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Aberrant right subclavian artery at 11 + 0 to 13 + 6 weeks of gestation in chromosomally normal and abnormal fetuses

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KEYWORDS: aberrant right subclavian artery; aortic arch; echocardiography; first-trimester screening; trimester 21

ABSTRACT

Objectives *To establish the feasibility of examining the subclavian artery at 11 + 0 to 13 + 6 weeks of gestation, and to determine the prevalence of aberrant right subclavian artery (ARSA) in chromosomally normal and chromosomally abnormal fetuses.*

Methods *Fetal echocardiography was performed prospectively in 516 patients before chorionic villus sampling at 11 + 0 to 13 + 6 weeks of gestation. Transabdominal sonography was carried out, and color flow mapping was used to identify the right subclavian artery and determine whether this was normal or aberrant (ARSA). Second-trimester fetal echocardiography was also carried out in a subgroup of 183 fetuses.*

Results *The median gestational age was 12 weeks and the median crown–rump length was 68 mm. Successful assessment of the right subclavian artery was achieved in 425/516 (82.4%) cases and the rate of failure to do so was significantly associated with decreasing fetal crown–rump length* ($r = 0.174$, $P < 0.001$) *and increasing maternal body mass index* ($r = 0.275$, $P < 0.001$). *An ARSA was observed in 2/353 (0.6%) fetuses with a normal karyotype, in 4/51 (7.8%) cases with trisomy 21 and in 2/20 (10.0%) with other chromosomal defects. In a subgroup of 183 fetuses examined in both the first and second trimester there were three cases of ARSA observed at both scans and an additional case in which ARSA was detected only at the second scan.*

Conclusions *Assessment of the position of the right subclavian artery is feasible at the 11 + 0 to 13 + 6-week scan and ARSA is more common in chromosomally abnormal than normal fetuses. However, ARSA in the first trimester is unlikely to be a useful marker of trisomy 21.*

INTRODUCTION

The normal aortic arch branches into three, the brachiocephalic trunk, the left common carotid artery and the left subclavian artery. After a short superior course, the brachiocephalic artery then divides into the right subclavian and right common carotid arteries. A developmental abnormality in the branching pattern of the aortic arch results in the presence of four branches: a right common carotid artery, a left common carotid artery, a left subclavian artery and a right subclavian artery, which arises anomalously from the descending aorta at its junction with the arterial duct. This origin of the right subclavian artery is to the left of the midline and, in order to reach the right arm, the artery passes behind both the trachea and the esophagus. This is termed an aberrant right subclavian artery (ARSA). Despite the unusual course of the artery, an ARSA has no implications in terms of symptoms from the cardiovascular point of view.

A pathological study in children and adults reported that an ARSA is found in about 3% of cases with congenital cardiac defects and in 0.1% of those without cardiac defects[1]. In trisomy 21 the prevalence of ARSA may be increased. Pathological or clinical studies in individuals with trisomy 21 reported that the prevalence of ARSA varies from 2.9% to 100% in those with cardiac defects, and from 0% to 5.4% in those without cardiac defects (Table 1)[2–8]. Recent prenatal ultrasound studies have reported that the incidence of ARSA in the second trimester is about 35% in trisomy 21 fetuses and 1.4% in chromosomally normal fetuses (Table 2)[9–12].

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Table 1 Studies investigating the incidence of aberrant right subclavian artery and cardiac defects in trisomy 21

		Aberrant right subclavian artery (n *(%))*	
Reference	*Type of study*	*Cardiac defect*	*No cardiac defect*
Evans (1950)[2]	Postmortem	1/28 (3.6)	0/35 (0)
Strauss (1953)[3]	Postmortem	1/6 (16.7)	0/6 (0)
Molz and Burri (1978)[4]	Postmortem	3/3 (100)	—
Rowe and Uchida (1961)[5]	Radiological, postmortem	2/70 (2.9)	5/92 (5.4)
Goldstein (1965)[6]	Radiological	10/27 (37.0)	0/1 (0)
Lo *et al.* (1989)[7]	Radiological, postmortem	24/149 (16.1)	—
Rathore and Sreenivasan (1989)[8]	Radiological	16/45 (35.6)	—
Total		57/328 (17.4)	5/134 (3.7)

Table 2 Prenatal ultrasound studies investigating the prevalence of aberrant right subclavian artery in normal fetuses and trisomy 21 fetuses

			Aberrant right subclavian artery (n *(%))*	
Reference	*Total number of cases*	*Gestation (weeks)*	*Normal*	*Trisomy 21*
Chaoui *et al.* (2005)[9]	54	18–33	0/40 (0)	5/14 (35.7)
Chaoui *et al.* (2005)[10]	906	15–34	13/905 (1.4)	1/1
Chaoui *et al.* (2006)[11]	14	< 14	—	4/14 (28.6)
Zalel *et al.* (2007)[12]	932	13–26	13/924 (1.4)	3/8 (37.5)
Total	1906		26/1869 (1.4)	13/37 (35.1)

The aim of this study was to establish the feasibility of examining the subclavian artery at 11 + 0 to 13 + 6 weeks of gestation, and to determine the prevalence of ARSA in chromosomally normal and chromosomally abnormal fetuses.

METHODS

This was a prospective study of 516 consecutive pregnancies before chorionic villus sampling (CVS) for fetal karyotyping. In all cases, screening for chromosomal defects had been undertaken by measurement of the fetal nuchal translucency (NT) thickness and maternal serum free beta-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein-A (PAPP-A) at 11 + 0 to 13 + 6 weeks[13].

Fetal echocardiography was performed transabdominally using a 4–8-MHz curvilinear transducer (Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) by sonographers with experience in first-trimester cardiac scanning. The four-chamber view of the heart, outflow tracts, arterial duct and aortic arch were assessed on cross-sectional imaging. Using color flow mapping with low velocity (pulse repetition frequencies ranging from 0.9 to 1.8 kHz), the transverse three vessels and trachea view was first imaged to confirm that the aortic arch crossed the trachea to descend on the left side of the fetus just anterior and to the left of the spine. The ultrasound beam was then moved slowly upwards (cranially) to the level of the clavicles. The normal right subclavian artery and, in some cases, the accompanying vein are seen anterior to the trachea coursing towards the right arm underneath the clavicle (Figure 1). The ideal fetal position is where the shoulder lies directly up towards or away from the transducer. The artery has a tortuous course above (cranial to) the level of the aortic arch. Usually the right and left subclavian arteries are imaged simultaneously. In contrast, an ARSA arises at a lower plane than normal in the thorax, at the junction of the arterial duct with the descending aorta, and is seen passing behind the trachea towards the right arm separate from the vein (Figure 1). Sonographers were instructed to allocate up to two periods of 3 min each for the examination and to record their findings as normal right subclavian artery, ARSA, or failure to achieve a conclusive assessment. The sonographers were unaware of the fetal karyotype at the time of the scan but obviously aware of other features on the scan, including NT thickness and the presence of fetal cardiac abnormalities.

Echocardiography was also carried out at 16–24 weeks in a subgroup of 183 pregnancies in our center and the findings of the two examinations were compared.

Statistical analysis

Regression analysis was used to examine the significance of the association between failed assessment of the right subclavian artery and fetal crown–rump length or maternal body mass index. Fisher's exact test was used to examine whether there was a significant difference in the prevalence of ARSA between the chromosomally normal and abnormal fetuses.

RESULTS

The median maternal age was 35 (range, 17–49) years and the median gestation at the time of CVS was 12 (range,

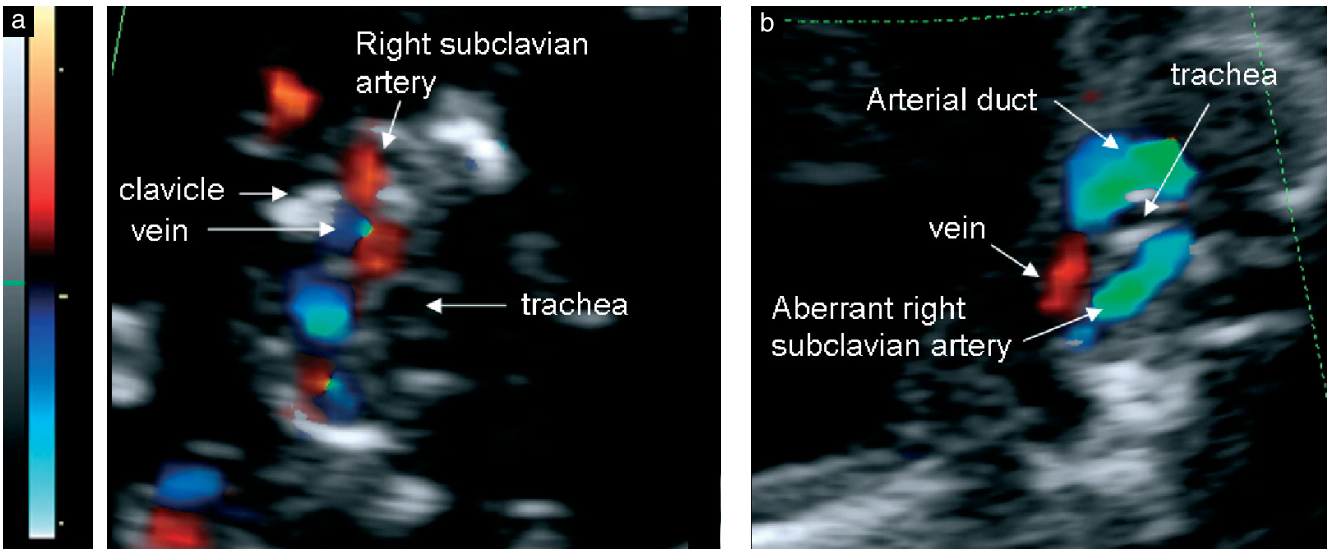

Figure 1 Ultrasound images showing (a) normal right subclavian artery coursing in front of the trachea, towards and underneath the right clavicle with the accompanying vein and (b) aberrant right subclavian artery arising from the junction of the aorta with the arterial duct crossing behind the trachea towards the arm; the accompanying vein is also seen.

11–13) weeks. The median crown–rump length was 68 (range, 47–84) mm. Successful assessment of the right subclavian artery was achieved in 425/516 (82.4%) cases and the rate of failure to do so was significantly associated with decreasing fetal crown–rump length ($r = 0.174$, $P < 0.001$) and increasing maternal body mass index ($r = 0.275$, $P < 0.001$) (Figure 2).

In the 425 cases that were successfully examined an ARSA was found in 2/353 (0.6%) with a normal fetal karyotype and in 6/71 (8.4%) with chromosomal defects ($P < 0.001$, Fisher's exact test), including 4/51 (7.8%) cases with trisomy 21 and 2/20 (10%) with other chromosomal defects (trisomy 18, $n = 10$; trisomy 13, $n = 2$; trisomy 22, $n = 1$; triploidy, $n = 3$; Klinefelter syndrome, $n = 2$; partial monosomy chromosome 3, $n = 1$; isodicentric chromosome 9, $n = 1$). The findings in the cases with ARSA are summarized in Table 3.

Fetal echocardiography demonstrated cardiac defects in 10/353 (2.8%) chromosomally normal fetuses (four at the first-trimester and six at the second-trimester scans), 13/51 (25.5%) fetuses with trisomy 21 (all in the first trimester) and 11/20 (55.0%) fetuses with other chromosomal defects (atrioventricular septal defect, $n = 9$; ventriculoseptal defect, $n = 3$; ventricular disproportion, $n = 9$; hypoplastic left heart, $n = 1$; tetralogy of Fallot, $n = 3$; aortic stenosis, $n = 1$; coarctation of the aorta, $n = 2$; pulmonary atresia, $n = 1$; tricuspid atresia, $n = 1$; transposition of the great arteries, $n = 2$; absent ductus venosus, $n = 1$; double-outlet right ventricle, $n = 2$; dysplastic atrioventricular valves, $n = 2$; note that in three cases there was more than one defect). The diagnosis of cardiac defects was made during the first-trimester scan in 9/11 pregnancies with other chromosomal defects and in the other two cases, in which the pregnancy was continued, the diagnosis was made during the second-trimester assessment.

Assessment for ARSA was also carried out at 16–24 (median, 20) weeks in our center in a subgroup of 183 of the 425 pregnancies. These included 177 with a normal karyotype, three with trisomy 21, and one each with trisomy 18, Klinefelter syndrome and partial monosomy chromosome 3. In the first-trimester scan an ARSA was observed in three of these cases (one with a normal karyotype, one with trisomy 21 and one with partial

Table 3 Cases with aberrant right subclavian artery, including eight cases diagnosed at the first-trimester scan and one case* diagnosed at the second-trimester scan

Case	*GA (weeks)*	*CRL (mm)*	*NT (mm)*	*Cardiac defect*	*Karyotype*	*Outcome*
1	13.0	70.8	2.8	No	Normal	Live birth
2	13.4	82.1	2.4	No	Normal	Live birth
3	12.6	65.4	2.5	No	Trisomy 21	Termination
4	12.2	61.8	2.9	No	Trisomy 21	Termination
5	12.0	66.9	2.7	No	Trisomy 21	Termination
6	12.6	71.8	3.2	No	Trisomy 21	Live birth
7	13.6	61.7	11.0	Ventricular disproportion	Trisomy 18	Termination
8	12.3	68.9	8.5	Tetralogy of Fallot	Partial monosomy 3	Termination
9*	12.2	64.8	2.6	No	Normal	Live birth

CRL, crown–rump length; GA, gestational age; NT, nuchal translucency.

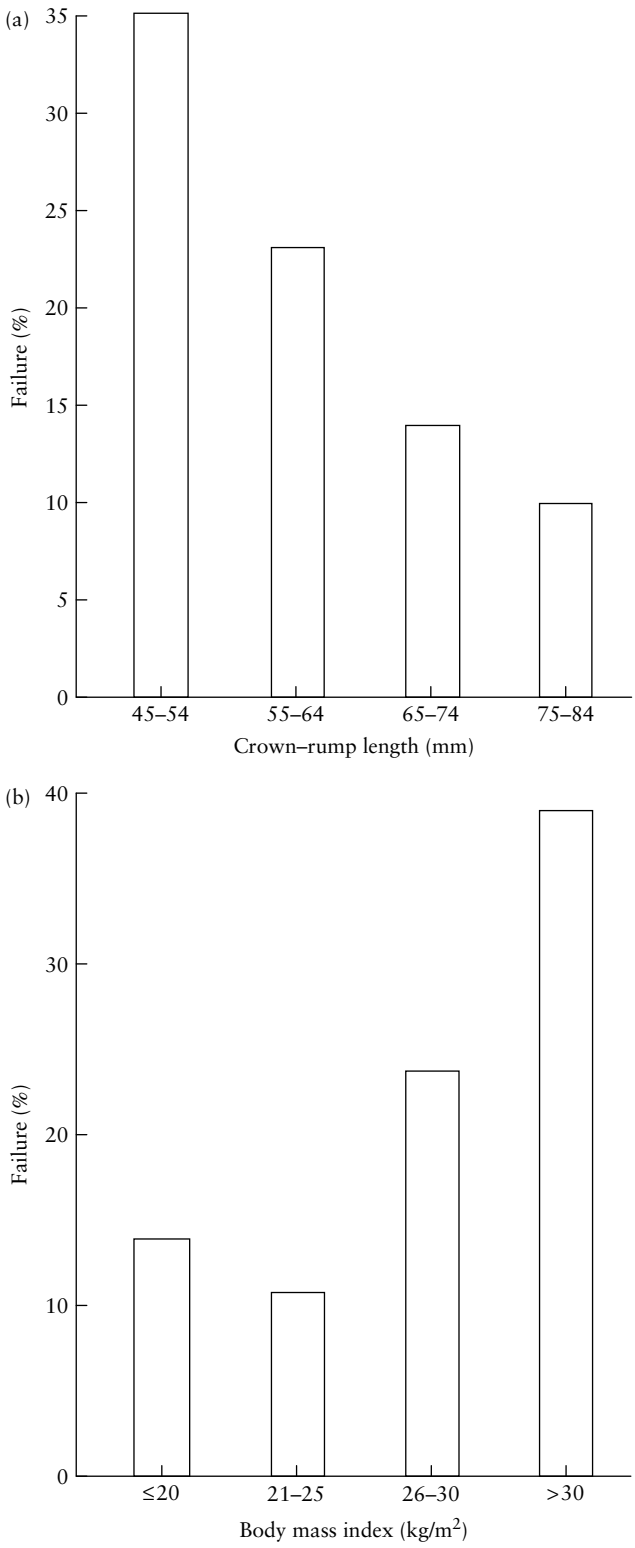

Figure 2 Failure to assess the right subclavian artery is associated with decreasing fetal crown–rump length (a) and increasing maternal body mass index (b).

monosomy chromosome 3). In the second-trimester scan the three cases with ARSA were confirmed and an additional ARSA was detected in 1/176 (0.6%) cases with a normal karyotype in which the right subclavian artery was thought to be normal at the first-trimester scan.

DISCUSSION

This study has demonstrated that it is possible to assess the position of the right subclavian artery in about 80% of cases by transabdominal ultrasound imaging at 11 + 0 to 13 + 6 weeks, and that feasibility of this assessment is highly dependent on the fetal crown–rump length and maternal habitus. Furthermore, it has shown that the prevalence of ARSA is higher in fetuses with chromosomal defects than in chromosomally normal fetuses.

A limitation of our study was that there was no postmortem examination to confirm the sonographic findings of presence or absence of ARSA in the case of chromosomal abnormalities when pregnancies were terminated. Nevertheless, if the first-trimester scan demonstrates an ARSA this is likely to exist, but in some cases the right subclavian artery is thought to be normal whereas in reality there is an ARSA. The first-trimester diagnosis of ARSA was confirmed in the subgroup of cases in which fetal echocardiography was also performed in the second trimester of pregnancy, but an ARSA was diagnosed at the second-trimester scan in 0.6% of cases in which the right subclavian artery was thought to be normal at the first-trimester scan.

Previous postnatal studies did not systematically investigate the prevalence of ARSA in chromosomally normal and abnormal individuals with and without cardiac defects. However, from their results several inferences could be made: first, ARSA is more common in those with than in those without cardiac defects (3% vs. 0.1%)[1]; second, the prevalence of ARSA among patients with cardiac defects is higher in those with trisomy 21 than in those with a normal karyotype (17%[2–8] vs. 3%[1]); and, finally, the prevalence of ARSA in patients without cardiac defects may be higher in those with trisomy 21 than in those with a normal karyotype (3.7%[2,3,5,6] vs. 0.1%[1]). In contrast, the prenatal ultrasound study by Chaoui *et al.* reported that ARSA is found in the second and third trimesters in more than a third of fetuses with trisomy 21 and that the prevalence is higher in those without than those with cardiac defects[9]. Similarly, in our study cardiac defects were observed in 13 of the 47 fetuses with trisomy 21 and a normal right subclavian artery but in none of the four with an ARSA. One possible explanation for the lower prevalence of ARSA in both trisomy 21 and chromosomally normal fetuses in our study than in previous prenatal studies is the use of transabdominal rather than transvaginal sonography.

In the first trimester of pregnancy effective screening for trisomy 21 is provided by a combination of fetal NT thickness and maternal serum free β-hCG and PAPP-A, with a detection rate of 90% for a false-positive rate of 5%[13]. The incorporation of additional sonographic markers, such as nasal bone, frontomaxillary facial angle, and tricuspid and ductus venosus flow, could increase the detection rate to more than 95% with a simultaneous reduction in false-positive rate to less than 3%[13].

This study has demonstrated that it may not be possible to assess the position of the right subclavian artery in

about 20% of cases at ultrasound scan at 11 + 0 to 13 + 6 weeks and that, although ARSA is more common in chromosomally abnormal than normal fetuses, in reality it is found only in about 8% of fetuses with trisomy 21. These findings suggest that ARSA in the first trimester is unlikely to be a useful marker of trisomy 21.

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