Infants with Esophageal Atresia and Right Aortic Arch: Characteristics and Outcomes from the Midwest Pediatric Surgery Consortium

Dave R. Lal1,*, Dave R. Lal, dlal@chw.org, Samir K. Gadepalli2, Cynthia D. Downard3, Peter C. Minneci4, Michelle Knezevich5, Thomas H. Chelius6, Cooper T. Rapp1, Deborah Billmire6, Steven Bruch2, R. Carland Burns5, Katherine J. Deans3, Mary E. Fallat7, Julia Grabowski8, Ferdynand Hebel8, Michael A. Helmrath9, Ronald B. Hirschl1, Rashmi Kabre8, Jonathan Kohler10, Matthew P. Landman6, Charles M. Leys10, Grace Z. Mak11, Daniel J. Ostlie10, Jessica Raque1, Beth Rymeski1, Jacqueline M. Saito12, Shawn D. St. Peter7, Daniel von Allmen1, Brad W. Warner12, Thomas T. Sato1 on behalf of the Midwest Pediatric Surgery Consortium.

1Division of Pediatric Surgery, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI
2Section of Pediatric Surgery, Department of Surgery, University of Michigan, Ann Arbor, MI
3Division of Pediatric Surgery, Hiram C. Polk, Jr., M.D. Department of Surgery, University of Louisville, Louisville, KY
4Center for Surgical Outcomes Research, The Research Institute and Department of Surgery, Nationwide Children’s Hospital, University of Ohio, Columbus, OH
5Division of Epidemiology, Institute for Health and Society, Medical College of Wisconsin, Milwaukee, WI
6Division of Pediatric Surgery, Department of Surgery, Indiana University School of Medicine, Indianapolis, IN
7Division of Pediatric Surgery, Department of Surgery, Children’s Mercy Hospital, Kansas City, MO
8Division of Pediatric Surgery, Department of Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago Northwestern University Feinberg School of Medicine, Chicago, IL
9Division of Pediatric Surgery, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
10Division of Pediatric Surgery, Department of Surgery, University of Wisconsin, Madison, WI
11Section of Pediatric Surgery, Department of Surgery, The University of Chicago Medicine and Biologic Sciences, Chicago, IL
12Division of Pediatric Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, MO

*Corresponding author.

Abstract

Purpose
Right sided aortic arch (RAA) is a rare anatomical finding in infants with esophageal atresia with or without tracheoesophageal fistula (EA/TEF). In the presence of RAA, significant controversy exists regarding optimal side for thoracotomy in repair of the EA/TEF. The purpose of this study was to characterize the incidence, demographics, surgical approach, and outcomes of patients with RAA and EA/TEF.

Methods
A multi-institutional, IRB approved, retrospective cohort study of infants with EA/TEF treated at 11 children’s hospitals in the United States over a 5-year period (2009 to 2014) was performed. All patients had a minimum of one-year follow-up.

Results
In a cohort of 396 infants with esophageal atresia, 20 (5%) had RAA, with 18 having EA with a distal TEF and 2 with pure EA. Compared to infants with left sided arch (LAA), RAA infants had a lower median birth weight, (1.96 kg (IQR 1.54-2.65) vs. 2.57 kg (2.00-3.03), p=0.01), earlier gestational age (34.5 weeks (IQR 32-37) vs. 37 weeks (35-39), p=0.01), and a higher incidence of congenital heart disease (90% vs. 32%, p < 0.0001). The most common cardiac lesions in the RAA group were ventricular septal defect (7), tetralogy of Fallot (7) and vascular ring (5). Seventeen infants with RAA underwent successful EA repair, 12 (71%) via right thoracotomy and 5 (29%) through left thoracotomy. Anastomotic strictures trended towards a
difference in RAA patients undergoing right thoracotomy for primary repair of their EA/TEF compared to left thoracotomy (50% vs. 0%, p=0.1). Side of thoracotomy in RAA patients undergoing EA/TEF repair was not significantly associated with mortality, anastomotic leak, recurrent laryngeal nerve injury, recurrent fistula, or esophageal dehiscence (all p>0.29).

Conclusion
RAA in infants with EA/TEF is rare with an incidence of 5%. Compared to infants with EA/TEF and LAA, infants with EA/TEF and RAA are more severely ill with lower birth weight and higher rates of prematurity and complex congenital heart disease. In neonates with RAA, surgical repair of the EA/TEF is technically feasible via thoracotomy from either chest. A higher incidence of anastomotic strictures may occur with a right-sided approach.

Level of Evidence
Level III

Keywords: Esophageal atresia, Right Aortic Arch, Thoracotomy, Anastomotic stricture, Complications

Introduction
Repair of esophageal atresia in the presence of a right aortic arch (RAA) is an often discussed but infrequently encountered anatomic variant, occurring in approximately 5 to 13% of cases [1-3]. Prior to advances in fetal and neonatal imaging, it was difficult to preoperatively diagnose laterality of the aortic arch, leading to intra-operative discovery of RAA during right thoracotomy for esophageal atresia repair. Preoperative diagnosis of aortic arch abnormalities, including RAA, has been greatly facilitated by contemporary fetal ultrasound and postnatal echocardiography [4,5]. These improved imaging modalities allow the surgeon to choose on which side to approach the esophageal repair, based on the presence of a right or left sided aortic arch. Despite improved preoperative accuracy, controversy remains on whether to use a right or left thoracotomy to repair esophageal atresia with RAA, and there are limited outcome data to define the most appropriate operative approach. We report the clinical characteristics, operative approach, and outcomes of a multi-institutional cohort of infants with esophageal atresia and RAA from 11 academic children’s hospitals.

1. Methods
1.1 Patients and study design

A multi-institutional retrospective cohort study was performed within the Midwest Pediatric Surgery Consortium (www.mwpsc.org; see Acknowledgments for list of centers) on infants diagnosed with esophageal atresia with or without tracheoesophageal fistula. Clinical practice and administrative databases were utilized to identify eligible patients. Individual Institutional Review Board approval was obtained at all eleven participating children’s hospitals. This study examines a specific subset of an entire esophageal atresia (EA) cohort that we have previously reported. Included patients underwent primary repair of esophageal atresia (ICD-9 750.3) from January 1, 2009 to January 1, 2014 and had a minimum of one-year follow-up.

Study data were stored and managed using REDCap (Research Electronic Data Capture) software hosted at The Medical College of Wisconsin [6]. All study data was entered locally and examined for completeness of data entry and accuracy both locally and centrally within the consortium. Missing data points were obtained when feasible and outliers were confirmed for accuracy.

1.2 Methods

Members of the consortium determined relevant data elements to collect and analyze prior to initiation of the study. Demographics, prenatal information, associated congenital anomalies, diagnostic imaging, physiologic status using American Society of Anesthesiology (ASA) Physical Status Classification at the time of esophageal repair were defined as preoperative variables. Perioperative data collection included, operative technique and findings, postoperative morbidity and mortality and need for further intervention(s) up to one year following esophageal anastomosis. Race/ethnicity was self-identified by parents at the time of hospital registration. Congenital heart disease was defined as clinically identified cardiac defects excluding patent ductus arteriosus and patent foramen ovale. Long gap esophageal
atresia was defined as a gap of three or more vertebral bodies between the proximal and distal esophageal segments determined on pre-operative chest x-ray utilizing an orogastric tube placed into the proximal pouch and the carina as a proxy for the tracheoesophageal fistula level or limited esophageal pouch contrast studies. Esophageal anastomotic stricture was defined as any need for dilatation within one year of surgical establishment of esophageal continuity. Anastomotic leak was defined as extravasation of contrast on a post-operative esophagram. Esophageal dehiscence was defined as complete separation of the two esophageal segments as determined by contrast study or at surgical exploration. Esophagrams were routinely obtained most commonly on post-operative day seven. Prenatal diagnosis or suspicion of EA/TEF was determined by prenatal ultrasound reports mentioning polyhydramnios and/or absent/small stomach with mention of a possible diagnosis of EA within the report. Similarly, the pre-operative side of the aortic arch was assessed by reviewing the prenatal ultrasound or postnatal echocardiogram reports when available.

1.3 Statistical analysis

Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA). Patients with missing data were excluded from the analysis. Continuous data were expressed as medians and interquartile ranges and discrete variables were expressed as percentages. For discrete variable comparisons, Pearson’s Chi-Square Test was used. Fisher’s Exact Test was used for associations of two binary variables with small cell sizes. The Wilcoxon Rank-Sum test was used to compare medians. A $p$-value less than 0.05 was considered statistically significant.

2. Results

2.1 Study Cohort and Demographics
Over the five-year study period, 396 infants with esophageal atresia with or without TEF were identified. The aortic arch was located on the left side in 364 (92%), right side in 20 (5%) and in 12 (3%) the arch side was unknown. Prenatal diagnosis of EA/TEF was diagnosed or suspected in 4 (20%) patients with RAA compared to 49 (13%) with a left sided arch.

Of the 20 infants with RAA, 11 (55%) were female, 18 (90%) were Caucasian, 1 (5%) African American, and 1 (5%) Hispanic. Ten (50%) had public insurance, 8 (40%) had private insurance and 2 (10%) self-pay. Esophageal atresia with distal TEF occurred in 18 infants with RAA; the remaining 2 had pure esophageal atresia. Infants with a right sided aortic arch had a significantly lower median birth weight and were more premature compared to infants with a left sided aortic arch (Table 1). Congenital heart disease was documented in 90% of infants with RAA versus 32% in those with a left sided arch (p<0.0001). The most frequent cardiac lesions in infants with RAA included ventricular septal defect (7/20, 35%), tetralogy of Fallot (7/20, 35%) and vascular ring (5/20, 25%).

2.2 Echocardiogram, Surgical Approach and Outcomes

Of the 20 infants with RAA (Figure 1), 5 underwent EA repair via a right thoracotomy without pre-operative echocardiography, 15 (75%) underwent preoperative echocardiography prior to repair. In these 15, 3 patients were excluded from analysis as none underwent successful EA repair (one died of multisystem organ failure/sepsis 5 months after birth, another of cardiac failure 26 months after birth and the third was lost to follow-up at 4 months of life after transfer to a different institution). Of the 12 remaining patients with pre-operative echocardiography, RAA was correctly identified in 9 (75%) and incorrectly interpreted as left sided in 3 (25%). In the 9 patients with a correctly identified RAA by echocardiogram prior to EA repair, 6 underwent initial left thoracotomy with successful primary EA repair achieved in 5 (83%). The remaining patient underwent conversion to right thoracotomy with successful
primary EA. Three infants (25%) underwent right thoracotomy with preoperative identification of RAA. Primary esophageal repair was successfully completed in all.

The three patients incorrectly diagnosed with left aortic arch by echocardiography and found intraoperatively to have RAA underwent successful EA repair through the right chest but subsequently all three developed anastomotic strictures requiring 1-2 dilations within 1 year of the esophageal repair. There were no anastomotic leaks, recurrent fistulas, esophageal dehiscences, vocal cord paresis/paralysis, chylothoraces or deaths in this group. Additionally, none required aortopexy or tracheopexy for tracheomalacia. All 3 patients had trans-anastomotic tubes placed intraoperatively and maintained in the postoperative period, and all were treated with postoperative acid suppression medication.

Ultimately, 11 patients underwent initial right thoracotomy for repair of their esophageal atresia (5 RAA infants without a pre-operative echocardiography, 3 infants incorrectly identified as having a LAA on pre-operative echocardiography and 3 with known RAA by pre-operative echocardiography). The success rate of esophageal atresia repair via the initial thoracotomy was 11/11 via a right thoracotomy and 5/6 (83%) via a left thoracotomy.

2. Right sided Aortic Arch compared to Left Sided Aortic Arch

A total of 364 infants with LAA were compared to 17 infants with RAA who underwent primary successful repair of their esophageal atresia (Table 2). There was no difference in the distribution of long EA gap length (defined as a ≥3 vertebral body gap), mortality, anastomotic stricture, anastomotic leak, recurrent fistula or other post-operative complications between the two groups (p>0.1 for all). Similarly, the use of trans-anastomotic tubes, postoperative acid suppression, and need for fundoplication or aortopexy were no different between groups (p>0.7 for all).
2.3 Right Sided Aortic Arch and Outcomes

Seventeen infants with RAA underwent primary successful repair of their esophageal atresia, 12 (71\%) via right thoracotomy and 5 (29\%) via left thoracotomy (Table 3). No patient with RAA underwent thoracoscopic EA repair. There was no difference in mortality or the incidence of anastomotic leak, recurrent fistula, esophageal dehiscence, vocal cord paralysis/paresis, or chylothorax between those undergoing right versus left thoracotomy (p>0.29 for all) for EA repair. Despite a similar distribution of long EA gap length and postoperative utilization of trans-anastomotic tubes (p=1.0 and 0.54, respectively), there was a trend toward increased anastomotic strictures in RAA infants who underwent right thoracotomy for EA repair compared to those infants repaired via left thoracotomy (50\% vs. 0, respectively, p=0.1). The use of postoperative acid suppression, fundoplication or aortopexy was similar between groups (p>0.3 for all).

3. Discussion

In this multi-institutional study, we identified a 5\% incidence of RAA in neonates with esophageal atresia. This incidence is slightly higher than the 3.6\% rate calculated in a recent systematic review incorporating 7 single-institution retrospective studies. [7] Similar to other studies [7], we found that infants with EA and RAA have a statistically significant increase of complex congenital heart disease compared to infants with EA and left aortic arch. The increased incidence of congenital heart disease may be a contributing factor to the lower birth weight and increased prematurity within the RAA cohort.

Historically, accurate preoperative identification of RAA by echocardiography has been low, ranging from 14\% to 62.5\%. [7-9] Our study reports the highest detection (80\%) of RAA in EA patients utilizing
preoperative echocardiography. This may reflect advances in fetal and antenatal echocardiographic technology and resolution. Additionally, consortium institutions are high volume, pediatric-specific academic medical centers with significant experience and expertise with fetal and neonatal imaging. However, the fact remains that the side of the aortic arch was incorrectly identified in 20%. Due to the low identification rate of RAA in previous studies, some authors recommend further imaging of EA infants with chest computed tomography, magnetic resonance imaging, or cardiac catheterization. Each of these additional tests expose infants to increased risks, including ionizing radiation and/or sedation/general anesthesia, and should be used selectively if arch anatomy is unclear by echocardiography. Three infants in our study with an incorrectly identified LAA by echocardiogram underwent right thoracotomy for EA repair, and all three had successful primary repair. All three developed postoperative anastomotic strictures that were treatable with dilation (1-2 dilations). Therefore, even with incidentally discovered RAA at the time of EA repair, it appears reasonable to attempt primary repair through the right chest if feasible rather than close and move to the left chest.

Our study failed to identify a significant association between the side of thoracotomy and the development of anastomotic strictures in infants undergoing EA repair with RAA. However, it is important to note that 50% of patients undergoing repair via a right thoracotomy developed an anastomotic stricture while no strictures occurred in the left thoracotomy group. It is likely that our sample size was insufficient to detect a significant difference. No other differences in postoperative complications were noted between groups, including recurrent fistula, esophageal dehiscence, vocal cord paresis, and chylothorax. Similarly, we found no differences between groups in factors commonly associated with an increased incidence of anastomotic strictures, including long gap length, anastomotic leak, and postoperative acid suppression. [10-12] Our consortium previously reported factors that contribute to anastomotic strictures in infants undergoing EA repair. [13] In a cohort of 292 infants
undergoing primary EA repair, only postoperative use of trans-anastomotic tubes was associated with anastomotic strictures on multivariate analysis. In this study, there was no difference in the use of postoperative trans-anastomotic tubes between infants with RAA undergoing EA repair through the right or left chest.

Although our study demonstrates that EA repair can be safely accomplished via either right or left thoracotomy in patients with RAA, left thoracotomy may be preferred as there is a trend toward a lower rate of anastomotic strictures. When RAA is discovered intraoperatively during right thoracotomy (incorrect or no preoperative imaging), attempting repair through right thoracotomy is reasonable with acceptable morbidity. The long-term risk of anastomotic dilation is predictably less than the morbidity associated with bilateral neonatal thoracotomies. In circumstances in which the EA cannot be repaired through a right thoracotomy due to the RAA, conversion to left thoracotomy is recommended.

Our study has several limitations. First, despite analyzing 396 patients, only 20 infants with EA had RAA, confirming the rarity of this anatomic variation. This low incidence limited the power of this study to detect differences in outcomes and the ability to perform subgroup analyses. Second, due to the retrospective nature of our study, inherent biases and an inability to establish causation between variables and outcomes exist. Lastly, although we examined many variables known to be associated with postoperative complications, we may have unintentionally excluded some or failed to account for confounding variables in our analysis. Despite these constraints, this is the first multicenter report on the surgical management of infants with esophageal atresia and right aortic arch and represents one of the largest cohorts of infants with esophageal atresia with RAA reported to date.

4. Conclusion
EA repair can be safely accomplished via either right or left thoracotomy in patients with RAA. The observation that half of RAA patients approached via a right thoracotomy for repair of their EA/TEF had anastomotic strictures, may be taken in to consideration when deciding the sidedness for surgical approach.

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Members of the Midwest Pediatric Surgery Consortium
Children’s Hospital of Wisconsin/Medical College of Wisconsin, Milwaukee, WI
American Family Children’s Hospital/University of Wisconsin, Madison, WI
C.S. Mott Children’s Hospital/University of Michigan, Ann Arbor, MI
Cincinnati Children’s Hospital/University of Cincinnati, Cincinnati, OH
Comer Children’s Hospital/University of Chicago, Chicago, IL
J. W. Riley Hospital for Children/Indiana University, Indianapolis, IN
Kosair Children’s Hospital/University of Louisville, Louisville, KY
Lurie Children’s Hospital/Northwestern University, Chicago, IL
Mercy Children’s Hospital/University of Missouri-Kansas City, Kansas City, MO
Nationwide Children’s Hospital/The Ohio State University, Columbus, OH
St. Louis Children’s Hospital/Washington University, St. Louis, MO

References


Figure 1. Summary of surgical management and outcomes in 17 infants with a right sided aortic who underwent successful repair of their esophageal atresia.

Table 1. Demographics of Infants with EA/TEF and a Right Sided Versus Left Sided Aortic Arch

<table>
<thead>
<tr>
<th></th>
<th>Right Sided Aortic Arch (n=20)</th>
<th>Left Sided Aortic Arch (n=364)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight (KG) median (IQR)</td>
<td>1.96 (1.54-2.65)</td>
<td>2.57 (2.0-3.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Median Gestational Age (wks)</td>
<td>34.5 (32-37)</td>
<td>37 (35-39)</td>
<td>0.01</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>90% (n=18)</td>
<td>32% (n=115)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proximal EA with distal TEF</td>
<td>90% (n=18)</td>
<td>85% (n=309)</td>
<td>0.75</td>
</tr>
<tr>
<td>Pure EA</td>
<td>10% (n=2)</td>
<td>7% (n=24)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 2. Outcomes after esophageal atresia repair comparing infants with a right sided aortic arch to those with a left sided aortic arch
<table>
<thead>
<tr>
<th></th>
<th>Right Aortic Arch (n=17, 4.5%)</th>
<th>Left Aortic Arch (n=364, 95.5%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality n(%)</td>
<td>3 (18%)</td>
<td>23 (6%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Anastomotic Stricture</td>
<td>6 (35%)</td>
<td>155 (43%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Anastomotic Leak</td>
<td>2 (12%)</td>
<td>85 (24%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Recurrent Fistula</td>
<td>1 (6%)</td>
<td>18 (5%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Esophageal Dehiscence</td>
<td>0</td>
<td>8 (2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vocal Cord Paresis</td>
<td>0</td>
<td>26 (7%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Long gap length*</td>
<td>3 (18%)</td>
<td>48 (13%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Trans-anastomotic Tube</td>
<td>14 (82%)</td>
<td>272 (76%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Acid Suppression</td>
<td>16 (94%)</td>
<td>323 (90%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Fundoplication</td>
<td>3 (18%)</td>
<td>50 (14%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Aortopexy</td>
<td>0</td>
<td>7 (2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>1 (6%)</td>
<td>8 (3%)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

*Gap length not reported in 2 patients who underwent a right thoracotomy. Long gap length considered a gap distance of ≥3 vertebral bodies.

Table 3. Outcomes comparing right thoracotomy to left thoracotomy for repair of esophageal atresia in infants with a right sided aortic arch

<table>
<thead>
<tr>
<th></th>
<th>Right Thoracotomy (n=12, 71%)</th>
<th>Left Thoracotomy (n=5, 29%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality n(%)</td>
<td>1 (8.3%)</td>
<td>1 (20%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Anastomotic Stricture</td>
<td>6 (50%)</td>
<td>0</td>
<td>0.10</td>
</tr>
<tr>
<td>Anastomotic Leak</td>
<td>2 (17%)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Condition</td>
<td>Count 1</td>
<td>Count 2</td>
<td>p-value</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Recurrent Fistula</td>
<td>0</td>
<td>1 (20%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Esophageal Dehiscence</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Vocal Cord Paresis</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Long gap length*</td>
<td>1 (8.3%)</td>
<td>1 (20%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Trans-anastomotic Tube</td>
<td>10 (83%)</td>
<td>3 (60%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>10 (83%)</td>
<td>5 (100%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Acid Suppression</td>
<td>12 (100%)</td>
<td>4 (80%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Fundoplication</td>
<td>2 (17%)</td>
<td>1 (20%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Aortopexy</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>1 (8.3%)</td>
<td>0</td>
<td>1.00</td>
</tr>
</tbody>
</table>

NA - not applicable, All test were performed by Fisher's Exact Test

*-Gap length not reported in 2 patients who underwent a right thoracotomy. Long gap length considered a gap distance of ≥3 vertebral bodies.
20 RAA infants

15 RAA infants underwent pre-op echo

12 RAA infants who underwent pre-op echo with follow-up

9 infants correctly identified as RAA by echo

6 infants initial repair via left thoracotomy

5/6 successful EA repair with initial Left thoracotomy

12 TOTAL underwent successful repair via LEFT thoracotomy

5 RAA infants without pre-op echo repaired via Right thoracotomy

8 RAA infants repaired via right thoracotomy

3 incorrectly identified as LAA: Repaired via Right thoracotomy

3 with initial attempt at repair via right thoracotomy

11 infants initial repair via right thoracotomy

11/11 successful EA repair with initial Right thoracotomy

12 TOTAL underwent successful repair via RIGHT thoracotomy

3 Excluded:
- 1 lost to follow-up
- 2 died prior to successful repair

1 required right thoracotomy for successful repair