

## CONGENITAL HEART DISEASE

# Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity

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**Objective:** To investigate whether antenatal diagnosis of coarctation of the aorta results in reduced mortality and improved preoperative haemodynamic stability compared with postnatal diagnosis.

**Design:** Retrospective review of all cases of coarctation of the aorta presenting to a tertiary fetal and neonatal cardiology service from January 1994 to December 1998.

**Methods:** Prenatal, postnatal, and necropsy records were reviewed to determine survival in the two groups. Markers of preoperative illness severity were recorded, including presence of femoral pulse, collapse, left ventricular function, ductal patency on echocardiography, coagulation status, duration of intensive care unit and total hospital stay, heart rate, respiratory rate, plasma creatinine, plasma potassium, and right upper limb blood pressure. A univariate and multivariate analysis was conducted on all variables and a cumulative score was created and subjected to logistic regression analysis.

**Results:** Both collapse and death were more common in the postnatally diagnosed group ( $p < 0.05$ ). Femoral pulses were more likely to be palpable and there was echocardiographic evidence of duct patency in the antenatally diagnosed infants ( $p < 0.001$  and  $p < 0.05$ , respectively). An increased respiratory rate was associated with postnatal presentation ( $p < 0.05$ ). Infants with haemodynamic instability preoperatively were more likely to have been diagnosed postnatally ( $p < 0.01$ ).

**Conclusions:** Antenatal diagnosis of coarctation of the aorta is associated with improved survival and preoperative clinical condition.

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Prenatal diagnosis of coarctation of the aorta has been possible for over 12 years.<sup>1</sup> It can, however, be a difficult diagnosis to make, as evidenced by the number of false positive and false negative diagnoses, even in the best centres.<sup>2</sup> Postnatally, coarctation often presents with cardiovascular collapse and acidosis as the arterial duct closes. Early diagnosis of coarctation should therefore improve preoperative haemodynamic stability with its associated risk of neurodisability and early neonatal death. Previous studies of coarctation<sup>3,4</sup> have not shown improved survival as a result of antenatal diagnosis but have suggested that the preoperative cardiovascular stability of affected infants is improved. These studies have examined coarctation as part of a group of mixed diagnoses and did not study necropsy cases. We therefore undertook a retrospective review of prenatally suspected coarctation to see whether the outcome was significantly better in this group than in infants diagnosed for the first time postnatally.

### METHODS

We included all cases of neonatal coarctation presenting to our cardiology department over a five year period from 1994. Prenatal, postnatal, and necropsy case records were reviewed. Outcome variables are shown in table 1. These were selected to assess the illness severity and were available in all cases. The acid-base status was not checked routinely on all neonates if they were considered to be in good or excellent condition, and these data are not included.

### Data analysis

Data were entered into STATA 6 for analysis. A univariate analysis was conducted on all variables with antenatal/postnatal diagnosis as the dependent variable. Categorical variables were analysed using Fisher's exact test. A Mantel-Haenszel test was used to test for trend. Continuous variables were analysed using a univariate logistic regression. A score

was created with the following variables: femoral pulse, collapse, left ventricular function, ductal patency, heart rate, respiratory rate, plasma creatinine, plasma potassium, right upper limb blood pressure, coagulation status, time on paediatric intensive care unit, and total hospital stay. Babies with a measurement value within normal neonatal limits were given a score of 0; those with a value greater than 2 SD outside the normal range were given a score of 2. A logistic regression of this score was conducted on antenatal versus postnatal diagnoses.

### Exclusion criteria

Coarctation presenting outside the first month of life was not included, as antenatal diagnosis of these late presentations has not been convincingly demonstrated and they are also less likely to become haemodynamically compromised as they are not duct dependent. Cases with complex heart disease in addition to coarctation were not included as it was not possible to match these with appropriate controls; however, patients with a ventricular septal defect or a bicuspid or stenotic aortic valve were included as these defects were common enough to be matched.

### RESULTS

Sixteen cases of coarctation were diagnosed antenatally during the five year study period. In three of these, coarctation was identified as part of more complex congenital heart disease and they were therefore excluded. In two additional cases coarctation was suspected prenatally but not confirmed postnatally. However, in both these infants there was narrowing of the aortic isthmus, with mildly increased Doppler velocity in the descending aorta. Both remain under surveillance. In a further case a fetus in whom coarctation was strongly suspected became hydropic and died at 20 weeks of gestation. Fetal maceration made it impossible to confirm the diagnosis at necropsy. No false negative prenatal diagnoses

**Table 1** Outcome variables

	Antenatal diagnosis	Postnatal diagnosis	p Value	M-H odds ratio (p)
Femoral pulse				
Good	10	1		
Weak	0	6	<0.0001	<0.0001
Absent	0	15		
Collapse/death				
Yes	0	10	<0.05	
No	10	15		
Left ventricular function				
Good	10	13	>0.05	>0.05
Poor	0	9		
Respiratory rate (mean) (breaths/min)	37.9	52.6	<0.05	
Arterial duct				
Open	8	6		
Restricted	2	9	<0.05	<0.05
Closed	0	7		
Heart rate (mean) (beats/min)	134.9	146.5	>0.05	
Systolic blood pressure (mean), R upper limb (mm Hg)	75.3	90.04	>0.05	
PT/APTT (mean)	1.2	1.3	>0.05	
Plasma potassium (mean) (mmol/l)	5.02	4.9	>0.05	
Plasma creatinine (mean) ( $\mu\text{mol/l}$ )	93.7	64.7	>0.05	
ITU stay (mean) (days)	6.9	6.9	>0.05	
Hospital stay (mean) (days)	22	18.2	>0.05	
Total score	3.00	6.59	<0.01	

APPT, activated partial thromboplastin time; ITU, intensive care unit; M-H, Mantel–Haenszel test; PT, prothrombin time; R, right.

were made. Thus there were 10 prenatally diagnosed fetuses who satisfied the inclusion criteria.

The most common indication for referral to the cardiac scanning clinic was an abnormal four chamber view on routine obstetric ultrasound ( $n = 5$ ), and in one case the arterial outlet view was abnormal. In two cases there was a history of a first degree relative with congenital heart disease and in two further cases the fetus had a non-cardiac anomaly.

The median gestation at prenatal diagnosis was 21.5 weeks (range 20–39 weeks). In the prenatal diagnosis group the right ventricle was larger than the left ventricle in all cases. Examination of the great arteries showed that the pulmonary artery diameter was twice that of the transverse arch in seven of the 10 cases.

Over the same period 22 infants who had had routine obstetric scanning but had not undergone dedicated cardiac assessment prenatally presented with coarctation in the neonatal period. Median age at presentation was seven days.

On clinical assessment at first presentation, femoral pulses were weak or impalpable in 21 of the 22 postnatally diagnosed infants, while they were palpable in all the antenatally diagnosed infants ( $p < 0.0001$ ). Echocardiography showed that the arterial duct was open in all the antenatally diagnosed patients; in contrast, in the postnatally diagnosed group the duct was open in only six of the 22 infants ( $p < 0.05$ ), in two of whom there was evidence that it was becoming restrictive. The median age of presentation in the postnatally diagnosed group was seven days, and most of this group were not delivered in a cardiac centre. All the antenatally diagnosed group were assessed on day 1.

Death before echocardiographic evaluation and presentation in a collapsed state—which we defined as having preoperative inotropic support or receiving colloid for resuscitation at initial presentation—were associated with postnatal diagnosis ( $p < 0.02$ ). There were 10 infants in these categories, seven of whom were successfully resuscitated and scheduled for operation; the remaining three were identified on review of

regional paediatric necropsy records. One of these infants also had aortic valve stenosis. All 22 cases who presented postnatally and were treated had undergone anomaly scans at 20 weeks. None of these had had a specific antenatal cardiac scan in a regional unit. All the antenatally diagnosed group were in good condition when reviewed on the first day of life. There was no intraoperative or postoperative mortality.

Increased respiratory rate at first assessment was associated with postnatal diagnosis ( $p < 0.05$ ). There was a trend towards tachycardia in children diagnosed postnatally ( $p < 0.08$ ). Abnormal values for heart rate, right upper limb blood pressure, coagulation status, potassium, and creatinine did not predict postnatal diagnosis. Raised plasma creatinine values recorded in the antenatally diagnosed group ( $93.7 \mu\text{mol/l}$ , *v*  $64.7 \mu\text{mol/l}$  in the postnatally diagnosed group) probably represented maternal values. Antenatally diagnosed cases did not have a significantly shorter paediatric intensive care unit or total hospital stay, as their stable clinical condition allowed them to be allocated to scheduled operating lists. No child died in hospital after diagnosis, either preoperatively or postoperatively.

All infants in this study had a normal karyotype. There were no cases of Turner's syndrome with coarctation in the analysis, as all such cases presented after 28 days of life.

Multivariate analysis of preoperative assessment scores for antenatally versus postnatally diagnosed cases showed that the overall score was significantly worse in infants in whom the diagnosis was made postnatally. Those infants with high cumulative scores indicating haemodynamic instability were 40% less likely to have been diagnosed antenatally (odds ratio 0.60, 95% confidence interval 0.41 to 0.87).

## DISCUSSION

Two earlier studies of prenatal diagnosis of coarctation of the aorta have established the criteria for the diagnosis of this condition.<sup>2 5</sup> All fetal hearts were therefore examined for ventricular disproportion, transverse aortic arch, and isthmic

hypoplasia, and the ratio of aortic to pulmonary artery size was determined. The false negative rates were 9/87 and 2/20 respectively. The false positive rate, only quoted in one study, was 24/87. Our smaller cohort did not have any false negative cases, but antenatal diagnosis is unlikely to detect all cases of coarctation. In particular, if the right ventricle is not enlarged, routine four chamber scanning in obstetric units will miss these cases. All of our patients had ventricular disproportion on the four chamber view. The two false positive cases remain under review for narrowing of the aortic isthmus and an associated increase in Doppler velocity. Both false positive cases were first seen after 30 weeks of gestation. This increased difficulty in antenatal diagnosis with advancing gestation has already been described.<sup>2</sup>

The crux of our hypothesis, however, was that prenatal diagnosis of coarctation improved both morbidity and mortality. Until recently there was little published evidence that antenatal diagnosis reduced mortality in infants with congenital heart disease. However, in a recent large series of 318 neonates with transposition of the great arteries, 68 of who were diagnosed antenatally, a reduction in both preoperative and postoperative mortality was observed.<sup>6</sup> Previous studies that included coarctation in addition to other congenital cardiac lesions have not shown improved survival in the antenatally diagnosed cohort, but necropsy records were not examined in those papers.<sup>3,4,7</sup>

Prenatal diagnosis has been shown to improve preoperative condition (but not survival) in hypoplastic left heart and transposition of the great vessels<sup>7</sup> and in a group of left heart obstructions including hypoplastic left heart and coarctation.<sup>4</sup> None of these studies looked specifically at coarctation. However, prenatal diagnosis of coarctation is easier to assess, as there is a low incidence of termination of pregnancy and a good surgical outcome, so surgical operative variables are removed.

Our study shows that prenatal diagnosis is potentially life saving, with three undiagnosed infants dying at home over the study period. All three children had a normal neonatal examination and were well at the time of discharge from hospital. Paediatric necropsy in the Oxford region is centralised to the John Radcliffe Hospital. A single dataset of cases of congenital heart disease first diagnosed at necropsy was examined in conjunction with the chief paediatric pathologist, and all cases of coarctation first diagnosed after the death of the infant were thus identified.

Antenatal diagnosis also improved preoperative condition—largely as a result of maintaining duct patency, which was 28% in the undiagnosed group but universal in the prenatally

diagnosed group. Severe deterioration with collapse or death occurred in 10 of the 22 undiagnosed cases but in none of the prenatally diagnosed group. The overall score for preoperative condition was significantly worse in those infants in whom the diagnosis was not known prenatally. This was despite the exclusion of three fatal cases in the analysis because of insufficient data.

It is unlikely that antenatal diagnosis will detect all cases of neonatal duct dependent coarctation. In particular if there is no ventricular disproportion referral will not be made for fetal cardiac scanning. There may well be cases of coarctation with both normal fetal ventricular proportions and normal transverse arch to pulmonary artery ratios, but these will probably be a minority. They are unlikely to be duct dependent and therefore will not be prone to collapse.

## Conclusions

Our retrospective review of a small number of cases of coarctation shows that an accurate diagnosis can be made antenatally. An early diagnosis may improve the preoperative condition of infants presenting for surgery and avoid the tragedy of death at home in undiagnosed cases of an eminently treatable condition.

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