimplantation of the aberrant subclavian artery to the ipsilateral carotid artery. Our institutional preference in the past seven years has been to perform reimplantation of the subclavian artery where possible for SAA.

1.4. Statistical analysis

The Fischer's exact test was used for categorical variables and the Mann-Whitney test for continuous variables with a $p < 0.05$ denoting statistical significance. (SPSS version 24, Released 2016; IBM Corp., Armonk, NY)

2. Results

2.1. Preoperative characteristics

Forty patients had SAA, and 23 patients had DAA. The majority of SAA patients (39) had a Neuhauser anomaly – a right sided aortic arch, an aberrant left subclavian artery with a left ligamentum. One SAA patient had mirror-imaging. The median age at the time of repair was 14.4 months (IQR 5.8–34.7 months) for the SAA group, and 5.3 months (IQR 1.3–10.1 months) for the DAA group. Preoperatively, 34 SAA (85%) had respiratory symptoms, and 25 (62.5%) had swallowing symptoms. All patients with DAA had respiratory symptoms, and 11 (48%) had swallowing symptoms (Table 1). CT was the most common diagnostic modality (82.5%, 52/63), followed by MRI (15.8%, 10/63). One patient was diagnosed by echocardiogram alone.

Of the 63 children with vascular rings, 16 (25.3%) had documented genetic abnormalities or syndromes (Table 2). The presence of genetic abnormalities or syndromes was not known for the remaining children. There was no difference in the median weight/height for the 16 patients [8.4 kg (IQR 6.2–13.1) and 72 cm (IQR 58–83)] compared to the remainder of the cohort [8.9 kg (5.3–12.6) and 71 cm (IQR 58.8–86.5)] ($p = 0.69$ and 0.49, respectively).

2.2. Perioperative bronchoscopy and postoperative morbidity and mortality

Preoperative or intraoperative bronchoscopy was performed based on surgeon preference. Thirty-eight children (23 SAA and 15 DAA) had flexible or rigid bronchoscopies. Two of the 23 SAA, and four of the 15 DAA had tracheomalacia. We do not have documentation of the presence or absence of tracheomalacia on the remaining 25 children in the series.

Table 1
Patient demographics

	Single aortic arch n = 40 (%)	Double aortic arch n = 23 (%)
Sex (male)	25 (62.5)	12 (52.2)
Median age at repair (months) (IQR)	14.4 mo (5.8–34.7 mo)	5.3 mo (1.3–10.1 mo)
Chromosomal abnormalities	15 (37.5)[a]	1 (4.3)
Pre-op respiratory symptoms	34 (85)	23 (100)
Pre-op swallowing symptoms	25 (62.5)	11 (47.8)

[a] $p = 0.004$

Table 2
Confirmed genetic abnormalities and syndromes*

	Single aortic arch n = 14
DiGeorge	3
Trisomy 21	3
Other mutation, deletion, duplication	6
CHARGE syndrome	1
PHACE syndrome	1
	Double aortic arch n = 2
Trisomy 21	1
Rosai-Dorman syndrome	1

* The genetics or syndrome status of the remaining children in the series is unknown. No patients had more than one abnormality or syndrome in our series.

There were no operative deaths. Six patients required a second operation. In the immediate postoperative period, three patients (1 SAA, 2 DAA) had postoperative chylothoraces requiring re-exploration.

Two SAA underwent a posterior aortopexy at a later admission due to persistent symptoms. One patient had persistent respiratory and swallowing symptoms; and the second SAA patient had swallowing symptoms. One DAA had anterior and posterior aortopexies due to respiratory symptoms.

2.3. Postoperative symptoms per outpatient chart review

At the most relevant last clinic visit, 45% (18/40) SAA and 65.2% (15/23) DAA had documented post-operative symptoms. The median time for the latest reported respiratory or swallowing symptom was 17.4 months (IQR 3.0–27.5 months) in the SAA group, and 10.9 months (IQR 0.99–33.1 months) in the DAA group. Persistent breathing difficulties were noted in 35% (14/40) SAA and 56.5% (13/23) DAA. Swallowing difficulties remained in 7 (17.5%) SAA and 3 (13.0%) DAA patients. Four patients had both swallowing and breathing difficulties (3 SAA, 1 DAA). There was no difference in the number of reported breathing and swallowing symptoms between the SAA and DAA groups (Fig. 2). Twelve of the 63 patients (19%) were followed long-term by a cardiologist.

2.4. Symptom focused survey results

Twenty-seven of 63 families (42.8%) were able to be reached by phone and consented to study participation. We obtained 14 responses. The median time from surgery to survey completion was 36 months for the DAA group, and 42.6 months for the SAA group. Ten responses were from the SAA group, and four from the DAA group. Five patients in the SAA group reported postoperative swallowing symptoms in the survey. Of those five patients, two had feeding gastrostomy tubes in place at the time of vascular ring repair due to other congenital conditions. Fig. 3 shows the patient survey endorsed symptoms according to arch anatomy.

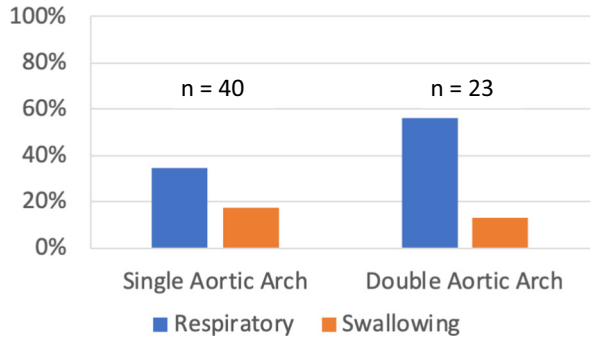

Fig. 2. Percentage of patients with respiratory and swallowing symptoms reported in the last outpatient clinic note based on arch anatomy

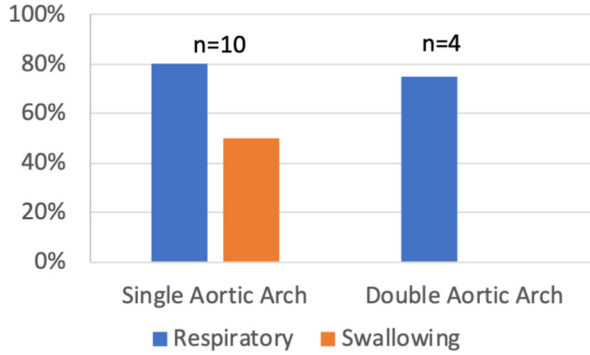

Fig. 3. Percentage of patients with respiratory and swallowing symptoms reported at time of symptom focused survey based on arch anatomy

2.5. Concordance between outpatient chart review and symptom focused survey

Of the eight SAA patients with respiratory symptoms on the survey, three had documented respiratory symptoms in their latest clinic notes. Only one patient of the five SAA with reported swallowing symptoms on the survey had documented symptoms in the clinic notes. For the DAA group, two of the three positive survey respondents had respiratory symptoms documented in the chart.

2.6. Postoperative symptoms following subclavian reimplantation

All 40 patients with SAA underwent division of the ligamentum arteriosum. Twenty-three of the 40 (57.5%) SAA patients underwent subclavian reimplantation. Of these 23 patients, five patients (21.7%) had isolated postoperative respiratory symptoms, two patients (8.7%) had isolated swallowing symptoms, and one patient had both breathing and swallowing difficulties per the last clinic visit notes.

Seven of the 23 patients who had subclavian reimplantation completed the postoperative symptom survey. Four patients had both breathing and swallowing difficulties postoperatively. Two had isolated respiratory issues, and one was asymptomatic. Of the six who reported respiratory symptoms, one had documented symptoms at last follow-up. Of the four who reported swallowing symptoms, one had documented symptoms at last follow-up.

The post-operative clinic records of the 23 SAA patients who underwent subclavian artery reimplantation and Kommerell's resection were compared to the 17 SAA who were not reimplanted. Eight of the 23 children (34.7%) reimplanted had persistent breathing or swallowing symptoms which was not different compared to the 10 of 17 (58.8%) symptomatic children who did not have their subclavian arteries reimplanted (58.8%) ($p = 0.13$).

3. Discussion

The presentation of vascular rings is uncommon as evidenced by our series of 63 patients in 11 years. Surgical division of a vascular ring is considered therapeutic. The majority of patients have an initial postoperative visit with their surgeon and subsequently follow-up with other care providers. However, it is unknown whether symptoms are completely relieved or persist. Based on our findings, post-operative symptoms may occur more commonly than previously thought.

3.1. Respiratory and swallowing symptoms following vascular ring repair

In our series, postoperative breathing issues appear to be the most common post-repair symptom, with others reporting frequent infections, and/or tracheomalacia as markers for symptom persistence [10, 13, 14]. In our retrospective cohort, we did not assess for the presence

of tracheomalacia or tracheal abnormalities. It is possible that we have a number of patients with airway issues that are unrecognized. In fact, Naimo et al. followed 132 patients after vascular ring repair (80, DAA, 50 SAA, 2 not specified) from 1978-2014. In their study, persistent tracheal compression was present in 2% of patients (2 DAA, 1 SAA). Seven patients also had mild tracheomalacia postoperatively with unspecified vascular ring anatomy (8.8%) [10]. Similarly, Bonnard et al. noted severe tracheomalacia in two of 38 (5.3%) postoperative patients from 1990-2000 [14]. In our contemporary cohort, 27 patients (42.8%, 13 DAA, 14 SAA) had respiratory symptoms at their most recent clinic follow-up of unclear etiology. We do not know if the symptoms were associated with tracheomalacia except in two patients with bronchoscopy documented tracheomalacia. Nor do we know the frequency of respiratory infections in our population. Further investigation with bronchoscopy is needed to help identify the etiology of persistent breathing symptoms in our cohort.

In addition to bronchoscopy to investigate persistent breathing difficulties, another option may be the use of pulmonary function tests in children who are old enough. Marmon et al. evaluated patients postoperatively for respiratory difficulty with pulmonary function tests. Their cohort included 54 patients from 1968-1983. Twenty-nine of their patients at follow-up were old enough to undergo testing and were asymptomatic. Nine (52.9%) of 17 "asymptomatic" patients flow-volume loops indicated central airway obstruction [15]. While we do not have children old enough for pulmonary function tests yet, pulmonary function tests with symptom surveys may be useful in evaluating the efficacy of our vascular ring repairs. Pulmonary function tests may also be used as a noninvasive study to triage to determine who may require bronchoscopy.

In our series, 35% (14) of SAA patients and 56.5% (13) of DAA patients had persistent respiratory symptoms documented in the medical record at a median follow-up of 17.4 months (SAA) and 10.9 months (DAA). These respiratory symptoms are unrelated to any known tracheal abnormalities. However as previously stated, we may have underdiagnosed tracheal issues. Our follow-up is shorter than Schmidt et al. but correlates with the reported 36% persistent respiratory symptoms (median follow-up 6.8 years over a 32-year period). The challenge of interpreting their study is the length of time (32 years) and the evolution of surgical technique for vascular ring repair. In addition, there was no arch anatomy reported [5]. Another study by Alsenaidi et al. similarly noted a high persistence of respiratory symptoms in 34% of DAA patients at a median follow-up of 6.5 months but had no data on SAA [3]. Other studies such as Francois et al. reported fewer postoperative symptoms in 23% of SAA and 14% of DAA patients at 6-month follow-up [6]. In follow-up beyond one year, Bonnard et al. reported complete symptom resolution in 68% of their patients, and partial symptom improvement in an additional 21% of their patients, with no symptom improvement in 11% of their patients [14]. Besides Naimo et al, the longest follow-up of respiratory symptoms was 37.2 months in Bonnard's cohort in 38 of their 62 patients with the remaining 24 patients having three months follow-up [10, 14].

Ten (15.8%) of our 63 patients (7 SAA, 3 DAA) experienced swallowing symptoms at last follow-up. One patient in our SAA group required late posterior aortopexy due to dysphagia. Persistence of swallowing symptoms occurred in 6% of the patients in the study from Naimo et al [10]. Our data and others show that vascular ring division may only be partially effective for relief of feeding difficulties [3, 10, 16]. However, few if any of our patients had esophagrams or upper endoscopies in follow-up.

The wide range of reported breathing and swallowing symptoms postoperatively suggests the need for closer and longer follow-up.

3.2. Family reported symptoms

In an attempt to correlate the accuracy of the medical record with family reported breathing and swallowing symptoms, we reached 27 of our 63 patients' families and requested a symptom focused survey. Fourteen families completed the survey (51.8% of the 27 – 10 SAA, 4 DAA). We compared these survey reports to the latest clinic notes. Eight patients in the SAA group had a range of respiratory symptoms on the survey. Only three of the eight patients had documented symptoms in their medical records. Three SAA patients had swallowing difficulties on survey (excluding the two with preoperative G-tubes) with no documented swallowing symptoms in the medical record. For the DAA group, two of the three patients with respiratory symptoms in the survey had documented symptoms in their chart. One potential reason for this discordance may be that the surveys focused on breathing and swallowing symptoms that may not be routinely asked in clinic. In addition, parents may be more likely to complete the survey if their child is experiencing symptoms. Humphrey et al. also utilized a symptoms focused survey, consisting of 10 questions regarding breath difficulties, swallowing difficulties, growth, exercise tolerance, and the child's concerns about their incision [16]. Twenty-four of their 38 patients responded. They noted over 50% symptom resolution with breathing and over 66% resolution with feeding symptoms. However, they did not report the median time to survey completion [16]. These results align closely with ours but with a higher completion rate and may indicate the need to simplify our survey in further follow-up. We may also achieve a higher completion rate by distributing the survey to our patients' pediatricians.

3.3. Role of surgical technique for SAA

In terms of surgical technique, the most common method of repair is through a thoracotomy. Some centers reimplant the aberrant subclavian artery for SAA and resect the diverticulum of Kommerell. Certainly, in terms of reoperative vascular ring surgery, Backer et al. in a series of 26 patients proposed resection of the Kommerell's diverticulum and reimplantation of the aberrant left subclavian artery for patients who had prior repair of SAA [17]. However, we do not know the degree of symptom relief in these patients who required reoperation. In our current practice for SAA, we prefer to resect the Kommerell's diverticulum and re-implant the aberrant subclavian artery at their initial operation when feasible. In our seven-year cohort, this was an evolving technique as in our SAA group, 24 of 40 (60.0%) patients underwent Kommerell's resection and 23 of 40 (57.5%) subclavian artery reimplantation. Of the 23 SAA patients who had reimplantation of the aberrant subclavian artery, six (26.1%) had persistent respiratory symptoms, and three other patients (13.0%) had swallowing symptoms at last clinic follow-up. It is unclear why these patients had persistent symptoms even with subclavian reimplantation. This underscores the need for long term follow-up especially when performing reimplantation during the index operation.

Our series did not have enough power to detect a difference and reflects the continued question of whether reimplantation of the subclavian artery for SAA is essential. Although it could be argued that a posterior aortopexy via from the contralateral chest for SAA patients with persistent post-operative symptoms may be facilitated by reimplantation at the index operation.

Some centers are performing SAA repair using video assisted thoracoscopic surgery (VATS). With this approach, the Kommerell's diverticulum is not resected nor is the aberrant subclavian artery reimplanted. Al-Bassam et al. reported safe perioperative outcomes in four SAA patients but did not have long term follow-up beyond 6 months with respect to symptom relief [18]. Riggle et al. compared their thoracoscopic experience to their open experience with SAA and DAA. Similar to Al-Bassam in the case of SAA, Kommerell's diverticulum was not resected (13 patients of 21 total SAA) or the aberrant subclavian artery reimplanted. Interestingly when they compared all SAA and DAA VATS patients to the open repair patients, they observed greater symptom relief in the VATS group compared to open group (90% vs. 31% respectively) [19]. The role of VATS may be of increasing interest if the symptom relief is better for children with symptomatic vascular rings.

3.4. Future directions

The high rates of respiratory and swallowing symptom persistence in our cohort as well as others, and the varying time frames of follow-up may underscore the need for comprehensive aerodigestive centers at programs performing vascular ring repairs. These centers can ensure multidisciplinary workup and care for persistent symptoms. Boesch et al. recently wrote a consensus statement about the structure and function of these programs, with a key definition of an aerodigestive patient as follows: "A pediatric aerodigestive patient is a child with a combination of multiple and interrelated congenital and/or acquired conditions affecting airway, breathing, feeding, swallowing, or growth that require a coordinated interdisciplinary diagnostic and therapeutic approach to achieve optimal outcomes. This includes (but is not limited to) structural and functional airway and upper gastrointestinal tract disease, lung disease because of congenital or developmental abnormality or injury, swallowing dysfunction, feeding problems, genetic diseases, and neurodevelopmental disability." [20]. This consensus statement provides a basic framework for coordinating multidisciplinary care for these patients. Work is currently underway at our institution to establish an aerodigestive center and will aid in a comprehensive multidisciplinary evaluation of our patients who have symptoms after repair. These centers are often led by gastroenterologists, pulmonologists, and otolaryngologists [21]. Since at least 25% of children in this series had a genetic abnormality or syndrome, genetic testing may be appropriate in these children in a broad context of an aerodigestive clinic. Similarly with the increasing resolution of fetal echocardiograms, vascular rings are being detected at our institution antenatally. The presence of a vascular ring is rarely an acute airway emergency; however, discussion is ongoing about antenatal parental counseling and the role of the clinic.

The role of the preoperative workup for vascular rings continues to evolve as some (Backer et al.) have advocated for the least imaging possible until the surgeon is comfortable with the operation needed. Backer and colleagues also note that low dose CT imaging has become one of the preferred methods over esophagram with routine echocardiogram screening due to the 12% incidence of associated cardiac issues [2]. Interestingly two years later, Snarr and Dyer advocated that barium esophagram and echocardiogram should be the first screening tools and CT/MRI reserved for abnormal or inconclusive findings on transthoracic echocardiogram [22].

4. Conclusions

We sought to answer the question of how well vascular ring repair alleviates respiratory and swallowing symptoms in the long term. Our median time of symptom persistence based on latest clinic follow-up was 17.4 months in the SAA group, and 10.9 months in the DAA group. Our follow-up was not as long as we had hoped because many patients may be following with providers outside of our system, and we are unlikely to be capturing all patients with persistent symptoms.

Nonetheless, our data indicates that we are not completely alleviating the breathing and swallowing symptoms of vascular rings with surgery. Respiratory symptoms persist, especially for patients with tracheomalacia. In addition, tracheomalacia does not explain swallowing difficulties. Patients who have undergone vascular ring repair would benefit from more frequent and focused postoperative visits using survey tools. Aerodigestive centers are becoming more common across the United States. These multidisciplinary centers will hopefully further aid in treating these patients. Given the small numbers of vascular rings across each center, a multicenter database or prospective trial would also help answer these questions.

4.1. Limitations

Our study is limited due to the retrospective design. There was limited genetic data on 16 of our 63 (25%) patients with known genetic anomalies. We were unable to determine if there were any genetic anomalies in the remaining 47 patients. There was also limited bronchoscopy data in regards to tracheomalacia, with 38 of the 63 (60%) of the children undergoing preoperative or intraoperative bronchoscopy. Of the patients with persistent symptoms, there was a paucity of postoperative imaging or testing to delineate a persistent anatomic cause for their symptoms. We also need longer follow-up to determine if our patients' symptoms improve into adolescence and adulthood. Attempts were made to conduct focused surveys, but the response rate was low. In addition, many families were unreachable. The nature of the survey is certainly open to bias as well as families may be more likely to complete surveys if their children are having symptoms.

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Disclosures

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