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Bet, B.B.; Snoep, M.C.; Leeuwen, E. van; Linskens, I.H.; Haak, M.C.; Rozendaal, L.; ... ; Pajkrt, E.

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Short-term outcome after the prenatal diagnosis of right aortic arch

Bo B. Bet[1,2] | Maartje C. Snoep[3] | Elisabeth van Leeuwen[1,2] | Ingeborg H. Linskens[2,4] | Monique C. Haak[3] | Lieke Rozendaal[5] | Ingmar Knobbe[6] | Joost van Schuppen[7] | Carlijn E. L. Hoekstra[8] | David R. Koolbergen[9] | Sally-Ann Clur[2,10] | Eva Pajkrt[1,2]

[1]Department of Obstetrics and Gynecology, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

[2]Amsterdam Reproduction and Development, Amsterdam, The Netherlands

[3]Department of Obstetrics and Fetal Medicine, LUMC, Leiden University, Leiden, The Netherlands

[4]Department of Obstetrics and Gynecology, Amsterdam UMC Location Vrije Universiteit, Amsterdam, The Netherlands

[5]Department of Pediatric Cardiology, LUMC, Leiden University, Leiden, The Netherlands

[6]Department of Pediatric Cardiology, Amsterdam UMC Location Vrije Universiteit, Amsterdam, The Netherlands

[7]Department of Radiology, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

[8]Department of Otorhinolaryngology, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

[9]Department of Cardiothoracic Surgery, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

[10]Department of Pediatric Cardiology, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands

Correspondence
Bo B. Bet, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands.
Email: b.bet@amsterdamumc.nl

Abstract

Objectives: To determine the proportion of children that require surgery in the first year of life and thereafter in order to improve the counseling of parents with a fetus with a right aortic arch (RAA).

Methods: Fetuses diagnosed with isolated RAA, defined as the absence of intra- or extracardiac anomalies, between 2007 and 2021 were extracted from the prospective registry PRECOR.

Results: In total, 110 fetuses were included, 92 with a prenatal diagnosis of RAA and 18 with double aortic arch (DAA). The prevalence of 22q11 deletion syndrome was 5.5%. Six pregnancies were terminated and five cases were false-positive; therefore, the follow-up consisted of 99 neonates. Surgery was performed in 10 infants (10%) in the first year of life. In total, 25 (25%) children had surgery at a mean age of 17 months. Eight of these 25 (32%) had a DAA. Only one child, with a DAA, required surgery in the first week of life due to obstructive stridor.

Conclusions: Children with a prenatally diagnosed RAA are at a low risk of acute respiratory postnatal problems. Delivery in a hospital with neonatal intensive care and pediatric cardiothoracic facilities seems only indicated in cases with suspected DAA. Expectant parents should be informed that presently 25% of the children need elective surgery and only incidentally due to acute respiratory distress.

Key points

What is already known about this topic?

- The detection rate of a fetal right aortic arch (RAA) has increased after the introduction of the three-vessel view (3VV) and three-vessel trachea view (3VTV) to fetal cardiac screening.

Sally-Ann Clur and Eva Pajkrt joint senior authors

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- Suspicion of fetal RAA may require advanced prenatal diagnostics and careful follow-up as it can coexist with intra- and extracardiac anomalies and chromosomal anomalies such as 22q11 deletion.
- An isolated RAA may be considered a benign condition, but sometimes requires surgical intervention due to respiratory or feeding problems.

What does this study add?

- A surgical intervention was required in 10% and 25% of the infants with a prenatal diagnosis of isolated RAA in the first year and first 5 years of life, respectively.
- A neonatal intervention for acute respiratory distress due to tracheal compression is rare, but may be required in cases with a double aortic arch (DAA).
- Delivery in a hospital with neonatal intensive care facilities is advised in all cases of suspected DAA.

1 | INTRODUCTION

A right aortic arch (RAA) is a congenital heart defect (CHD) in which the aortic arch deviates to the right instead of the left. The prevalence of RAA is estimated at 0.1%, but may be higher as it may remain undetected and asymptomatic throughout life.[1–3] The prenatal detection rate in the past was low but has significantly increased since the addition of three-vessel view (3VV) and three-vessel trachea view (3VTV) to fetal screening protocols.[4–6] In the Netherlands, the 3VV was added as a mandatory view in 2012.[7] Although the 3VTV has been taught and implemented in hospital settings, as per ISUOG guidelines, it is not yet mandatory in the national screening program.[8,9]

Variations in the aortic arch anatomy result from the abnormal regression of the primordial paired aortic arches during embryonic development.[2,10,11] They may require advanced prenatal diagnosis and careful follow-up as they can coexist with intra- and extracardiac anomalies and chromosomal anomalies such as 22q11 deletion.[12–15] Normal development leads to a left aortic arch (LAA) and a left-sided arterial duct (LAD). An RAA can exist with LAD or right-sided arterial duct (RAD) and may occur with aberrant origin of the left subclavian artery (ALSA), RAA with a mirror-image branching pattern, or be part of a double aortic arch (DAA).[3,14] When an isolated RAA (i.e. without associated intra- or extracardiac anomalies) forms part of a vascular ring encircling the trachea and esophagus, symptoms such as stridor or dyspnea can occur at any time from birth and dysphagia may develop once solid food is started.[4,11,16,17] Surgical treatment is then required.[2,11,14] The timing of symptom onset and of possible surgery should be discussed during prenatal counseling and may affect the birth plan.

There are currently no guidelines addressing the postnatal follow-up of an isolated RAA. Therefore, we aimed to evaluate the short-term outcome of these fetuses and to determine the incidence of surgical interventions in the first year of life, the differences between prenatal and postnatal diagnoses, the incidence and onset of symptoms, and the use of postnatal diagnostic methods.

2 | METHODS

2.1 | Design and population

We conducted a cohort study including pregnant women with fetuses diagnosed with an isolated RAA. Cases were included from January 2007 until December 2020 from three fetal medicine units in the Netherlands: Leiden University Medical Center and Amsterdam University Medical Centers (Amsterdam UMC), location AMC and VUmc that are united in the formation of the Center for Congenital Heart Disease Amsterdam-Leiden (CAHAL). All patients diagnosed with and treated for congenital heart defects (CHDs) in the three hospitals are recorded prospectively in a collective registry PRECOR.[18] We included only fetuses with a prenatal diagnosis of an RAA, which means we excluded cases with associated intracardiac or other structural anomalies. Fetuses with genetic syndromes without extracardiac anomalies were included. Only cases with at least 1 year of postnatal follow-up available were included. In all newborns with a prenatal diagnosis of an RAA, transthoracic echocardiography was performed postnatally, sometimes followed by a CT-thorax and/or diagnostic laryngo-tracheo-bronchoscopy (dLTB). Typically, diagnostic tests were performed when the child became symptomatic; however, in location AMC, dLTB at around one year of age was advised in asymptomatic babies as well from 2017 to assess the degree of airway compression. A CT-thorax was performed in all cases of (suspected) DAA to confirm the diagnosis as surgical correction was anticipated. When dysmorphic postnatal findings were detected, genetic testing was also offered, if it was not already performed prenatally.

This manuscript is written in alignment with Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[19] The

Medical Ethics Committee of the Amsterdam UMC approved this study (W21_361).

2.2 | Outcomes

The primary outcome measure was surgical intervention before the age of 1 year. In addition, the incidence and clinical presentation of symptoms related to the RAA were registered as well as the pre-surgical diagnostic work-up. Secondary outcomes were delivery-related outcomes, such as preterm birth, signs of acute respiratory distress, and admission to the neonatal intensive care unit (NICU) directly after birth.

2.3 | Data collection and analysis

All data were collected in a Castor EDC online database. The electronic patients' records were evaluated to collect additional information on maternal and fetal characteristics: Maternal age, obstetric history, positive family history of CHD, multiple pregnancy, gestational age at diagnosis, diagnosis of RAA subtype, estimated fetal weight, and outcome of prenatal genetic testing. In this study, RAA was divided in four subtypes: RAA with LAD, RAA with RAD, DAA, and RAA without further specifications. Sonographic evaluation of the thymus was not performed routinely; therefore, this data was not collected. Data on pregnancy and neonatal outcomes were retrieved from electronic patients' records of the mother and child and consisted of gestational age at delivery, type and place of delivery, APGAR scores, birth weight, postnatal diagnosis of RAA subtype, genetic testing, admission to NICU, incidence and type of symptoms, age at presentation of symptoms, incidence of surgical intervention, age at surgical intervention, type of surgical intervention, and complications after surgery. The results of imaging prior to surgery were collected and consisted of postnatal echocardiography, dLTB, CT-thorax, and/or a barium swallow test, all assessed by experienced radiologists. Postnatal confirmation of the diagnosis of an RAA was made by transthoracic echocardiography or CT-thorax, in which the CT-thorax or findings at surgery were taken as the gold standard.

Patient characteristics were described as number (%) for categorical data and as mean with standard deviation (±SD) or median with interquartile range for continuous data. Prenatal and postnatal diagnoses of RAA subtypes were compared. The incidence of surgical intervention was presented in a Kaplan-Meier curve and compared between RAA (all subtypes) and DAA using Mantel-Cox log rank tests. The mean age at surgical interventions was compared between subtypes using Independent Student *T*-tests and the median age at the onset of symptoms by the Mann-Whitney *U* test. The incidence of surgical intervention between subtypes was compared using a chi-square test. *p*-values below 0.05 were considered statistically significant. Statistical analyses were done using IBM Corp SPSS Statistics version 28.0 and *R* Studio version 1.2.1335.[20,21]

3 | RESULTS

In total, 175 cases with an RAA were diagnosed between 2007 and 2021. Due to intracardiac or associated extracardiac anomalies, respectively, 50 (29%) and 10 (6%) cases were excluded. The intracardiac anomalies consisted mainly of CHDs such as tetralogy of Fallot, double-outlet right ventricle, or atrioventricular septal defect. Among the excluded cases with additional anomalies, chromosomal or genetic abnormalities were present in 13 (22%) and consisted of trisomy 21 ($n = 7$), 22q11deletion ($n = 2$), trisomy 18 ($n = 1$), chromosome 6-duplication ($n = 1$), 15q-deletion ($n = 1$), and FGFR-1-mutation ($n = 1$). Five cases were excluded because of incomplete follow-up. Subsequently, 110 cases of RAA were included in this study, and due to the termination of pregnancy ($n = 6$) and false-positive cases ($n = 5$), the follow-up consisted of 99 cases.

With a mean of 47,900 second-trimester anomaly scans made in our region every year, Figure 1 shows that there was an increasing number of detected cases over time. In the period 2010–2012, there were approximately 0.4 cases detected per 10,000 anomaly scans, and in 2018–2020, almost 4 cases detected per 10,000 anomaly scans. There were no prenatal diagnoses of isolated RAA made in 2007–2009.

Table 1 shows the baseline characteristics of this cohort. The mean gestational age at diagnosis at the fetal medicine unit was 20 + 5 weeks. The majority was referred for suspected CHD ($n = 98$, 89%) at the standard anomaly scan. Other reasons for advanced ultrasonography were suspicion of other anomalies ($n = 6$), high-risk pregnancy ($n = 3$), increased nuchal fold ($n = 2$), and incomplete routine screening ($n = 1$). Six of the included cases were diagnosed with 22q11 deletion syndrome (5.5%).

In 92 (84%) of the included cases, an RAA was prenatally diagnosed of which the arterial duct (AD) was described as left sided in 72 (78%), right sided in 9 (10%), and not specified in 11 (12%) cases. The other 18 fetuses (16%) were prenatally diagnosed with a DAA. In 44 of the 110 cases (40%), an abnormal origin of the left subclavian artery (ALSA) was described, and in two cases (2%), an abnormal origin of the right subclavian artery was described, both cases with a DAA.

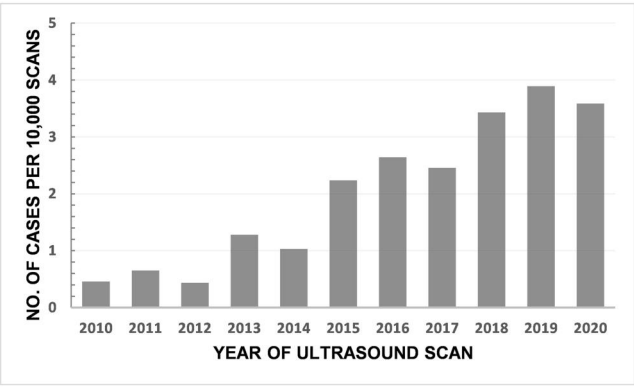

FIGURE 1 Number of detected isolated right aortic arch (RAA) cases per 10,000 anomaly scan performed yearly in the North-West region of the Netherlands.

TABLE 1 Baseline characteristics of the included cases.

Characteristics	*n* (%), mean ± SD, median [IQR]
Maternal age (years)	31.5 ± 4.6
BMI (kg/m^2)—Missing (*n* = 12)	24.4 ± 4.7
Nulliparous	53 (48%)
Singleton pregnancy	107 (97%)
Family history of CHD—Missing (*n* = 2)	6 (5.5%)
Male gender—Missing (*n* = 1)	56 (51%)
Prenatal screening—Missing (*n* = 20)	
cfDNA	35 (39%)
First-trimester combined test	21 (23%)
Not performed	34 (38%)
Invasive prenatal diagnostics	52 (47%)
Postnatal genetic testing	23 (21%)
Genetic diagnosis	
22q11-deletion	6 (5.5%)
Gestational age at diagnosis (weeks + days)	20 + 4 [20 + 0 – 21 + 1]

Abbreviations: BMI, body mass index; cfDNA, cell-free DNA; CHD, congenital heart defect.

In 52 (47%) of the 110 cases, the parents opted for invasive prenatal testing and chromosome analysis. Five (4.5%) cases were diagnosed with 22q11 deletion and the remaining were all normal. Postnatal chromosome analysis revealed one other case with 22q11 deletion. Consequently, the prevalence of 22q11 deletion syndrome in cases with RAA as only fetal anomaly was 5.5% (6/110) in our cohort. This was compared between cases with a prenatal diagnosis of RAA and DAA, respectively, 5.4% (5/92) and 5.5% (1/18).

In six of the 110 cases (5.5%), the parents opted for a termination of pregnancy. Four pregnancies were terminated after the genetic diagnosis of 22q11 deletion (RAA, *n* = 3; DAA, *n* = 1). Additionally, two pregnancies were terminated (1.8%; RAA, *n* = 1, DAA *n* = 1) despite a positive counseling regarding the prognosis of the findings. The decision of termination was a specific parental request (at a gestational age of 21 and 23 weeks, respectively), and termination on social indication is regulated by law up to 24 weeks in the Netherlands.

3.1 | Accuracy of diagnosis

Of the 104 newborns with a prenatal diagnosis of RAA or DAA, the diagnosis was confirmed postnatally in 99 (95%), by echocardiography only in 62 cases, and by CT-thorax in 37 cases. Five false-positives occurred with the postnatal diagnosis of a LAA. Prenatal ultrasound resulted in a diagnostic accuracy of 95%. None of the children had extracardiac anomalies after birth, thus confirming that all cases were isolated.

Of the 88 newborns that were prenatally diagnosed with RAA, 83 (94%) were confirmed. In three and two cases, respectively, the postnatal diagnosis showed LAA and DAA (Figure 2). Both DAA cases were diagnosed as RAA + LAD prenatally. In one of them, the CT-thorax showed an atretic segment of the smaller LAA (see Figure 3). Of the 16 cases with a prenatal diagnosis of DAA, the diagnosis was correct in seven cases (44%). In seven other cases, the postnatal diagnosis was RAA not DAA. In three of these, a vascular ring was present due to the LAD, ALSA, and the existence of a Kommerell's diverticulum. A diagnosis of LAA was made postnatally in the remaining two cases. Figure 2 shows the flowchart of cases and diagnoses with the postnatal diagnosis of LAA being the normal anatomical situation. The 9 (9%) incorrect diagnoses (DAA not RAA, RAA not DAA) were in all cases confirmed by CT-thorax. In two cases with RAA not DAA, there was an inconsistency between postnatal echocardiography (signs of DAA) and CT-thorax (RAA).

Additionally, in 13 of 99 neonates (13%), an additional cardiac anomaly was diagnosed postnatally. A ventricular septal defect was found in nine cases of which two were clinically significant. In two, crossed pulmonary arteries were found; in one, a bicuspid aortic valve; and in one, a hypoplastic left pulmonary artery.

3.2 | Follow-up after birth

After excluding the newborns with an LAA (*n* = 5), the follow-up consisted of 99 neonates: 90 with RAA and 9 with DAA (Figure 2). Median duration of follow-up was 46 months [27–74] with a minimum of 13 months and maximum of 11 years. No deaths occurred

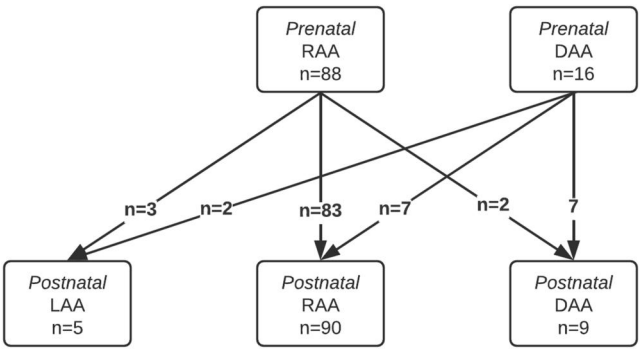

FIGURE 2 Flowchart of diagnoses and the difference between prenatally and postnatally. DAA, double aortic arch; LAA, left aortic arch; RAA, right aortic arch.

during the follow-up. The characteristics of the delivery and the direct neonatal period are presented in Table 2.

In the first year of life, 18 children (18%) developed symptoms related to the RAA of which 12 out of 18 (67%) had respiratory symptoms, two (11%) had dysphagia, and four (22%) demonstrated both. In the first month of life, only one child (1%) underwent emergency surgery due to inspiratory stridor due to tracheal compression from a DAA. This case presented directly after birth with respiratory insufficiency and APGAR scores of 9, 8, and 6. The CT-thorax on day 1 and dLTB on day 3 showed severe tracheal compression and tracheomalacia, leading to surgery on day 7. The last prenatal echocardiogram was made at 27 weeks of gestation and showed unremarkable DAA images and no polyhydramnios. During

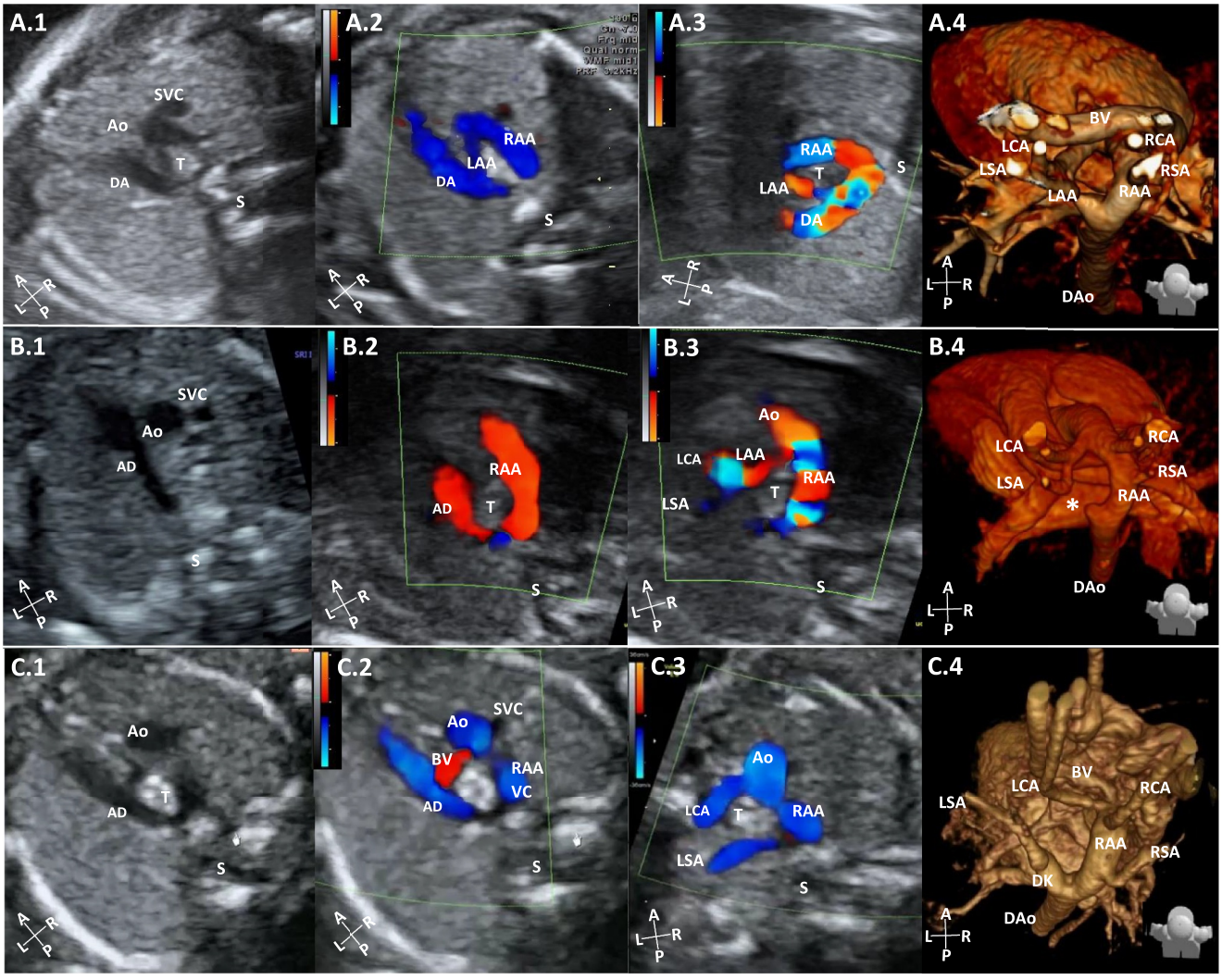

FIGURE 3 Three vessel and/or three vessel and trachea views and postnatal 3D reconstructions of postnatal CT-scans of three vascular rings. A DAA is seen in images (A 1–4), a DAA with an atretic segment is shown in images (B 1–4) and an RAA with an LAD in images (C 1–4). In (A 1 and 2), the splitting of the ascending Ao into LAA and right RAA can be seen. Images (A 3 and 4) show the tight "0" ring formed by the DAA. Images (B 2 and 3) can be confused with those in (C 2 and 3). Image (B 2) shows a "U" shape similar to that seen in (C 1 and 2), and the usually smaller LAA can be confused with the LCA (images B 3 and C 3). The 3D reconstruction (B 4) shows the atretic segment (*) of the DAA, which, with its fibrous continuity, causes a vascular ring that is tighter than the ring seen in (C 4). Images (C 1–2) and (C 4) show the typical "U" ring of an RAA with an LAD and aberrant origin of the LSA from the DAo. The diverticulum of Kommerell is seen in (C 4). A, anterior; AD, arterial duct; Ao, aorta; BV, brachiocephalic vein; DAA, double aortic arch; DAo, descending aorta; DK, diverticulum of Kommerell; L, left; LAA, left aortic arch; LAD, left sided arterial duct; LCA, left carotid artery; LSA, left subclavian artery; P, posterior; R, right; RAA, right aortic arch; RCA, right carotid artery; RSA, right subclavian artery; S, spine; SVC, superior caval vein; T, trachea. [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Characteristics of the delivery and neonatal period (n = 99).

Characteristics	n (%), mean ± SD, median [IQR]
Gestational age at birth (weeks)	39 + 0 ±2 + 0
Premature birth	12 (12%)
Birthweight (gram)—Missing n = 5	3367 ± 619
Type of delivery—Missing n = 19	
Vaginal	63 (79%)
Caesarean section	17 (21%)
NICU admission not related to prematurity or dysmaturity—Missing n = 4	14 (14%)
Due to respiratory insufficiency	6 (12%)
Age at postnatal diagnosis (days)	17 [1–32][a]

Abbreviation: NICU, neonatal intensive care unit.

[a]One case was excluded here as the child underwent confirmatory echocardiography at 5 years of age specifically for this study as he/she had been lost to follow-up.

the 1-year follow-up, the rate of surgical intervention was 10/99 (10%) due to compression of the trachea and/or esophagus. Six patients had a DAA and four had an RAA. The age at surgery in the first year tended to be older in the RAA cases: DAA cases underwent surgery at 1, 8, 8, 12, 17, and 19 weeks and RAA at 25, 36, 47, and 50 weeks, respectively. Figure 4 displays the Kaplan-Meier curves of time free of surgery, displayed separately for RAA and DAA cases at 1-year follow-up. There was a significant difference between RAA and DAA cases ($p < 0.001$).

After the first year, additional nine children developed symptoms. Therefore, in total, 27 children (27%) developed symptoms related to the RAA, of which 15 (56%) had respiratory symptoms, six (22%) had dysphagia, and six (22%) demonstrated both. The most common symptoms were stridor, chronic coughing, refusal of solid food, and choking incidents. The median age at the onset of symptoms was 9 [1–14] months. Symptoms occurred in 20 (22%) of the children with postnatal RAA diagnosis and in 7 (78%) of the children with postnatal DAA diagnosis ($p = 0.003$). The median ages at the onset of symptoms for RAA and DAA were 10 [6–15] and 1 [0–9] months, respectively ($p = 0.062$). Among the symptomatic children with RAA, there was only one child without a vascular ring (RAA and RAD). This child had apneas and a CT scan was performed, but the symptoms were eventually attributed to reflux.

Besides echocardiography, in 41 children, a CT-thorax ($n = 37$), a dLTB ($n = 27$), and/or a barium swallow test ($n = 9$) were performed. Six of these children underwent all three types of imaging and 18 underwent both CT scan and dLTB. In seven children, the dLTB was performed at the time of the surgery. The mean age at which the CT-thorax was performed was 14 ± 15 months, for dLTB 14 ± 10 months, and at the barium swallow test 20 ± 17 months. Additional postnatal diagnostics were performed mainly in symptomatic children, but CT-thorax and dLTB were performed in 14 and 6 asymptomatic children, respectively, as well. These diagnostics showed tracheal and/or esophageal compression in 10/14 (71%) and 6/6 (100%).

During the entire follow-up period, 25 (25%) children had surgery. Double aortic arch cases underwent surgery significantly more often during the follow-up than RAA cases, 8 out of 9 (89%) and 17 out of 90 (19%) children had surgical intervention, respectively ($p < 0.001$). Among the operated RAA cases, ALSA was diagnosed in 15/17 cases (88%). As expected, there were no surgical interventions in the group with a prenatal RAA and RAD. The mean age at surgery in the total cohort was 17 ± 12 months, cases with DAA on average at 6 ± 7 months' age, and RAA on average at 22 ± 11 months' age ($p < 0.001$). No operations were performed after the 5 years of life. Figure 5 displays the Kaplan-Meier curves of time free of surgery, separated for RAA and DAA cases at 5-year follow-up. Again, a significant difference between RAA and DAA was observed ($p < 0.001$). In this cohort, cleavage of the ductal ligament, resection of Kommerell's diverticulum, and if indicated, reimplantation of the LSA in the left carotid artery, or ligation thereof if reimplantation was not possible, were performed for RAA. For DAA, the smallest arch (usually the left arch) was interrupted and the ductal ligament cleaved. An aortopexy was also performed in some cases ($n = 3$). Two complications occurred after surgical intervention. One due to complications of a thoracic drain and one due to a postoperative hemorrhage, both children needed a second surgical intervention.

4 | DISCUSSION

4.1 | Main findings

Overall, the prognosis of children with a prenatal diagnosis of isolated RAA was good with a low risk of acute postnatal problems. The surgical intervention rate in the first year of life was 10%. Twenty-seven children developed RAA-related symptoms at a mean of 10 months, and 25% needed surgery at a mean age of 17 months. Surgical intervention was performed in 89% of the children with a

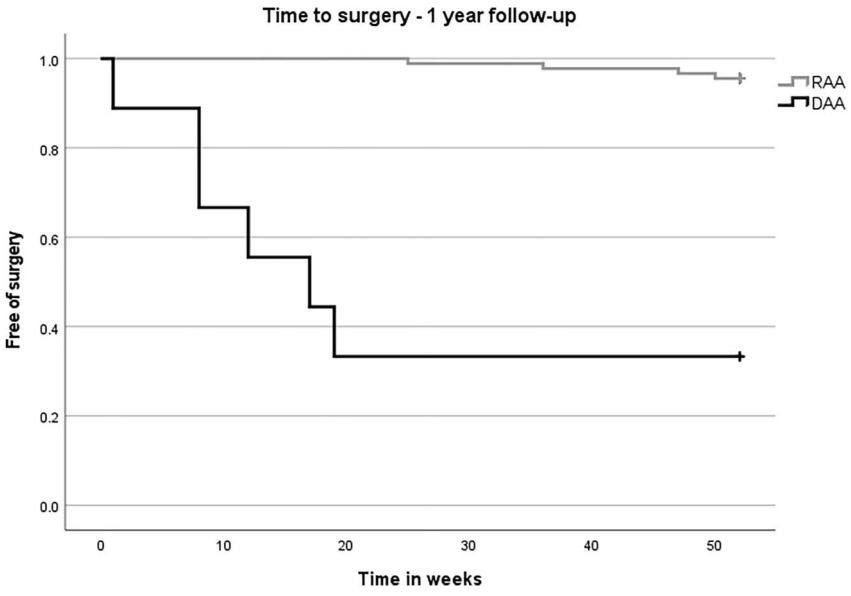

FIGURE 4 Time to surgery in the first year of follow-up separately for RAA and DAA cases. As all cases had a complete follow-up in this first year, there were no censored cases. DAA, double aortic arch; RAA, right aortic arch.

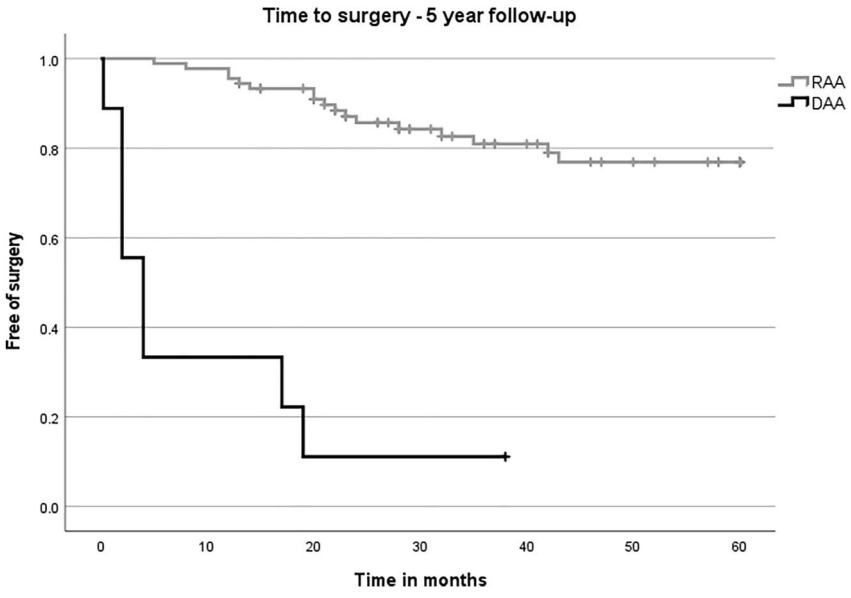

FIGURE 5 Time to surgery in 5 years of follow-up separately for RAA and DAA cases. The vertical lines represent the moment a case is censored based on the end of follow-up. DAA, double aortic arch; RAA, right aortic arch.

DAA and in 19% of those with an RAA. This is important information, which needs to be included in the counseling of isolated RAA.

4.2 | Interpretation

The rate of prenatally detected cases of isolated RAA in our cohort is compared to the 0.05% reported by Mogra et al.[1] but lower than the expected 0.1%.[2] However, we showed an increasing trend of prenatal diagnosis after the introduction of the 3VV, which was in line with the results of Babuoglu et al.,[22] and we expect the prenatal diagnosis to increase even further with the implementation of the 3VTV as a mandatory view in our country.

Earlier prenatal studies have reported surgical rates of 0%–79%.[14–17,23,24] Our results are difficult to compare with these studies as most cases were not isolated, were selected from both high- and low-risk populations, or different follow-up periods were used. Moreover, the decision for a surgical intervention can be institution-dependent, because there is currently no guideline for the treatment of RAA.[25] However, our results are in line with the meta-analysis of D'Antonio et al., reporting a pooled surgical intervention rate of 18%.[14] Our mean age at surgery of 17 months is also compared with other studies.[4,17,26] Additionally, the surgical rate was higher in children with a DAA compared to an RAA + LAD, as one may expect as the vascular ring of a DAA is generally tighter. These findings are consistent with recent studies, in which the majority or all of the children with a DAA required surgery.[4,26,27]

A detailed prenatal diagnosis of the type of RAA is essential as this influences the prenatal counseling and the location of delivery. As all but one of our patients, who had a DAA and who was operated

on day 7, required non-emergency intervention, delivery in a hospital with NICU and cardiothoracic service is advised for DAA cases. The other types of RAA can safely be delivered in a local hospital as long as the diagnosis is secure.

To establish the indication for surgery, additional imaging might be indicated in both symptomatic and asymptomatic children. In this cohort, 41% underwent CT-thorax, dLTB and/or barium swallow test, and interestingly, the dLTB showed tracheal compression in 6/6 asymptomatic children. This discordance between symptoms and findings supports a proposal to perform these investigations as part of the standard postnatal workup of these patients. More research is needed to establish the best method and timing of these interventions.[28–30]

4.3 | Strength and limitations

To our knowledge, our study is one of the largest cohort studies on isolated RAA addressing neonatal follow-up and surgical intervention. This study was possible due to the collaboration of three academic hospitals in CAHAL and covered approximately 30% of prenatal care in the Netherlands.[31] Moreover, the prospective registry PRECOR is a well-established database and makes it unlikely that we missed any cases.[18,32] Furthermore, we only had a 4% loss-to-follow-up rate (5/115 isolated cases), which was mostly due to international migration and is normal in such cohort studies. However, some limitations need to be mentioned. First, the prevalence of 22q11 deletion syndrome in our cohort was 5.5% and resembled that of current literature,[14] but amniocentesis or postnatal genetic testing was not routinely offered, especially in the early years of this cohort study. Therefore, as 22q11-deletion syndrome is one of the most common genetic anomalies and has a variable, subtle phenotype, we might have missed some of these diagnoses.[33,34] Moreover, genetic testing has expanded recently with possibilities as whole exome sequencing.[35] Therefore, it is possible that the incidence of genetic anomalies is actually higher.

Third, the amount of detail of the prenatal diagnosis differed in our cohort; in some cases, the course of the AD and subclavian arteries were not described. This information is very important for the risk evaluation and we may have missed relevant data here. This can be explained partly by improved ultrasound techniques, but also by differences in years of experience and specialist training of the ultrasonographers. Despite this, the accuracy of prenatal ultrasound was high, 95%, in our cohort. We could not determine one specific factor that contributed to the false-positive rate. Potential factors of influence were diverse including limited imaging quality in older cases, absence of a follow-up echocardiogram in the third trimester and the presence of a cardiac anomaly that affected the left-right interpretation of the 3VV (PLVCSS; large AD, both diagnosed postnatally). The discordant finding of seven cases with RAA not DAA and two cases with DAA not RAA demonstrates that it can be difficult to differentiate between anatomical variants.[36,37] However, more tools to help differentiating between DAA and RAA are currently studied.[38,39] In one case of DAA, prenatally diagnosed as RAA + LAD, the CT scan showed an atretic, fibrous segment of the smaller LAA explaining the misdiagnosis (see Figure 3). It is important to be aware of this anatomical possibility and in cases where there is any doubt regarding the diagnosis of a DAA or where an atretic segment of a DAA is suspected as delivery in a well-equipped hospital is warranted. Some research indicates that a fetal MRI may assist in the identification of cases at a high risk for tracheal compression and thus may require surgery soon after birth.[40–42] Fourth, there is no standardized follow-up for children with an RAA. There has been an increasing tendency to perform a dLTB in asymptomatic children as research has shown that symptoms are not directly related to the extent of tracheal and/or esophageal compression.[17] The true incidence of tracheal and/or esophageal compression is thus likely to be higher than reported. Untreated compression of the trachea can possibly lead to irreversible tracheomalacia, making it important to investigate tracheal compression thoroughly.[30] A standardization of follow-up in children with RAA is therefore of clinical importance and may lead to an increased surgical intervention rate in the early postnatal years.

5 | CONCLUSION

This study shows that the prognosis of children with a prenatal diagnosis of an RAA is good with a low risk of acute postnatal respiratory problems. A detailed fetal echocardiogram is needed to provide an accurate prenatal diagnosis with information about the location of the AD and the origin of the subclavian arteries. A delivery in a hospital with NICU and cardiothoracic service is only indicated in cases with suspected DAA. Expectant parents can be informed that presently 25% of the children need surgery in the first years of life and that children rarely develop acute respiratory distress.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Bo B. Bet https://orcid.org/0000-0003-2200-9607
Maartje C. Snoep https://orcid.org/0000-0002-7327-1915

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