Arterial distensibility in children and teenagers: normal evolution and the effect of childhood vasculitis

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Background: Polyarteritis nodosa is a necrotising vasculitis of the medium sized and small muscular arteries. The inflammatory and subsequent reparative processes may alter the arterial mechanical properties. The effect of vasculitic damage on arterial distensibility has never been explored however.

Aim: To determine the normal values and the effect of childhood vasculitis on arterial distensibility in children and teenagers.

Methods: Distensibility of the brachioradial arterial segment was studied using pulse wave velocity (PWV ∝1/distensibility), in 13 children with polyarteritis nodosa at a median age of 11.8 (range 4.9–16) years. As a control group, 155 healthy schoolchildren (6–18 years, 81 boys) were studied. PWV was assessed using a photoplethysmographic technique; blood pressure was measured by an automatic sphygmomanometer (Dinamap). Data from patients were expressed as z scores adjusted for age and compared to a population mean of 0 by a single sample t test. Determinants of PWV in normal children were assessed by univariate and multivariate linear regression analyses.

Results: Age, height, weight, and systolic blood pressure correlated individually with the brachioradial PWV. Multivariate analysis identified age as the only independent determinant. Ten of the patients were in clinical remission, while three had evidence of disease activity at the time of study. The PWV in the patient group as a whole was significantly greater than those in healthy children (mean z score +0.99). Raised C reactive protein concentration (>2 mg/dl) in the three patients with active disease was associated with a higher PWV when compared to those in remission (z score +2.78 v +0.45). The diastolic blood pressure of the patients was higher than those of the controls (z score +1.04) while the systolic pressure was similar (z score −0.36).

Conclusions: PWV in the brachioradial arterial segment increases gradually during childhood independent of body weight, height, mass, and blood pressure. Increased PWV, and hence decreased distensibility, in this peripheral arterial segment occurs in polyarteritis nodosa and is amplified during acute inflammatory exacerbation.
analysed using custom made software. A non-weighted four point running average technique was used to smooth the signal. The transit time was determined from the time delay between the foot of the corresponding brachial and radial pulse waves, as this point is relatively free of wave reflection. The foot was determined by an algorithm that identified the point at which the second derivative of the diameter waveform is maximum. The pulse wave velocity was derived by dividing the measured distance between the two probes by the transit time.

**Results**

**Control subjects**

Age (in both boys and girls), height, weight, and systolic blood pressure significantly and positively correlated with brachial-radial pulse wave velocity (table 1). As the height and weight variables had a strong linear relation with age (tolerance of height and weight was 0.11 and 0.17, respectively) when included in the multiple linear regression model, they were removed from the model and instead the body mass index was included. Age was identified as the only independent determinant by multivariate analysis (standardised $\beta = 0.57$, $p < 0.001$; table 1). Pulse wave velocity was therefore normalised for age and expressed as z score (measured value minus mean value/standard deviation) for comparison between different patient groups and controls (fig 1).

**Children with polyarteritis nodosa**

Thirteen children with polyarteritis nodosa were studied at a median age of 11.8 (range 4.9–16) years. Median duration of the illness since diagnosis was 3.1 (range 0.4–11.5) years. Ten were in clinical remission, while three had clinically active disease at the time of study that coincided with an increase in C reactive protein ($> 2$ mg/dl). Their medications included steroids ($n = 11$), cytotoxics ($n = 10$), antiplatelet agents ($n = 8$), cyclosporin A ($n = 2$), and antihypertensive drugs ($n = 2$).

Pulse wave velocity in children with polyarteritis nodosa was significantly greater than that in healthy children ($z$ score $+0.99 (0.92)$, $p = 0.037$; fig 2). Diastolic blood pressure of the

| Table 1 Univariate and multivariate analysis of variables relating to pulse wave velocity |
|-----------------------------------|-------------------------------|-------------------------|
| Variables                          | Univariate analysis | Multiple linear regression |
| Age (years)                        | $0.40$ ($<0.001$) | $0.57$ ($<0.001$) |
| Boys                               | $0.46$ ($<0.001$) |
| Girls                              | $0.28$ ($0.015$)    |
| Sex (male)                         |                  |
| Height (cm)                        | $0.41$ ($<0.001$) |
| Weight (kg)                        | $0.32$ ($<0.001$) |
| Body mass index (kg/m$^2$)         | $0.13$ ($0.1$)    | $-1.64$ ($0.08$) |
| Systolic blood pressure (mm Hg)    | $0.16$ ($0.047$)  | $-0.017$ ($0.87$) |
| Diastolic blood pressure (mm Hg)   | $0.04$ ($0.64$)   | $-0.11$ ($0.31$) |
| Mean blood pressure (mm Hg)        | $0.14$ ($0.09$)   | $0.16$ ($0.20$) |
| Pulse rate (per minute)            | $-0.09$ ($0.29$)  | $0.16$ ($0.09$) |

**Figure 1** Scatter plot of pulse wave velocity against age. The lines represent the mean (solid line) and the 95% prediction interval (dashed lines).

**Figure 2** Vertical scatter plots of z scores of pulse wave velocity in patients and controls. The error bar represents mean (SEM); z scores of the three patients with flare of disease activity at the time of study are marked by asterisks.
patients was higher than that of the controls (z score: +1.04 (0.91), p = 0.028), while systolic blood pressure was similar between the two groups (z score -0.36 (1.08), p > 0.4). Raised C reactive protein concentration (>2 mg/dl) in three patients with flare of disease activity at the time of study was associated with a higher pulse wave velocity (z score +2.78 (1.84), compared with those in remission (+0.45 (0.89), p = 0.012)). There was, however, no significant correlation between the z scores of pulse wave velocity and the duration of illness from diagnosis (r = -0.29, p = 0.36).

**DISCUSSION**

Our data show that there is a gradual increase in pulse wave velocity of the brachioradial arterial segment, hence a decrease in arterial distensibility, during childhood independent of body weight, height, mass, and blood pressure. The arterial distensibility is significantly decreased in children with polyarteritis nodosa. Importantly, this abnormality is amplified during inflammatory exacerbation.

By constructing a multivariate model, we identified age as the only significant determinant that correlates positively with the distensibility of peripheral arteries in the upper limb of children and teenagers. Previous investigators have found no consistent change in distensibility of the radial or brachial arteries with age. Bramwell and Hill and Avolio and colleagues found a linear increase in pulse wave velocity in the upper limb from 3 to 89 years of age, while Avolio and colleagues, in another population studied, and Ho, who studied adults >20 years of age, reported little age related changes. Nonetheless, the scatter plots of Avolio and colleagues suggested, on closer examination, a steep rise in pulse wave velocity in the upper limb from birth to 20 years of age which then plateaux off in adulthood. However, our findings, and those of the others, fail to confirm a peak in arterial compliance at around 10 years of age, as reported by Laugum and Gosling. This is perhaps not surprising as progressive medial degeneration is probably the major underlying factor. The rate of elastin synthesis increases to a maximum in the perinatal period and falls rapidly thereafter. With the cyclic mechanical stress, fragmentation of the elastin fibres and transfer of the stress to much stiffer collagen fibres inevitably result in progressive reduction in vascular compliance. Our findings echo those of Avolio and colleagues and refute the suggestion that change in pulse wave velocity with age is entirely owing to difference in systemic blood pressure.

Of interest to note, however, is that the type of blood pressure measurement is known to be associated with increased pulse wave velocity, which is justified in light of the predilection of its involvement in polyarteritis nodosa, the ascending aortic load presented to the left ventricle would inevitably increase with increased impedance in any of these vascular beds. The arterial damage in polyarteritis nodosa may therefore prejudice later cardiovascular health by decreasing arterial distensibility, increasing characteristic impedance and cardiac load.

In summary, normal aging is associated with a progressive reduction in arterial distensibility. Chronic vasculitis leads to a significantly reduced distensibility, the magnitude of which is amplified during the acute inflammatory stage of the disease.
REFERENCES