Gestational Age and Birth Weight in Relation to Aortic Stiffness in Healthy Young Adults: Two Separate Mechanisms?

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Background: Impaired vascular development due to intrauterine growth retardation and postnatal-induced vascular damage by an unfavorable cardiovascular risk profile may both cause stiffer arteries in later decades.

Methods: Of 524 young adults, participating in the Atherosclerosis Risk in Young Adults (ARYA) study, data on birth characteristics were obtained from the original medical records of the Municipal Health Service and the extent of aortic stiffness was assessed using carotid–femoral pulse wave velocity (PWV).

Results: The PWV showed an inverse trend with gestational age (linear regression coefficient ($\beta$) = -0.07 m/sec per 1 week; $P = .064$) whereas it was positively related to birth weight ($\beta$ = 0.33 m/sec per 1 kg; $P = .020$), adjusted for blood pressure (BP), gender, age, and each other. After exclusion of the 26 prematurely born infants, the association with gestational age was attenuated ($\beta$ = -0.03 m/sec per 1 week; $P = .582$), whereas the relation with birth weight hardly changed ($\beta$ = 0.30 m/sec per 1 kg; $P = .041$). In an analysis in which we excluded the 26 subjects with diabetic mothers the birth weight–PWV relation was attenuated ($\beta$ = 0.21 m/sec per 1 kg; $P = .169$).

Conclusions: Our findings suggest that prematurity drives the relation of gestational age and PWV, whereas risk of impaired glucose tolerance drives the relation of birth weight and PWV. We hypothesized that two separate mechanisms might be involved in the development of arterial stiffness in healthy young adults. Am J Hypertens 2003;16:76–79 © 2003 American Journal of Hypertension, Ltd.

Key Words: Arterial stiffness, birth weight, gestational age, young adults.


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We explored whether low birth weight and premature birth are independently involved in the process of arterial stiffening and whether these relations are independent of BP, gender, and age in healthy young adults.

Methods

Study Population

The Utrecht-cohort of the Atherosclerosis Risk in Young Adults (ARYA) study includes 750 young adults born between 1970 and 1973, who attended secondary school in the city of Utrecht in The Netherlands and of whom the original medical records from the Municipal Health Care were available. From October 1999 to December 2000, the participants visited our clinic twice within a 3-week period. The ARYA study was approved by the Medical Ethical Committee of the University Medical Center Utrecht and all participants gave written informed consent. The present report is restricted to the 524 participants in whom measurement of aortic stiffness was performed.

Information on birth weight, birth length, and gestational age was obtained from the original medical records of the Municipal Health Service.

Assessment of the Adult Cardiovascular Risk Profile and Aortic Stiffness

At each visit, peripheral BP was measured twice, in the left brachial artery with a semiautomated device (Dinamap, Critikon Inc., Tampa, FL). Data on systolic and diastolic BP are the average of the four measurements. During the first visit, anthropometric measurements were performed with indoor clothes without shoes and a written standardized questionnaire was completed on cardiovascular risk factors, such as smoking pattern, alcohol intake, physical activity, and family history for cardiovascular disease, diabetes mellitus, and hypertension. During the second visit, a fasting venous blood sample was drawn.

The PWV was measured noninvasively in the carotid–femoral segment using the SphygmoCor device (PWV Medical, Sydney, Australia). Two distances were measured in a straight line using a compass to reduce the influence of body contours: (a) from the sternal notch to the proximal sampling site on the carotid artery and (b) from the sternal notch to the distal sampling site on the femoral artery. The carotid to femoral path length was estimated by subtracting distance (a) from distance (b). The PWV was determined by sequential acquisition of pressure waveforms from the carotid and the femoral arteries by applanation tonometry (Millar SPT 301 pressure transducer, Millar Instruments, Sydney, Australia). The timing of these waveforms was compared with that of the R-wave on the simultaneously recorded electrocardiogram. The PWV was determined by calculation of the difference in the carotid-to-femoral path length divided by the difference in R-wave-to-waveform foot times. The average of 10 successive measurements was used in the analyses to cover a complete respiratory cycle. The whole procedure was repeated three times per subject and the average PWV value was used for the analysis.

Data Analysis

The relations between PWV and birth characteristics were investigated using linear regression models. Due to equipment failure, usable PWV data were only available in 524 participants (46% men). Of those, only 422 had complete data on both birth weight and gestational age. We compared the baseline characteristics across the groups with and without missing data. No major differences were found. Also, it is not likely that “missingness” is related to either PWV, gestational age, or birth weight. Therefore, we assume that missingness is a random phenomenon and does not bias our findings.

Results

Mean (SD) birth weight, birth length, and gestational age were 3438 g (554 g), 50.7 cm (2.6 cm), and 39.8 weeks (2.0 weeks), respectively; 26 subjects were born prematurely (<37 weeks). As expected, prematurely born infants had significantly lower gestational age and birth weight and were significantly shorter at birth than term infants (Table 1). At young adulthood, mean (SD) age,
Table 2. Studies on arterial stiffness and birth size

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Martyn6</th>
<th>Kumaran7</th>
<th>Montgomery8</th>
<th>Styczynski9</th>
<th>ARYA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/women</td>
<td>N = 208</td>
<td>N = 435</td>
<td>N = 528</td>
<td>N = 142</td>
<td>N = 422</td>
</tr>
<tr>
<td>Age (y)</td>
<td>49.5 ± 4.8</td>
<td>25.0 ± 0.8</td>
<td>20.9 ± 1.1</td>
<td>28.2 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>Men, 3270; women, 3136</td>
<td>Men, 2785; women, 2707</td>
<td>Men, 47.9; women, 47.6</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Current MAP (mm Hg)</td>
<td>Overall, ± 107</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Current BMI (kg/m^2)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>PWV method</td>
<td>Optical method</td>
<td>Not reported</td>
<td>Optical method</td>
<td>Optical method</td>
<td>Optical method</td>
</tr>
<tr>
<td>Measured segment</td>
<td>AI; FPT^o</td>
<td>1) zero (P = .5)</td>
<td>1) Not reported</td>
<td>1) Not reported</td>
<td>1) Not reported</td>
</tr>
<tr>
<td>β (BW and PWV)</td>
<td>2) neg (P = .05)</td>
<td>2) zero (P = .8)</td>
<td>2) zero (P = .71)</td>
<td>2) zero (P = .71)</td>
<td>2) zero (P = .71)</td>
</tr>
<tr>
<td></td>
<td>3) zero (P = .94)</td>
<td>3) zero (P = .94)</td>
<td>3) zero (P = .94)</td>
<td>3) zero (P = .94)</td>
<td>3) zero (P = .94)</td>
</tr>
</tbody>
</table>

ARYA study = Atherosclerosis Risk in Young Adults; MAP = mean arterial pressure; BMI = body mass index; PWV = pulse wave velocity; AI = aortoiliacal; FPT = femoropopliteal tibial; AR = aortoradial; AF = aortofemoral; ATP = aorto-tibial posterior; ADP = aorto-dorsalis pedis; ATa = aorto-tibial anterior; CF = carotid femoral; BW = birth weight.

Discussion

Our findings support the hypothesis that intrauterine underdevelopment, as a consequence of premature birth, is associated with increased arterial stiffness. Because intrauterine growth retardation often leads to dysmaturation of arteries, the PWV showed an inverse trend with gestational age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03). Both age (linear regression coefficient (β) = -0.07 m/sec per 1 week; P = 0.041). In an additional analysis, we compared the mean PWV of full-term subjects with those of preterm subjects, with full-term age (β = 0.33 m/sec per 1 week; P = 0.03).
taken into account in the analysis, make these reports incomparable (Table 2). Moreover, none of these studies discussed the relation between gestational age and arterial stiffness. This is remarkable, as most of the studies that use birth weight as a determinant usually also have information about gestational age.

In conclusion, our results show that premature birth as well as a higher birth weight were related to increased aortic PWV, independent of BP. Further studies are needed to elucidate whether two separate mechanisms are involved in the development of arterial stiffness in healthy young adults.

References