SCIENTIFIC LETTER

Aortic coarctation: prognostic indicators of survival in the fetus

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Prenatal diagnosis of aortic coarctation (AoCo) is feasible and has been shown to improve survival of affected neonates.[1] However, AoCo represents the main determinant of both false negative and false positive diagnoses of congenital heart disease (CHD) in the fetus.[2 3] As a primary lesion, it accounts for 7.1–8.3% of CHD in fetal series and is significantly associated with chromosomal and extra-cardiac anomalies.[2 3] We report here a retrospective analysis conducted on a population of 68 fetuses diagnosed with AoCo confirmed at necropsy or after birth.

The objectives of this study are to analyse the characteristics, associations, and outcome of AoCo when diagnosed in the fetus and to evaluate the prognostic impact of these characteristics on survival.

METHODS

This study is an observational analysis including all fetuses with a primary diagnosis of isolated AoCo seen at two referral centres over an eight year period (1995–2002). Of the original 166 fetuses, 98 were excluded (association with other major CHDs in 71 cases, lesion unconfirmed at birth in 18 cases, necropsy/surgical confirmation not available in nine cases). The remaining 68 cases with confirmed AoCo represent the study population. All fetuses underwent fetal echocardiography and a detailed anomaly scan. All examinations were performed with high resolution ultrasound systems (Prosound 5000 and 5500 Aloka, Tokyo, Japan; Toshiba Powervision 6000, Tokyo, Japan). The following variables were entered in the analysis: indication for fetal echocardiography; gestational age at diagnosis; additional ventricular septal defect (VSD); additional bicuspid aortic valve (BAV); associated extra-cardiac anomalies; karyotype; fetal growth restriction (FGR); pregnancy and neonatal outcome. Karyotype was available in 57/68 (83.8%) cases. Fetal growth data were available in 66/68 (97%) cases.

Statistical analysis was performed using the SPSS 8.0 package for Windows 98 (SPSS, Illinois). Differences in frequencies and means were assessed by χ^2 test and one way analysis of variance (ANOVA) test, respectively. Multivariate logistic regression analysis was employed to evaluate impact of different binary variables on survival; probability values of $p < 0.05$ were considered significant. Significance was expressed by odds ratio with confidence intervals.

RESULTS

Mean gestational age at the time of diagnosis was 25.1 weeks (range 17–37 weeks), with 34/68 cases diagnosed < 24 weeks of gestation. Indication for fetal echocardiography was: suspicion of CHD in 34 cases (50.0%); extra-cardiac anomalies in 23 cases (33.8%); positive family history in five cases (7.4%); other indications in six cases (8.8%). Of the 68 cases, 29 (42.7%) had an additional VSD and 10 (14.7%) a BAV, with 24/29 VSDs and 5/10 BAV detected prenatally. Extra-cardiac anomalies were associated in 27/68 cases (39.7%) (table 1). An abnormal karyotype was present in 20/57 cases in which it was known, which yields an aneuploidy rate of 35.1% (29.4% of the whole series) (table 1). FGR was present in 29.4% of all cases (20/68) and in 21.6% (8/37) of euploid ones. In the latter group, six cases had a birth weight < 5th centile (5 < 1500 g) and two < 10th centile. In these five cases, gestational age at delivery ranged between 31–34 weeks.

Table 1 Extra-cardiac anomalies associated with AoCo by system*

System	Anomalies
Central nervous system	Agenesis of the corpus callosum, Dandy-Walker anomaly†, holoprosencephaly†, NTD†, hydrocephalus†, CPC†, encephalocele
Facial	CLP†, micrognathia†, hypotelorism†
Gastrointestinal	Oesophageal atresia, diaphragmatic hernia†, exomphalos†, gastroschisis, anorectal atresia
Urogenital	Bilateral renal agenesis, MKK†, pyelectasis, PKK, vesico-ureteral reflux, hypospadia, horseshoe kidney†
Skeletal	Osteogenesis imperfecta type III, clubfoot, rockerbottom foot†, clinodactily†, hesadactily†, thanatophoric dwarfism, arthrogriposis†, bilateral radial aplasia†
Syndromes	Ellis van Creveld, Cornelia de Lange, Roberts, Jeune
Other	Cystic hygroma† single umbilical artery, eye anomalies, external ear anomalies
Chromosomal	Monosomy X (7 cases), trisomy 21 (3 cases), trisomy 18 (3 cases), trisomy 13 (2 cases), microdeletion 22q11, unbalanced translocation 2–21, unbalanced translocation 5–6, del 16q, trisomy 16q (1 case each)

*More than one anomaly per fetus.
†Associated with chromosomal anomalies.
CPC, choroid plexus cyst; CLP, cleft lip and palate; MKK, multicystic kidney; NTD, neural tube defect; PKK, polycystic kidney.

Feto-neonatal outcome was as follows: 21 (30.9%) terminations of pregnancy, 4 (5.9%) intrauterine deaths, 7 (10.3%) early neonatal deaths, 5 (7.4%) late postoperative deaths, and 31 (45.6%) survivors. Mean gestational age at birth was 38.3 weeks (range 31–41 weeks). Of the 12 dead neonates, major extra-cardiac anomalies were present in two cases (normal birth weight) and five cases had a birth weight < 1500 g. Excluding cases undergoing termination of pregnancy and those with extra-cardiac or chromosomal anomalies, the adjusted overall survival rate is 79.3% (23/29), with no significant difference between isolated coarctation and coarctation plus VSD (85.7% *v* 73.3%). Considering only cases diagnosed at 24 weeks gestation or earlier, 58.8% (20/34) underwent termination of pregnancy. However, 15 (75%) of them had associated chromosomal or extra-cardiac anomalies.

The impact of the above mentioned variables on survival was then evaluated in a multivariate logistic regression model with survival as dependent variable. The following binary

Abbreviations: AoCo, aortic coarctation; BAV, bicuspid aortic valve; CHD, congenital heart disease; FGR, fetal growth restriction; VSD, ventricular septal defect

variables were entered in the model: additional VSD; extra-cardiac anomalies; karyotype; FGR. According to the multivariate analysis, which excluded cases undergoing termination of pregnancy and those with an abnormal karyotype, the only significant independent prognostic factor was the presence of FGR; survival was 88.0% in appropriately grown fetuses and 37.0% in growth retarded ones (n = 33, odds ratio 11.73, 95% confidence interval 1.59 to 86.47; $p < 0.01$).

DISCUSSION

The first issue to take into consideration is that the rate of additional intra-cardiac lesions detected in this fetal series is consistent with postnatal data: 42.7% *v* 37–53% for VSDs,[4] and 14.7% *v* 18.8% for BAV. As to the already reported high association rate with extra-cardiac and chromosomal anomalies, our figures are consistent with the those of Allan and co-workers[2] (29.4% and 29%, respectively) but significantly higher than the 11.8% reported postnatally.[4] The significant discrepancy with postnatal figures is easily explained considering the high number of referrals for extra-cardiac anomalies (34% of the whole series), which is likely to have acted as a selection bias; in fact, 15/20 cases with an abnormal karyotype had major extra-cardiac abnormalities detected at routine ultrasound, whereas minor anomalies were detected in the remaining five cases only after referral.

However, we believe that the most interesting finding of this report is the strong prognostic significance of FGR shown by the multivariate logistic regression analysis. In this series, growth restriction complicated 21.6% of euploid cases and was responsible, among euploid fetuses not undergoing termination of pregnancy, for a significant drop in survival ($p < 0.01$). This finding should be kept in mind while counselling patients about the surgical outcome of prenatally diagnosed coarctation, for weight represents one of the most important variables affecting neonatal survival in cardiac surgery,[5] and has been shown here to also play a role when detected prenatally. However, since the incidence of FGR in the present series is not that different from the incidence seen in small for gestational age neonates in the Baltimore-Washington infant study (21.6% *v* 15.4%),[4] some other factors could be responsible for the overall surgical mortality, which is higher than that reported in most surgical cohorts (79% *v* 90–95%).[5] The relatively small population size, barely relevant in comparison with the robust populations of the Baltimore-Washington infant study, is the most likely explanation for this significant discrepancy.[4] In addition, the presence of major extra-cardiac anomalies in two of the neonates has certainly contributed to the low survival rate.

In conclusion, we have confirmed that AoCo, when diagnosed in the fetus, is significantly associated with extra-cardiac and chromosomal anomalies. In addition, we have shown that, at least in this series, there is a consistent risk of FGR (21.6%) which, in addition, represents the single and most important bad prognostic indicator. These data should be considered during prenatal counselling in cases of suspected AoCo.

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REFERENCES

1 **Franklin O**, Burch M, Manning N, *et al*. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart* 2002;**87**:67–9.
2 **Allan LD**, Sharland GK, Milburn A, *et al*. Prospective diagnosis of 1006 consecutive cases of congenital heart disease in the fetus. *J Am Coll Cardiol* 1994;**23**:1452–8.
3 **Paladini D**, Russo MA, Teodoro A, *et al*. Prenatal diagnosis of congenital heart disease in the Naples area during the years 1994–1999. The experience of a joint fetal-pediatric cardiology unit. *Prenat Diagn* 2002;**22**:545–52.
4 **Perry LW**, Neill CA, Ferencz C, *et al*. Infants with congenital heart disease: the cases. In: Rubin DJ, Loffredo AC, Magee AC, eds. *Epidemiology of congenital heart disease.The Baltimore-Washington Infant Study 1981–1989. Perspectives in Pediatric Cardiology*. 4. New York: Mount Kisco Futura Publishing Co, 1993:33–62.
5 **Bacha EA**, Almodovar M, Wessel DL, *et al*. Surgery for coarctation of the aorta in infants weighing less than 2 kg. *Ann Thorac Surg* 2001;**71**:1260–4.