

# Birth Weight and Cardiac Structure in Children

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## ABSTRACT

**OBJECTIVE.** Epidemiologic studies have shown associations between impaired fetal growth and risk for coronary heart disease in adults. The underlying mechanisms are unknown. We investigated whether restricted intrauterine growth affects cardiac structure.

**METHODS.** We performed echocardiography on 216 9-year-old children who were measured previously at birth. The diameter of the coronary left and right main branches was derived from the widest dimension; total coronary artery diameter was calculated by adding the diameters of the left and right coronary arteries. Aortic root diameter, left atrial diameter, left ventricular diameter, left ventricular outflow tract diameter, and left ventricular mass were measured.

**RESULTS.** On average, children who had weighed less at birth had a smaller total coronary artery diameter, aortic root diameter, and left ventricular outflow tract diameter after adjustment for gender, gestational age, current height and weight, and maternal height and prepregnant weight. For each SD increase in birth weight, total coronary diameter rose by 0.10 mm, log aortic root diameter rose by 1.5%, and log left ventricular outflow tract diameter rose by 1.6%.

**CONCLUSION.** Impaired fetal growth may have long-term effects on cardiac structure. This may help to explain why adults whose birth weight was low are at greater risk for coronary heart disease.

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### Key Words

cohort studies, echocardiography, epidemiology, fetal growth

### Abbreviation

CI—confidence interval

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**E**PIDEMIOLOGIC STUDIES IN several countries have shown that impaired fetal growth is associated with an increased risk for coronary heart disease in later life.<sup>1-5</sup> The mechanisms that underlie this relation are unclear. One possibility may be that poor fetal growth has effects on cardiac structure that persist into childhood and beyond, increasing the risk for coronary artery disease.

We used echocardiography to examine a group of 216 children who were aged 9 years and had been measured at birth. Our aim was to investigate the relation between birth weight and cardiac chamber, aortic root, and coronary artery diameters.

## METHODS

The mothers of the children in this study all had taken part in an earlier study of nutrition during pregnancy between April 1992 and June 1993. White women who were aged 16 years or more and had singleton pregnancies of <17 weeks' gestation were recruited during their first visit to the midwives' antenatal booking clinic at the Princess Anne Maternity Hospital in Southampton, UK; women who had diabetes and those who had undergone hormonal treatment to conceive were excluded. There were routine obstetric data about the pregnancy and delivery, and anthropometric data on the child were collected at birth. Gestation was estimated from menstrual history and scan data.<sup>6</sup> In total, 559 children were followed up to the age of 9 months, and these children form the sampling frame for this study.

When the children approached 9 years of age, we asked the Community Pediatric Service in Southampton to write to their parents with an invitation to take part in an additional follow-up study to investigate the effect of early growth on the structure and function of the heart and blood vessels, on cognitive function, and on bone mass. We chose to study the children at 9 years of age because measurements of cognitive function made at this age tend to be stable into adulthood and because we wanted to measure the children before they reached puberty. All of the children in the cohort had previously been flagged on the child health computer at the Central Health Clinic in Southampton. Letters were sent to all 461 families who were still living in the Southampton area. Of 461 invited, 216 (47%) attended for anthropometry and echocardiography. The children sat quietly in a temperature-controlled room ( $20 \pm 2^\circ\text{C}$ ) for at least 10 minutes. When pulse rate and blood pressure measurements indicated hemodynamic stability, transthoracic echocardiography (Acuson 128 XP and a 3.5-MHz phased array transducer) was performed by a single echocardiographer (B.J.) with the child in the left lateral recumbent position. Two-dimensional, M-mode, and Doppler echocardiograms were recorded over 5 consecutive cardiac cycles, and measurements were made off-

line. Aortic root diameter, left ventricular diameter, left atrial diameter, and left ventricular outflow tract diameter were measured. Left ventricular mass was calculated according to American Echocardiography Society convention. The left main and right coronary arteries were detected in the short axis of the aortic valve, and their cavity diameter was derived from the widest dimension.<sup>7</sup> Total coronary artery diameter was calculated by adding the diameters of the left and right coronary arteries. The decision to measure coronary artery diameter was made after the start of the study, so these measurements were available for 157 children.

The Local Research Ethics Committee approved the study, and the children and their mothers gave informed consent. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Where necessary, variables were transformed using logarithms to satisfy statistical assumptions of normality. We used the 2-sample *t* test and the Wilcoxon rank-sum test to examine characteristics of the study participants. Linear regression was used to examine the relation between birth weight, expressed as SD scores, and cardiac dimensions. Weight and height measurements made at the 9-year examinations were adjusted for exact age using the British 1990 growth reference data,<sup>8</sup> obtained from the Child Growth Foundation.

## RESULTS

Characteristics of the 216 children and their mothers are shown in Table 1. Cardiac dimensions all were significantly smaller in girls. Girls were shorter than boys, although their weights both at the age of 9 years and at birth were similar. The children who had an echocardiogram ( $n = 216$ ) did not differ from the nonresponders ( $n = 245$ ) in mean birth weight ( $P = .10$ ). There were no differences between the first 59 children examined, whose echocardiogram did not include measurement of coronary artery diameter, and the remaining 157 children in birth weight ( $P = .92$ ) or weight at 9 years ( $P = .27$ ), although they were on average 2 cm shorter ( $P = .05$ ).

As expected, all cardiac dimensions tended to be larger in children who were taller or heavier at the age of 9 years. There were no statistically significant differences in cardiac dimensions according to mother's social class or her smoking status during pregnancy, but in univariate analysis, all dimensions tended to be larger in children whose mother was taller. Children whose mother's prepregnant weight was higher had, on average, a larger left atrial diameter and left ventricular mass.

We examined the relation between each cardiac dimension and birth weight SD scores in separate multivariate linear regression analyses, adjusting for gender and gestational age at birth, current height and weight, and maternal height and prepregnant weight (Table 2). On average, children who had weighed less at birth had

**TABLE 1** Characteristics of the 216 Study Participants and Their Mothers

Characteristics	Boys (n = 115)	Girls (n = 101)
Child		
Birth weight, mean (SD), kg	3.37 (5.9)	3.26 (6.5)
Premature, %	7.8	6.9
Weight at 9 y, kg	28.1 (25.7–31.8)	28.2 (25.1–31.9)
Height at 9 y, mean (SD), cm	132.0 (6.0)	129.5 (6.2)
Total coronary artery diameter, mean (SD), mm	4.32 (0.29)	4.18 (0.24)
Aortic root diameter, cm	2.23 (2.13–2.36)	2.11 (2.0–2.19)
Left atrial diameter, mean (SD), cm	2.47 (0.24)	2.34 (0.21)
Left ventricular mass, g	85 (76–97)	74 (66–74)
Left ventricular outflow tract diameter, cm	1.59 (1.52–1.66)	1.51 (1.45–1.59)
Left ventricular diameter, cm	1.40 (1.32–1.44)	1.35 (1.31–1.40)
Mother		
Height, mean (SD), cm	163.3 (7.3)	162.2 (6.1)
Prepregnant weight, kg	59.0 (54.0–65.0)	59.0 (52.3–66.5)
Smoked during pregnancy, %	17.4	25.7
Social class, %		
I/II	29.2	22.0
III	52.2	62.0
IV/V	18.6	16.0

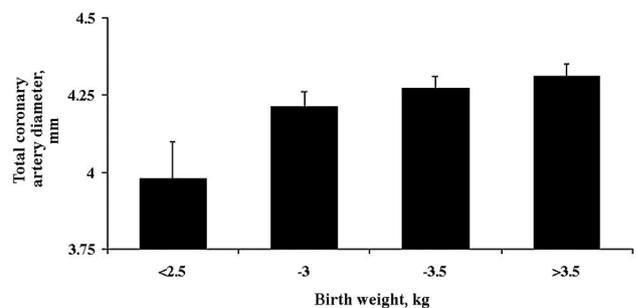
Values are medians (interquartile ranges) unless stated otherwise.

**TABLE 2** Results of Separate Multivariate Linear Regression Analyses: Change in Each Cardiac Dimension Per SD Score Increase in Birth Weight

Cardiac Dimension	Change in Cardiac Dimension <sup>a</sup> (95% CI), Adjusted for Gender and Gestation	P Value	Change in Cardiac Dimension <sup>a</sup> (95% CI), Adjusted for Gender, Gestation, Current Weight and Height, and Maternal Prepregnant Weight and Height	P Value
Total coronary artery diameter, mm	0.09 (0.03 to 0.15)	.002	0.10 (0.03 to 0.16)	.003
Left atrium diameter, cm	0.03 (–0.01 to 0.08)	.120	–0.02 (–0.06 to 0.02)	.298
Aortic root diameter	2.9% (1.6% to 4.2%)	<.001	1.5% (0.1% to 2.8%)	.028
Left ventricular mass	8.5% (5.1% to 12%)	<.001	2.4% (–1% to 5.1%)	.090
Left ventricular outflow tract diameter	3.0% (1.9% to 4.1%)	<.001	1.6% (0.5% to 2.7%)	.003
Left ventricular diameter	3.0% (1.8% to 4.1%)	<.001	0.9% (–1% to 1.9%)	.095

<sup>a</sup> Expressed as regression coefficient or, for those cardiac dimensions that had been log-transformed, percentage change.

a smaller total coronary artery diameter, aortic root diameter, and left ventricular outflow tract diameter after adjustment for gender, gestational age, current size, and maternal prepregnant size. For each SD increase in birth weight, total coronary artery diameter increased by 0.10 mm (95% confidence interval [CI]: 0.03–0.16), log aortic root diameter increased by 1.5% (95% CI: 0.1%–2.8%), and log left ventricular outflow tract diameter rose by 1.6% (95% CI: 0.5%–2.6%). These associations were similar using birth weight unadjusted for duration of gestation and in boys and girls and were affected little by adjustment for systolic or diastolic blood pressure or by exclusion of 16 children who were born before 37 weeks' gestation (data not shown). Figure 1 shows the relation between coronary artery diameter and birth weight; the relation remained significant when we omitted the 10 children with birth weight <2.5 kg. There were no significant associations between birth weight and left ventricular mass, left ventricular diameter, or left atrial diameter

**FIGURE 1**

Mean (standard error) total coronary artery diameter (mm), adjusted for gender, gestational age, current height and weight, and maternal height and prepregnant weight, according to birth weight.

## DISCUSSION

In this study of 9-year-old children, we found that total coronary artery diameter, aortic root diameter, and left ventricular outflow tract diameter were significantly smaller in children who had weighed less at birth, after adjustment for current body size and for maternal

prepregnant size. There were no significant associations between birth weight and left ventricular mass, left ventricular diameter, or left atrial diameter.

One of the limitations of this study was our inability to follow up all children in the original cohort. This was partly because some had moved away from the area in which the original study took place and it was not possible to trace them and partly because some declined to participate. Mean birth weight, however, was similar in the groups that did and who did not take part in the current phase of the study, and we think that it is unlikely that nonresponse or our inability to follow up children who had moved away will have introduced bias. Another limitation is that data on total coronary artery diameter were not available for some of the children in the study: the first 59 to attend the clinic for an echocardiogram. These children were slightly shorter than the remaining 157 children who attended the clinic, but as there was no difference between the groups in mean birth weight or current weight, it is unlikely that our findings on the relation between birth weight and total coronary artery diameter would have been different had we had complete data on all 216 children.

Echocardiography of normal neonates has shown a linear increase in aortic root diameter with increasing birth weight.<sup>9</sup> Our findings that children who weighed less at birth have smaller aortic root diameters after taking account of current size suggest that restricted prenatal growth could have persisting effects on the structure of the heart and great vessels and add to the evidence on the determinants of aortic root diameter.<sup>10</sup> A narrow left ventricular outflow tract diameter has been linked with vibratory innocent murmurs in normal children,<sup>11,12</sup> but it is unclear whether prenatal effects on the left ventricular outflow tract and aortic root have other clinical implications. However, it is possible that small differences in the mechanical and physical properties of the heart and aortic root in early life have a disproportionate influence on cardiac risk in adulthood.<sup>13</sup> Longitudinal studies are needed, however, to confirm such a hypothesis.

Echocardiographic studies of the coronary arteries in healthy children with normal hearts have shown that diameter increases with weight and height.<sup>14,15</sup> Our finding that birth weight was associated with total coronary artery diameter in 9-year-old children, independent of current weight and height, suggests that growth during fetal life may have a lasting effect on coronary artery size. Experimental evidence that intrauterine influences can have persisting effects on the coronary circulation has come from studies of sheep that were made anemic during fetal life.<sup>16</sup> Adult sheep that in utero had been made anemic by isovolemic hemorrhage for a 10-day period in late gestation showed greater maximal conductance in the coronary circulation.<sup>16</sup> Fetal anemia led to

increased coronary reserve and a greater cardiac functional response to acute hypoxic stress in the adult sheep.<sup>17</sup>

Intrauterine influences on the development of the coronary circulation of human infants could have important implications. People who have a smaller coronary artery diameter have a higher prevalence of atherosclerotic lesions,<sup>18</sup> and they are likely to be at increased risk for luminal occlusion as atherosclerosis progresses.<sup>19</sup> They also have a poorer outcome after cardiac interventions such as angioplasty or coronary artery bypass surgery,<sup>20</sup> perhaps as a result of a higher likelihood of thrombosis in smaller vessels.<sup>21</sup> The results of this study showing that birth weight is an independent predictor of total coronary artery diameter in children may help to explain the findings linking low birth weight and increased risk for coronary heart disease in adults.<sup>1-5</sup>

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