Sex specific difference in the relation between birth weight and arterial compliance in young adults: The Young Hearts Project

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Low birth weight and small size at birth have been related to raised blood pressure in both childhood and adult life¹ and a previous report has demonstrated lower arterial compliance in middle aged adults who were small at birth.² It has been hypothesised that, in the growth retarded fetus, reduced arterial compliance results from impaired elastin synthesis in the walls of large arteries.³ Elastin synthesis in blood vessels seems to be primarily limited to the fetal and perinatal periods³ with no appreciable synthesis during adulthood. Investigation of the relation between birth weight and arterial compliance in young people, as in this study, presents an opportunity to test this hypothesis and has the advantage that the relation should not be obscured by existing atherosclerosis, which is related to both birth weight and arterial compliance.

Methods

Subjects were recruited from 1015 randomly selected children who participated in a survey of cardiovascular risk factors performed in Northern Ireland in 1989 (the Young Hearts cohort). All subjects were invited to attend further screening between 1997 and 1999, when aged 21 to 25 years (the Young Hearts 3 survey). Altogether 489 (48.2%) of the original subjects attended (251 men, 238 women). Clinical and questionnaire data were collected on a large number of cardiovascular risk factors. The screening procedure included measurement of blood pressure (Hawksley Random Zero Sphygmomanometer) and pulse wave velocity (the speed of propagation of the systolic pressure wave along the length of an artery) in three arterial segments (aorto-iliac, aorto-radial, aorto-dorsalis pedis) by a non-invasive optical method.² Pulse wave velocity (PWV) is inversely proportional to arterial compliance. Data on PWV for all three segments were available for 456 subjects (93%,

228 men, 228 women). Recorded birth data, including weight and gestational age, were obtained from computerised birth records held by the Department of Health and Social Services and Public Safety (Northern Ireland).

Generalised linear models (SPSS for Windows, Version 10) were constructed in accordance with Lucas *et al*⁴ with PWV in the three arterial segments as dependent variables and birth weight as a predictor variable. Gestational age, age at screening, adult body mass index (BMI) and systolic and diastolic blood pressure were included as covariates in the models. A sex/birthweight interaction term was also constructed and included in the models. This term was significant ($p < 0.01$) in all models, so separate models were constructed for each sex.

Results

We achieved a modest response rate (48.2%) but mean birth weight was the same in responders and non-responders (3393 g versus 3349 g, $p=0.2$). Mean PWV in all segments were significantly higher in men than women; aorto-iliac, 3.26 m/s versus 2.92 m/s, $p < 0.01$; aorto-radial, 4.33 m/s versus 4.15 m/s, $p < 0.01$; and aorto-dorsalis pedis, 5.16 versus 4.76, $p < 0.01$. The unadjusted and adjusted regression coefficients for the relations between birth weight and PWV in the arterial segments are shown in table 1. For both the aorto-iliac and aorto-dorsalis pedis segments the PWV and birth weight relations were positive for men and negative for women. The PWV/birth weight relation in the aorto-radial segment was negative in both sexes, but was much stronger in women than in men. Adjustment of the relations between birth weight and PWV in any segment for adult BMI made little difference to observed regression coefficients. Further adjustment for systolic and diastolic blood pressure did not affect the relations in men but attenuated those seen in women.

Table 1 Unadjusted and adjusted difference in pulse wave velocity (PWV) in the three arterial segments per kilogram difference in birth weight

Measure of arterial compliance	Unstandardised regression coefficients (95% CI)			
	Unadjusted	Adjusted for age and gestational age	Further adjustment for adult BMI	Further adjustment for systolic and diastolic blood pressure
PWV in aorto-iliac segment (m/s)				
Men	0.12 (0.01, 0.23)	0.20 (0.06, 0.34)	0.23 (0.09, 0.37)	0.23 (0.09, 0.36)
Women	-0.12 (-0.22, -0.03)	-0.12 (-0.22, -0.02)	-0.13 (-0.26, 0.01)	-0.09 (-0.19, -0.01)
PWV in aorto-radial segment (m/s)				
Men	-0.01 (-0.13, 0.12)	-0.01 (-0.13, 0.12)	-0.01 (-0.18, 0.16)	-0.01 (-0.17, 0.16)
Women	-0.13 (-0.25, 0)	-0.13 (-0.26, 0)	-0.12 (-0.20, 0.01)	-0.07 (-0.20, 0.05)
PWV in aorto-dorsalis pedis segment (m/s)				
Men	0.12 (-0.01, 0.24)	0.09 (-0.08, 0.26)	0.09 (-0.08, 0.25)	0.08 (-0.08, 0.24)
Women	-0.07 (-0.20, 0.06)	-0.06 (-0.20, 0.07)	-0.06 (-0.20, 0.07)	-0.01 (-0.14, 0.11)

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Discussion

The men who participated in this study had substantially higher PWV (lower arterial compliance) in each of the arterial segments than the women, with the difference most marked in the elastic arteries of the aorto-iliac segment. Differences between the sexes in body mass index, blood pressure, smoking habit, alcohol consumption, total and HDL-cholesterol and triglycerides explained part but not all of the sex differences in pulse wave velocities (data not shown). There were also clear differences between the sexes in the nature of the relation between birth weight and arterial compliance. The negative relations between birth weight and PWV seen in women, which were largely unaffected by adjustment for adult BMI, support the hypothesis by Martyn *et al*³ that impaired growth in utero may affect elastin synthesis in blood vessels and result in diminished arterial compliance in adulthood. However, the findings in men are equally strong and are in the opposite direction to that which would be expected if the hypothesis held. Previous reports have failed to show associations between birth weight and arterial compliance in young adults⁵⁻⁶ but these studies did not examine the sexes separately. Our finding of a sex difference in the relation between birth weight and arterial compliance is in keeping with that of some previous investigators who have shown that the negative relation between birth weight (and other measures of fetal undernutrition) and blood pressure at age 8–11 years is almost entirely confined to girls.⁷ We cannot, however, offer a coherent explanation for the apparent sex difference in the

relation between birth weight and arterial compliance. Chance is one possibility, despite the significant interaction tests,⁸ and in one study that also found no overall association between birth weight and arterial compliance⁵ there was little evidence of any sex difference (Alan Montgomery, personal communication). We suggest that future studies examining this association should present data separately for men and women.

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