Supplemental Material

Supplemental tables

Table S1: Table of variables collected:

fetal cardiac centre
gestation at prenatal diagnosis
referral indication
prenatal diagnosis
prenatal extra-cardiac anomalies
CVS/Amniocentesis performed and result
NIPT performed
pregnancy outcome
postnatal genetic test performed and result
postnatal detected extra-cardiac anomalies
postnatal diagnosis
additional cardiac anomalies diagnosed pre and postnatally
symptoms
surgery
age at surgery
weight at surgery
surgical details
hospital length of stay for vascular ring surgery
surgical complications
age at last follow-up
symptoms at last follow-up
alive or died.

Table S2: Uptake of FASP anomaly screening in 2018/19 in the different regions of England and the percentage with a prenatally diagnosed arch anomaly. The percentage prenatally diagnosed in the London region was greater than the other regions.

Region	**Number of fetuses screened**	**Number with arch anomaly**	**Percentage with prenatally diagnosed anomaly**	**95% Confidence Limits**	**P-value**
London	115,653	146	0.13%	0.11-0.15%	
West midlands & East	151,532	54	0.04%	0.03 – 0.05%	<0.0001
North	116,378	96	0.08%	0.07-0.10%	0.01
South	136,327	48	0.04%	0.03-0.05%	<0.0001

Table S3: Table of Genetic Differences found and associated ECA and Cardiac anomalies

Genetic anomaly	Variant of unknown significance	number (%)	Aortic arch type	Prenatal extracardiac anomaly	Prenatal cardiac anomaly	Any prenatal anomaly	Pregnancy outcome	Postnatal extracardiac anomaly	Postnatal cardiac anomaly	Vascular ring surgery
22q11 deletion	No	28 (35.00%)	RAA-LD-ALSCA 17; RAA-LD-MI 2; RAA-RD 2; DAA 2; RAA Unknown 5	7/28	5/28; 3 muscular VSD, 2 Bilateral SVC	11/28	Liveborn 24/28; TOP 3/28; lost to follow-up 1/28	7/24	7/24	7/24
Trisomy 21	No	9 (11.25%)	RAA-LD-ALSCA 5; RAA-LD-MI 1; DAA 1; RAA Unknown 2	1/9	0	1/9	Liveborn 8/9 TOP 1/9	1/8	3/8	5/8
CHARGE syndrome, CHD7	No	3 (3.75%)	RAA-LD-ALSCA 1; RAA Unknown 2	2/3	1/3	2/3	Liveborn 3/3	3/3	2/3	0
Duplication at 22q11.21	No	2 (2.50%)	RAA-LD-ALSCA 2	0	0	0	Liveborn 2/2	0	0	0
XXY Kleinfelters	No	2 (2.50%)	RAA-LD-ALSCA 2	0	0	0	Liveborn 2/2	0	0	1/2
16p 13.11 duplication	No	2 (2.50%)	RAA-LD-ALSCA 2	1/2	0	1/2	Liveborn 2/2	1/2	0	0
chromo 1 deletion	No	1 (1.25%)	RAA Unknown	No	Small Muscular VSD	Yes	TOP	Not relevant	Not relevant	Not relevant
Chromosome 1q duplication	No	1 (1.25%)	DAA	No	No	No	Liveborn	No	No	Yes
2q21.3q22.1 microdeletion	No	1 (1.25%)	RAA Unknown	No	No	No	Liveborn	No	No	No
Duplication of terminal region of long arm chromosome 3	No	1 (1.25%)	RAA - ALSCA	No	No	No	TOP	Not relevant	Not relevant	Not relevant
7q36 deletion	No	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	No
8q22.3 & 9p24.3 duplication	No	1 (1.25%)	DAA	No	No	No	Liveborn	Yes	No	Yes
Chromosome 8 inversion	No	1 (1.25%)	RAA-ALSCA	No	No	No	Liveborn	Yes	No	Yes
Mosaic 8	No	1 (1.25%)	RAA-MI	Yes	No	Yes	Liveborn	Yes	No	Yes
Duplication of short arm of chromosome 12 at band 12p12.1	No	1 (1.25%)	RAA-ALSCA	No	No	No	Liveborn	Yes	Yes	Yes
15q11.2	No	1 (1.25%)	DAA	No	No	No	Liveborn	No	No	Yes
15q24 deletion	No	1 (1.25%)	DAA	No	No	No	Liveborn	Yes	No	Yes
17q23.1q23.2 microdeletion	No	1 (1.25%)	RAA-ALSCA	Yes	No	Yes	Liveborn	Yes	No	No
noonans syndrome	No	1 (1.25%)	RAA-ALSCA	No	No	No	Liveborn	Yes	No	Yes
Polands anomaly	No	1 (1.25%)	DAA	No	No	No	Liveborn	Yes	No	Yes
Robinow syndrome	No	1 (1.25%)	RAA Unknown	Yes	No	Yes	Liveborn	Yes	Yes	No
Rubinsten Taybi syndrome	No	1 (1.25%)	DAA	No	No	No	Liveborn	Yes	Yes	Yes
Smith Magenis syndrome	No	1 (1.25%)	RAA Unknown	No	No	No	Liveborn	Yes	Lost to follow-up	Yes
Verheij syndrome (8q24.3 deletion)	No	1 (1.25%)	RAA-RD	Yes	No	Yes	Liveborn	Yes	Yes	No
Williams syndrome	No	1 (1.25%)	RAA Unknown	No	No	No	TOP	Not relevant	Not relevant	Not relevant
arr (1 - 22) x 2, (x,y) x 1	No	1 (1.25%)	RAA-RD	No	No	No	Liveborn	No	Yes	No
compound heterozygous c.-22-2A>C and c.35del.p in GJB2	No	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	No
Delta F508	No	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	Yes
Mitochondrial MT-TE mutation	No	1 (1.25%)	True conflict	No	No	No	Liveborn	Yes	No	No
No details	No	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	No	Yes	Yes
21q21.1 duplication	Yes	1 (1.25%)	RAA Unknown	No	No	No	Liveborn	No	No	No
ALG8 gene variant	Yes	1 (1.25%)	RAA - ALSCA	Yes	No	Yes	Liveborn	Yes	No	No
Amplification of chr 10	Yes	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	No
Complex imbalance of band q36.3 in the long arm of chromosome 7	Yes	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	No
Two changes on BRF1	Yes	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	Yes	No	No
Microdeletion on 6 and 13	Yes	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	No	No	Yes
Microduplication at 19p13.2	Yes	1 (1.25%)	RAA - ALSCA	No	No	No	Liveborn	No	Yes	Yes
Copy number imbalance 2q23.1	Yes	1 (1.25%)	DAA	No	No	No	Liveborn	No	No	Yes
Copy number imbalance of uncertain significance, no further detail	Yes	1 (1.25%)	DAA	No	No	No	Liveborn	No	No	Yes
Copy number variation on short arm of sex chomosome	Yes	1 (1.25%)	DAA	No	No	No	Liveborn	No	No	Yes

Table S4: Modified-Poisson regression to investigate predictors for genetic abnormality, assuming normal genetics if no genetic test performed (n=1046).

	Risk Ratio (RR, 95% CI)	**Lower 95% Confidence limit**	**Upper 95% Confidence limit**	**P value**	**Missing data (%)**
(intercept)	0.08	0.03	0.20	<0.0001	
RAA-LAD-MIB	0.34	0.09	1.36	0.11	7 (0.7)
RAA-LAD-ALSA	0.85	0.34	2.84	0.76	7 (0.7)
RAA-LAD-unknown branching pattern	0.62	0.22	2.19	0.40	7 (0.7)
DAA	0.91	0.32	3.24	0.87	7 (0.7)
Prenatal ECA	3.39	1.89	5.73	<0.0001	0 (0)
Prenatal additional cardiac anomaly	2.06	0.86	4.22	0.07	0 (0)

Table S5: Percentage of patients free of vascular ring surgery and symptoms at 1 year, 2 years and 4 years of age.

	1 year (%, 95%CI)	**2 years (%, 95%CI)**	**4 years (%, 95%CI)**	**Hazard ratio (HR, 95% CI)**
Symptoms				
RAA	84.4 (81.7-87.1)	80.4 (77.4-83.4)	78.6 (75.5-81.8)	0.29 (0.22-0.39)
DAA	54.8 (46.5-64.6)	49.5 (41.2-59.5)	46.1 (37.7-56.4)	1.00
Vascular ring surgery				
RAA	91.5 (89.5-93.6)	84.7 (82.1-87.4)	82.2 (79.4-85.1)	0.13 (0.10-0.16)
DAA	39.3 (31.9-48.5)	30.4 (23.5-39.2)	24.9 (18.5-33.4)	1.00
Symptoms				
RAA-LAD-ALSA	78.8 (75.0 – 82.8)	73.5 (69.4- 77.9)	71.0 (66.8 -75.6)	0.41 (0.30-0.56)
All other RAA	93.6 (90.6 – 96.6)	91.9 (88.6 -95.3)	91.3 (87.9 – 94.9)	0.11 (0.07-0.18)
DAA	54.8 (46.5 – 64.6)	49.5 (41.2-59.5)	46.1 (37.7 -56.4)	1.00
Vascular ring surgery				
RAA-LAD-ALSA	89.0 (86.2-91.9)	79.0 (75.4 -82.8)	74.6 (70.5 – 78.9)	0.18 (0.14-0.23)
All other RAA	96.1 (93.8-98.5)	95.3 (92.8-97.9)	94.4 (91.5-97.3)	0.04 (0.02-0.06)
DAA	39.3	30.4	24.9	1.00

	(31.9-48.5)	(23.5 -39.2)	(18.5 -33.4)	

Table S6: Modified-Poisson regression to investigate predictors for surgical relief of a vascular ring (n=986).

	Risk Ratio (RR, 95% CI)	**Lower 95% Confidence limit**	**Upper 95% Confidence limit**	**P value**	**Missing data (%)**
(intercept)	0.03	0.00	0.12	<0.001	
RAA-LAD-MIB	1.10	0.16	21.5	0.93	7 (0.7)
RAA-LAD-ALSA	8.57	1.92	150.95	0.03	7 (0.7)
RAA-LAD-unknown branching pattern	1.67	0.31	30.87	0.63	7 (0.7)
DAA	26.37	5.89	464.67	0.001	7 (0.7)
Prenatal ECA	0.78	0.42	1.32	0.40	0 (0)
Prenatal additional cardiac anomaly	1.17	0.56	2.16	0.64	0 (0)
Genetic anomaly	1.68	1.13	2.43	0.01	0 (0)

Supplemental figures

Figure S1

Figure 1 Supplementary material: Number of fetuses diagnosed with RAA or DAA each year in the study.

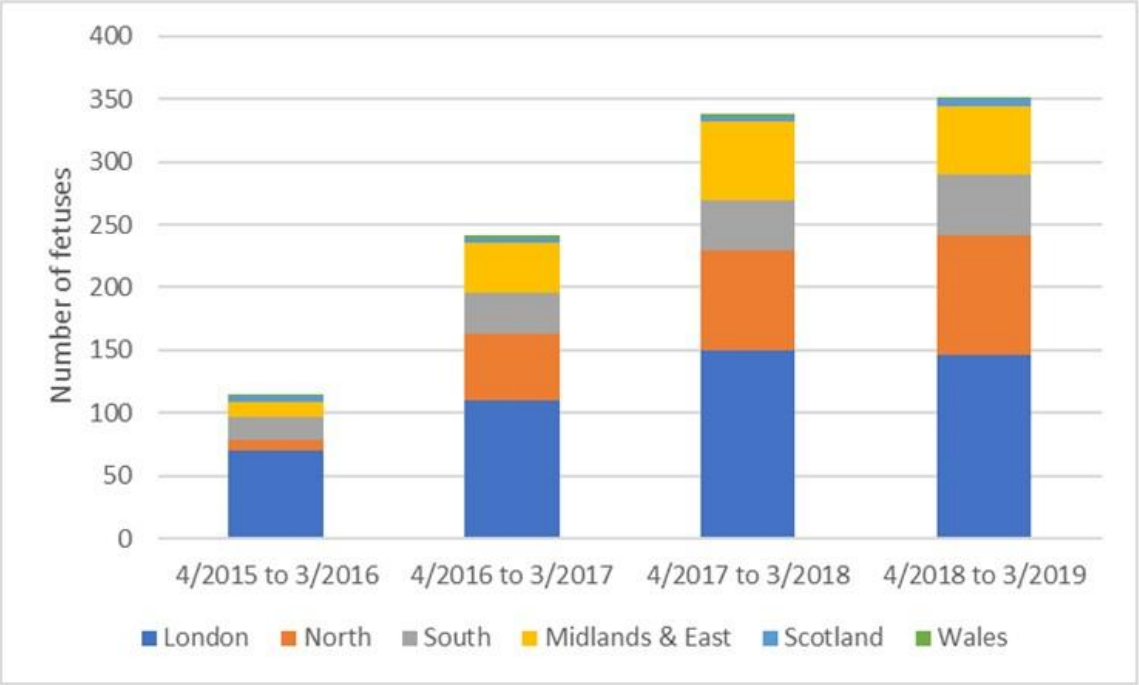

Figure S2

Frequency and type of tracheoesophageal compressive symptoms/signs reported.