

Prenatal Detection, Comorbidities, and Management of Vascular Rings



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The 3-vessel and trachea view is now integrated into obstetrical screening and facilitates prenatal detection of vascular rings. We examined trends in prenatal detection, associated cardiac and extracardiac anomalies, and surgical management in this population. We reviewed a population-based cohort of pediatric vascular ring patients diagnosed prenatally and postnatally between 2002 and 2017 in Alberta, Canada. Of 106 cases, 28 (26%) had a prenatal diagnosis. Prenatal detection increased over time: 0/29 from 2002 to 2009, 4/28 (14%) from 2009 to 2011, 7/23 (30%) from 2012 to 2014, and 17/26 (65%) from 2015 to 2017 ($p < 0.01$). The prenatal group more commonly had right aortic arch/left ductus/aberrant left subclavian artery (24/28 vs 53/78, $p = 0.04$) and associated cardiac pathology (18/28 vs 33/78, $p = 0.05$). The rate of genetic anomalies was overall higher than previously reported (34%) and did not differ between groups (11/28 vs 25/78, $p = 0.48$). Those with a prenatal diagnosis were less likely to require cross-sectional imaging (9/28 vs 48/78, $p < 0.01$), modifying the vascular ring subtype diagnosis in 2 patients. Surgical intervention was common and did not differ between groups (24/28 vs 66/78, $p = 0.89$). In conclusion, prenatal detection of vascular rings has increased. Despite differences in vascular ring subtype and associated cardiac pathology, the incidence of genetic anomalies and need for surgical intervention is not associated with timing of diagnosis. Genetic counseling should be universally offered. The diagnostic accuracy of echocardiography suggests additional imaging may not be routinely required. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1703–1708)

Vascular rings are caused by a variety of embryological abnormalities of the great arteries which result in the trachea and esophagus being encircled by vascular structures.¹ Vascular rings are relatively rare with an incidence of 2 to 10/10,000. As a result, publications have provided descriptive information from relatively small cohorts of patients.^{2–17} Vascular rings are diagnosed prenatally with the 3-vessel and trachea view (Figure 1).¹⁸ Obstetric anomaly screening is offered to all pregnant women in Canada and this view has been part of national screening guidelines since 2009.^{19–21} We hypothesized that prenatal diagnosis rates of vascular rings have increased resulting in an opportunity to better understand the clinical spectrum, presentation, and need for surgery in this population. In order to improve the accuracy of prenatal counseling, our study aimed to quantify frequency of associated anomalies,

precision of fetal echocardiography in diagnosing the anatomical subtype and need for surgery in patients with vascular rings.

Methods

This is a retrospective population-based cohort study of fetal and pediatric patients born between January 1, 2002 and December 31, 2017 with a diagnosis of a vascular ring in the province of Alberta, Canada. There are 2 fetal cardiology centers in Alberta and a single pediatric cardiac surgical program. Subjects were identified through institutional fetal cardiology, imaging, and surgical databases and included if they had a diagnosis of vascular ring, confirmed at the time of surgery when possible. Pulmonary slings and isolated right aortic arches were excluded. Subjects were then divided into 2 cohorts: those diagnosed prenatally and those diagnosed only after birth. Medical records were reviewed for demographics, genetic anomalies, echocardiogram results, additional imaging modalities used, need and indication for surgery, and age and weight at surgery. Approval was obtained from local institutional review boards. All statistical analyses were completed using SPSS Statistics (IBM Corp, Version 25.0. Armonk, NY). The data are descriptive, with frequencies reported for categorical variables. Chi-square analyses were used to compare categorical variables between groups. Student's *t* test was used to compare mean values for continuous variables. The Cochran-Armitage test for trend was used to assess changes in the rate of prenatal detection over time.

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Table 1
Patient demographics and outcomes

	Total (n = 106)	Prenatal diagnosis (n = 28)	Postnatal diagnosis (n = 78)	p Value
Female	52%	50%	53%	0.82
Age at diagnosis		23 weeks (range 15-33 weeks)	24 months (range 1 day-13 years)	NA
Type of vascular ring				
RAA/ALSA	77 (73%)	24 (86%)	53 (65%)	0.04*
DAA	26 (24%)	3 (11%)	23 (32%)	
Other	3 (3%)	1 (3%)	2 (3%)	
Additional cardiac lesions	51 (48%)	18 (64%)	33 (44%)	<0.05*
Genetic abnormalities/syndromes/associations	36 (34%)	11 (39%)	25 (32%)	0.48
Additional investigations				
Barium swallow	19 (18%)	1 (4%)	18 (23%)	0.02*
Bronchoscopy	20 (19%)	3 (11%)	17 (22%)	0.20
CT/MRI	56 (53%)	9 (32%)	48 (62%)	<0.01*
Need for surgery	89 (84%)	24 (86%)	66 (85%)	0.89
Indication for surgery				
Symptoms	43 (48%)	8/24 (33%)	39/66 (59%)	0.01*
Additional cardiac lesion	46 (52%)	16/24 (67%)	27/66 (41%)	0.03*
Unknown	16 (15%)	4 (14%)	12 (15%)	0.89
Age at surgery (months)	6 (3 days-14 years)	4 (3 days-3 years)	8 (5 days-14 years)	0.02*
Weight at surgery (percentile)		35 ± 36	40 ± 35	0.56
Need for surgery, isolated vascular rings (n = 51)	39 (76%)	6/10 (60%)	33/45 (73%)	0.71
Age at surgery, isolated vascular rings (n = 51) (months)	32 (3 days-14 years)	6 (3 days-14 months)	38 (11 days-14 years)	0.05

CT = computed tomography; DAA = double aortic arch; MRI = magnetic resonance imaging; RAA/ALSA = right aortic arch/aberrant left subclavian/left ductus.

* Statistically significant.

prenatal and postnatal groups ($p = 0.62$). There was no statistically significant difference in the proportion of genetic anomalies diagnosed in isolated vascular rings versus those with associated cardiac lesions (15/55, 27% vs 22/51, 43%; $p = 0.87$). The genetic abnormalities and associations identified included 22q11 microdeletion (21/36, 58%), trisomy 21 (10/36, 28%), CHARGE syndrome (2/36, 6%), Goldenhar syndrome (1/36, 3%), VACTERL association (1/36, 3%), and 22q11 microdeletion with VACTERL association (1/36, 3%).

In the prenatal diagnosis group, 1 vascular ring diagnosis was modified following postnatal computed tomography (CT). Prenatally, DAA was suspected, but a diagnosis of right aortic arch, mirror image branching with left posterior ductus arteriosus was confirmed by CT and at surgery.

In the postnatal diagnosis group transthoracic echocardiography led to the suspicion of an undefined vascular ring in 1 case, which was clarified by CT to be left aortic arch, aberrant right subclavian artery, and right ductus arteriosus/ligamentum. In the postnatal group, 4 cases had a fetal echocardiogram where the vascular ring was missed, of which 1 had a DAA and the other 3 had RAA/ALSA. These cases were screened in 2011, 2012, 2014, and 2015.

In patients with a prenatal diagnosis, only 9 (32%) received additional imaging beyond echocardiography with a CT or magnetic resonance imaging (MRI). Although 48 (62%) of those diagnosed after birth had a CT or MRI ($p < 0.01$). Those with a prenatal diagnosis of vascular ring were less likely to undergo barium swallow study ($p = 0.02$). However, there was no difference in the rate of

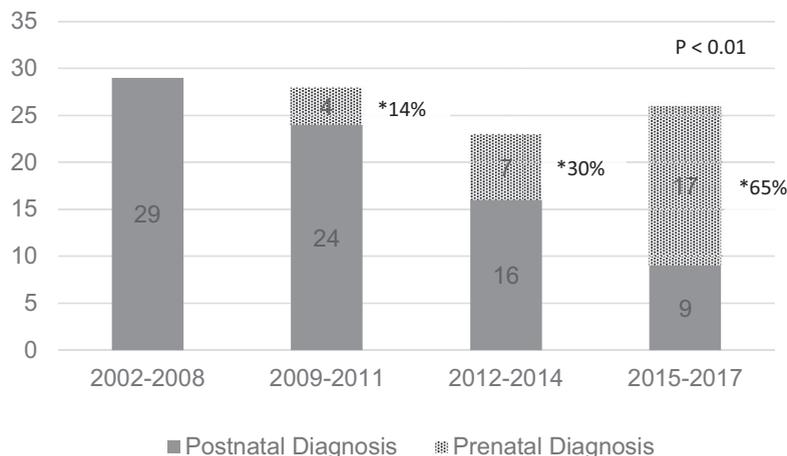


Figure 2. Prenatal detection rates of vascular rings over time. *Percentage of total with prenatal diagnosis.

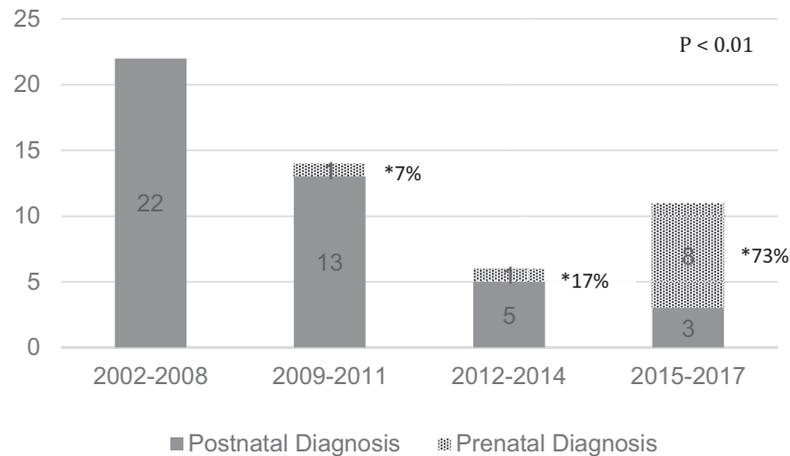


Figure 3. Prenatal detection rates of isolated vascular rings over time. *Percentage of total with prenatal diagnosis.

bronchoscopy before surgical repair based on timing of diagnosis of a vascular ring ($p = 0.20$).

Vascular ring division was common and the incidence comparable between the prenatal and postnatal diagnosis cohorts with 90 of 106 (85%) requiring surgical intervention overall; 24/28 (86%) in the prenatal diagnosis group and 66/78 (85%) in the postnatal diagnosis group ($p = 0.89$). There was also no difference in ring division rates for isolated compared with nonisolated vascular rings (37/51, 73% vs 42/55, 77%, $p = 0.65$). In the overall cohort, surgery was indicated due to symptoms in 47 (53%), due to additional cardiac lesions in 40 (45%) and to expose the trachea for a tracheoesophageal fistula repair in 1 (1%). In those with an isolated vascular ring who underwent surgery, the indications included airway symptoms (23/40, 58%), dysphagia (13/14, 32%), airway symptoms with dysphagia (3/40, 8%), and exposure of the trachea for tracheoesophageal fistula repair (1/40, 2%). Those in the prenatal diagnosis group more often underwent surgery due to the presence of additional cardiac lesions requiring surgery than for respiratory symptoms or dysphagia. More of those in the postnatal diagnosis group underwent surgery due to symptoms than the presence of additional cardiac lesions requiring surgery ($p = 0.01$). There was no mortality in those who underwent ring division.

In the overall cohort, 9 patients required cardiac surgery in the first month of life. In the prenatal group 2/28 (7%) had neonatal surgery, 1 for hypoplastic left heart syndrome and 1 to divide a vascular ring to better expose a tracheoesophageal fistula for repair. In the postnatal group, 7/78 (9%, $p = 0.09$) had neonatal surgery, 3 for additional cardiac lesions and 4 for respiratory symptoms. The additional cardiac lesions included truncus arteriosus, transposition of the great arteries, and coarctation of the aorta. In those with an isolated vascular ring, all of those requiring neonatal surgery had DAA anatomy.

The overall median age at surgery was 6 months (range 3 days to 14 years). The prenatal diagnosis group were younger at the time of surgery compared with those in the postnatal diagnosis group ($p = 0.02$). Those with an isolated vascular ring underwent surgery at a median age of 32 months (range 3 days to 14 years) compared with those

with an associated cardiac lesion who underwent surgery at a median age of 4 months (range 5 days to 5 years; $p = 0.09$). The weight percentile at surgery did not differ between those with a prenatal or postnatal diagnosis ($p = 0.56$).

Discussion

This study reports a large contemporary cohort of complete vascular ring subjects with a prenatal or postnatal diagnosis. The first report of a prenatal diagnosis of a vascular ring was made in 1998.² Our study indicates that the rate of vascular ring detection in utero has significantly increased over the past decade. In fact, there were no prenatal diagnoses of vascular rings in Alberta before 2009. Our findings are consistent with previously published data from Evans et al in a cohort of vascular rings.⁴ These findings are also concomitant with increasing rates of prenatal detection of transposition of the great arteries in Alberta as we have recently reported.²²

A fetal diagnosis of vascular ring was more often associated with additional cardiac pathology. We suspect the presence of additional cardiac pathology facilitated recognition of CHD in the pregnancy prompting fetal cardiology referral that led to the additional vascular ring diagnosis in many. This highlights that there is still room for improvement in detection of isolated vascular rings in utero by obstetric screening. It is also of interest that those in the prenatal diagnosis cohort who had additional cardiac lesions all had RAA/ALSA. Identification of any vascular ring, but particularly RAA/ALSA, should prompt a thorough evaluation for additional cardiac lesions; most commonly ventricular septal defect, tetralogy of Fallot, and atrioventricular septal defect.

The subtype of vascular ring most often diagnosed was RAA/ALSA. This is consistent with the most recently published data, including the study by Evans et al.⁴ It does differ from earlier studies in which DAA was the most common subtype.⁶

Our study demonstrates a high rate of genetic diagnoses in patients with vascular rings. Other investigations have reported lower rates of genetic diagnoses in mixed cohorts.^{4,5}

D'Antonio et al performed a meta-analysis of RAA in 2016 and found 6% had 22q11 microdeletion and 14% had an abnormal karyotype.⁵ Only 48% of the fetuses included in the latter review had a complete vascular ring. Two other studies reported a 5% incidence of 22q11.2 deletion and 9% incidence of other chromosomal abnormalities.^{16,17} The high rate of genetic abnormalities and associations in our group may relate to the inclusion of vascular ring patients only. Our relatively high rate of genetic testing likely has also impacted the genetic diagnosis rate. Families should be counselled about the high risk of genetic abnormalities once a diagnosis of vascular ring has been made, to inform decisions regarding genetic testing and pregnancy planning.

A prenatal diagnosis of vascular ring may confer an advantage to patients in terms of a reduction in the rate of additional investigations. Importantly, prenatally diagnosed cases of vascular ring were less likely to require a CT or MRI and the attendant costs and risks of radiation exposure or anesthesia than those with a postnatal diagnosis. Before vascular ring surgery, it is common in many centers to perform additional cross-sectional imaging.^{6,23,24} With fetal echocardiography, much of the vascular ring anatomy is defined. The presence of a patent ductus arteriosus before birth provides a full understanding of the vascular structures encircling the trachea and esophagus. Postnatally, by the time infants and children present with symptoms, many have had spontaneous closure of the ductus arteriosus. This leaves only a ligamentum arteriosum that cannot be evaluated by echocardiography. In our experience, only 2 cases had a change in the vascular ring diagnosis subtype after CT. This would suggest echocardiography alone is likely adequate for the majority of patients. There was also a reduction in the time to diagnosis and surgery in those with a prenatal diagnosis which may theoretically reduce the risk of residual symptoms following vascular ring ligation. However, it is possible that a prenatal diagnosis may also bias physicians to exaggerate symptoms and the need for surgery. Overall, the need for surgery among those with a vascular ring is commonplace and does not differ between those with a prenatal or postnatal diagnosis and families can be counseled as such.

The major limitation of this study is that the true denominator remains unknown as there may be asymptomatic patients in our province who have not received a diagnosis. This would contribute to an overestimation of prenatal detection rates. In addition, this study is retrospective, and we acknowledge that the case numbers remain relatively low despite being one of the largest series to date.

In summary, we have reported a large contemporary cohort of vascular ring subjects and illustrated major improvements in prenatal detection rates over time. We have documented rates of genetic abnormalities, associations, and the need for vascular ring division in this rare population that can be used to better counsel families both before and after birth. Surgical division for vascular ring is required in the vast majority of diagnosed cases, irrespective of the timing of diagnosis. Children with a prenatal diagnosis have fewer nondiagnostic investigations and have surgery at a younger age. The diagnostic accuracy of echocardiography in both prenatal and postnatal groups suggests that additional imaging may not routinely be required for

surgical planning. The rate of genetic abnormalities and associations is higher than previously reported, highlighting the need for genetic counseling and screening at diagnosis.

Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2019.02.030>.

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