Cardiology in the Young (2012), **22**, 451–456
doi:10.1017/S104795111200008X

Original Article

Aortic stiffness and flow-mediated dilatation in normotensive offspring of parents with hypertension

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Abstract *Objectives:* Although hypertension has been shown to be one of the most important risk factors for atherosclerosis, data about the presence of subclinical atherosclerosis in normotensive offspring with parental history of hypertension are scarce. Accordingly, the current study was designated to evaluate flow-mediated dilatation and aortic stiffness, which are early signs of atherosclerosis in young subjects with parental history of hypertension. *Methods:* A total of 102 healthy, non-obese subjects in the age group of 18–22 years were included in this study and divided into two groups. The first group included 70 offspring of hypertensive parents and the second group included 70 offspring of normotensive parents as controls. In all subjects, endothelium-dependent and endothelium-independent vasodilatation of the brachial artery and aortic elastic parameters were investigated using high-resolution Doppler echocardiography. *Results:* Offspring of hypertensive parents demonstrated higher values of aortic stiffness (7.1 plus or minus 1.88 and 6.42 plus or minus 1.56, respectively) but lower distensibility (9.47 plus or minus 1.33 and 11.8 plus or minus 3.36 square centimetres per dyne per 10^6) and flow-mediated dilatation (4.57 plus or minus 1.3 versus 6.34 plus or minus 0.83 percent, p equals 0.0001, respectively) than offspring of hypertensive parents. *Conclusion:* We observed blunted endothelium-dependent dilatation and aortic stiffness in offspring of hypertensive parents compared with offspring of hypertensive parents. This is evident in the absence of overt hypertension and other diseases, suggesting that parental history of hypertension is a risk for subclinical atherosclerosis and it may contribute to the progression to hypertension and overt atherosclerosis in later life.

Keywords: Hypertension; family history; non-invasive indicators of atherosclerosis; endothelial function

Received: 13 July 2011; Accepted: 3 December 2011; First published online: 21 February 2012

ALTHOUGH THEIR BLOOD PRESSURE LEVELS ARE often well below the hypertensive range, the offspring of hypertensive parents tend to have higher blood pressure levels, increased blood pressure response to exercise, and increased stiffness of the carotid artery compared with offspring of normotensive parents.[1,2] In addition, some cardiovascular abnormalities such as increased left ventricular mass index and a reduced venous compliance were reported in offspring of hypertensive parents.[3]

In the past few years, several new non-invasive tools have emerged that can detect atherosclerosis in its subclinical phase. Measurement of flow-mediated dilatation and aortic stiffness are two such promising tools, which are early markers for the detection of asymptomatic atherosclerotic lesions and/or structural changes resulting from hypertension.[4,5] In previous longitudinal studies, it is demonstrated that aortic stiffness was an independent predictor of cardiovascular mortality in hypertensive patients, in patients with end-stage renal disease, and in elderly people.[6–8] The assessment of flow-mediated dilatation of the brachial artery has been widely used as a simple and non-invasive method for determining endothelial function.[9,10] Recently, it has been shown that flow-mediated dilatation is reduced in patients with coronary risk factors and in patients with coronary artery disease.[11] Although it has been shown that

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hypertension is one of the most important predictors of reduced arterial elasticity and flow-mediated dilatation independent of age and also that offspring of hypertensive parents have higher blood pressure, increased blood pressure response to exercise than offspring of hypertensive parents, data about the large-artery elastic properties and flow-mediated dilatation and their clinical impact in offspring of hypertensive parents are scarce.

Accordingly, the aim of this study was to investigate the early signs of atherosclerosis in healthy offspring of hypertensive parents.

Material and methods

Study Protocol

A total of 140 subjects (ages 22.9 standard deviation equals 1.8 years) were studied and divided into two groups on the basis of their family history of hypertension. The first group included 70 offspring with parental history of hypertension and the second group included 70 offspring of normotensive parents. In the first group, at least one parent of each subject studied had hypertension verified by the investigators and defined as high clinical blood pressure levels (systolic pressure above 140 millimetres of mercury, and/or diastolic blood pressure 90 millimetres of mercury as the mean of three different measurements in at least three different visits at 1-week intervals) or using antihypertensive medication. All subjects in the study were clinically healthy. Exclusion criteria from the study were coronary artery disease, congestive heart failure, valvular heart disease, impaired glucose tolerance, diabetes mellitus and any other chronic medical illnesses or family history of diabetes, and obesity (body mass index must be less than 30 kilogram per square metre). All subjects were free from cardiac medications and drugs known to affect echocardiographic parameters and all had a similar lifestyle. The study was approved by the ethical committee of our institutions.

Echocardiographic measurements

All measurements were performed by M-mode echocardiography with the subjects in the left lateral decubitus position. Vivid 7 Doppler echocardiographic unit (GE Vingmed Ultrasound, Horten, Norway) with 2.5 Megahertz probe was used. Echocardiographic tracings were recorded at a sweep speed of 50 millimetres per second. The aortic diameter was recorded by M-mode echocardiography at a level 3 centimetres above the aortic valve.[12] Internal aortic diameters were measured by means of a caliper in systole and diastole as the distance between the trailing edge of the anterior aortic wall and the leading edge of the posterior aortic wall. Aortic systolic diameter was measured at the time of full opening of the aortic valve, and diastolic diameter was measured at the peak of QRS. In all, 10 consecutive beats were measured routinely and averaged. The aortic systolic and diastolic diameter indexes for each subject were calculated by dividing the aortic systolic and diastolic diameter by the body surface area. The percentage change of the aortic root was calculated as 100 multiplied by (aortic systolic diameter minus aortic diastolic diameter) divided by aortic diastolic diameter to obtain the aortic strain.

Blood pressure

All patients had their blood pressure measured in the supine position with a mercury sphygmomanometer. Korotkoff phases I and V were used to determine the systolic and diastolic pressures, respectively, and the average of three readings was regarded as the clinical blood pressure. Pulse pressure was obtained as systolic minus diastolic blood pressure, and the following indexes of the elastic properties of the aorta were calculated: (1–5) aortic root distensibility equals 2 multiply (aortic systolic diameter minus aortic diastolic diameter) divided by pulse pressure multiply aortic diastolic diameter, in square centimetre per dynes, and (2–5) aortic stiffness index equals (systolic blood pressure divided by diastolic blood pressure) divided (aortic systolic diameter divided by aortic diastolic diameter) divided aortic diastolic diameter (pure number) (18–5, 19–5).

Sampling of blood

Blood samples for analysis of plasma concentrations of total cholesterol, triglycerides, high-density lipoprotein cholesterol, and fasting glucose were obtained at wake-up time (7:20 am) and processed at the hospital laboratory according to routine procedures.

Vascular reactivity study

The technique for assessing endothelium-dependent and endothelium-independent vasodilation by non-invasive ultrasound has been described in detail by Celermajer.[9] Briefly, the diameter of the brachial artery was measured in triplicate at rest, during reactive hyperaemia, and after administration of sublingual glyceryltrinitrate using a high-resolution ultrasound device with a 12.0 Megahertz linear array transducer (Vivid 7 dimension, GE Vingmed Ultrasound, Norway). Longitudinal images of the brachial artery were obtained proximal to the antecubital fossa. Transmit focus zones were set approximately to the depths of the anterior and the posterior vessel walls. Images were magnified,

https://doi.org/10.1017/S104795111200008X Published online by Cambridge University Press

and depth and gain settings were used to optimise the image of the vessel wall, particularly the media–adventitia interface. Other investigators have demonstrated that conduit artery dilation changes in response to increased flow are endothelium dependent,[13] whereas the dilator response to glyceryltrinitrate is endothelium independent.[14]

Brachial artery ultrasound was performed in a quiet room. All patients rested for at least 10 minutes before the first scan. Increased flow was then induced by inflation of a pneumatic tourniquet placed around the forearm to a pressure of 300 millimetres of mercury for 4–5 minutes. A second scan was obtained 45–60 seconds after cuff deflation. After a recovery phase of 15 minutes, sublingual glyceryltrinitrate (0.4 milligrams) was administered and 3–4 minutes later the last scan was obtained. Vessel diameters after reactive hyperaemia and glyceryltrinitrate administration were compared with the resting diameters and expressed as a percentage to the average lumen diameter at rest, which was considered 100% (flow-mediated dilatation percent equals ((vessel diameters reactive hyperaemia minus vessel diameters at rest) multiply by 100) divided by vessel diameters at rest; glyceryltrinitrate percent equals ((vessel diameters after glyceryltrinitrate minus vessel diameters at rest) multiply by 100) divided by vessel diameters at rest). Arterial blood flow was measured as Doppler flow velocity multiplied by the cross-sectional area ($\pi \times \text{radius}^2$).

Statistics

All analyses were performed by the computerised SPSS 11.5 package program (Statistical Package for Social Sciences, SPSS Inc.). Results are given as mean ± standard deviation. Student's t test or one-way Analysis of variance, as appropriate, was used to compare continuous variables, and the chi-square test was used to compare proportions among groups. Linear regression analysis with Pearson's coefficients was used to assess the strength of association between variables and p-value less than 0.05 was considered statistically significant.

Results

Basic characteristics of subjects

The study population consists of 140 healthy subjects (94 men, mean age: 22.9 plus or minus 1.8 years). The characteristics of the subjects are summarised in Table 1. There was no statistically important difference among offspring of hypertensive parents and offspring of hypertensive parents (p greater than 0.05), according to age, gender, height, weight, body mass index, smoking habits, systolic blood pressure, diastolic blood pressure, and pulse pressure. Plasma levels of total cholesterol, triglycerides, high-density lipoprotein cholesterol, and fasting glucose were also similar between the two groups.

Echocardiographic parameters

Table 1 outlines echocardiographic data of the groups. We compared aortic elastic parameters between offspring of hypertensive parents and normotensive parents. The systolic and diastolic diameters of the aorta were similar between two groups, but the aortic distensibility and strain were significantly lower in offspring of hypertensive parents than in offspring of normotensive parents (p equals 0.01 and 0.013, respectively). However, aortic stiffness index was significantly greater in offspring of hypertensive parents than in controls. Endothelial parameters in groups are shown in Table 1 also. Similarly, baseline artery diameter, hyperaemic percent change in velocity, and glyceryltrinitrate-induced vasodilatation of groups were nearly equal but flow-mediated dilatation was significantly lower in offspring of hypertensive parents than offspring of normotensive parents (p equals 0.009; Fig 1). The age was positively correlated with strain and negatively correlated with glyceryltrinitrate-induced vasodilatation (r equals 0.17, p equals 0.04 and r equals −0.18, p equals 0.03, respectively). In addition, we found a significant positive correlation between body mass index and aortic stiffness index, but negative correlation with aortic distensibility (radius equals 0.22, p equals 0.008 and radius equals −0.20, p equals 0.01, respectively).

Reproducibility of the echocardiographic measurements

The intraobserver regression coefficient was 0.87 (p equals 0.001) and the interobserver regression coefficient was 0.85 (p equals 0.001) for all echocardiographic measurements.

Discussion

The main finding of the present study was that the offspring with parental history of arterial hypertension had decreased endothelial-dependent vasodilation and higher aortic stiffness indices compared with offspring with normotensive parents, although they had similar systolic blood pressure, diastolic blood pressure, and pulse pressure in the absence of other classic vascular risk factors.

Development of new non-invasive tools for detection of subclinical atherosclerosis, such as measurement of aortic stiffness and brachial artery flow-mediated vasodilatation, has added a new

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Table 1. Comparison between offspring of hypertensive parents and offspring of normotensive parents.

	Offspring of hypertensive parents (n = 70)	Offspring of normotensive parents (n = 70)	p-value
Demographic characteristics			
Age (years)	22.9 ± 2.2	22.8 ± 1.4	0.6
Gender (male/female)	46/24	48/22	0.85
Weight (kg)	63.2 ± 10	64.9 ± 10.6	0.34
Height (cm)	171 ± 9.1	172 ± 8.7	0.74
BMI (kg/m^2)	21.4 ± 2.1	21.9 ± 2.2	0.22
Smoking (%)	8.6	5.7	0.46
SBP (mmHg)	114 ± 7.4	114.3 ± 7.5	0.78
DBP (mmHg)	73.1 ± 4.9	72.9 ± 4.9	0.83
Pulse pressure	42.7 ± 5.4	41.7 ± 6	0.28
Blood samples			
Total cholesterol (mg/dl)	166.7 ± 31.9	157.9 ± 38.1	0.14
Triglycerides (mg/dl)	85.6 ± 22.3	86.2 ± 18.9	0.81
HDL-c (mg/dl)	46.1 ± 11.3	45.8 ± 10.6	0.91
Fasting serum glucose (mg/dl)	79.2 ± 9.5	79.5 ± 9.1	0.83
Endothelial parameters			
Baseline artery diameter (mm)	4.33 ± 0.68	4.32 ± 0.67	0.89
Hyperaemia (% change in velocity)	412.2 ± 44.5	424.2 ± 52.7	0.8
FMD (%)	5.94 ± 1.6	7.2 ± 3.6	**0.009**
GTN-induced dilatation (%)	14.2 ± 0.8	14.3 ± 0.9	0.7
Aortic elastic parameters			
Systolic diameter (cm)	3.22 ± 0.11	3.26 ± 0.15	0.11
Diastolic diameter (cm)	2.93 ± 0.10	2.95 ± 0.14	0.24
Distensibility ($cm^2/dyn/10^6$)	4.81 ± 2.21	5.79 ± 2.18	**0.01**
Strain (%)	10 ± 4	11.8 ± 4.3	**0.013**
Stiffness index	5.96 ± 2.29	4.85 ± 1.4	**0.001**

BMI = body mass index; DBP = diastolic blood pressure; FMD = flow-mediated dilatation; GTN = glyceryltrinitrate; HDL-c = high-density lipoprotein cholesterol; SBP = systolic blood pressure
Bold values = p-value < 0.05 considered significant

dimension to cardiovascular research and clinical cardiology practice. Our study suggests that offspring of hypertensive parents are associated with impaired endothelial-dependent vasodilatation, even in the absence of hypertension or other chronic disease. These results are corroborated by the finding of the current study suggesting that flow-mediated dilation in large arteries significantly deteriorates with a parental history of hypertension, whereas glyceryltrinitrate-induced vasodilation appears unrelated to the history of parental hypertension. Owing to the fact that flow-mediated dilatation depends to a high extent on the endothelial generation of nitric oxide, whereas glyceryltrinitrate-induced dilation primarily reflects endothelium-independent dilatory function, our findings suggest that the nitric oxide-dependent dilatory capacity of the arterial wall decreases with history of parental hypertension.[15] To the best of our knowledge, this study is the first to investigate endothelial functions and aortic elastic properties in offspring of hypertensive parents.

Flow-mediated brachial artery reactivity is impaired in persons with overt atherosclerosis and in asymptomatic persons with risk factors for coronary disease.[16,17] In the current study, however, subjects with history of any of these factors were excluded. Statistical control of remaining variability in blood pressure or body mass index had no effect on the relationship between the history of parental hypertension, aortic elastic properties, and flow-mediated dilatation. Therefore, it may be concluded that the history of parental hypertension duration may be an independent predictor of impaired endothelial function and aortic elastic properties in healthy subjects with a parental history of hypertension. Moreover, because reduced flow-mediated dilatation has been suggested as an early event in the development of atherosclerosis, it may be speculated that endothelial dysfunction is a physiologic or epidemiologic co-factor behind the atherosclerotic structural lesions at an early age.[9,17]

Changes in the elastic properties of the aorta are associated with coronary artery disease.[12,18] It has been demonstrated that increased aortic stiffness and decreased distensibility, which indicate impairment in the elastic structure of the aorta, are associated with coronary artery disease and its risk factors.[19–21] Aortic stiffness has been shown to have good correlation with cardiovascular end points.[22] Our study showed that the aortic stiffness index

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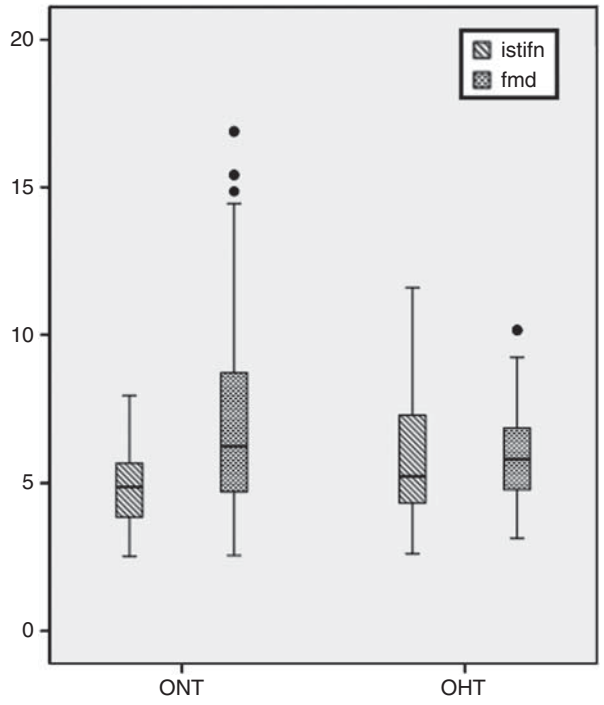

Figure 1.
Box plot graph for the flow-mediated dilatation and aortic stiffness index in the offspring of hypertensive and normotensive parents. ONT = offspring of normotensive parents; OHT = offspring of hypertensive parents; FMD = flow-mediated dilatation; istifn = aortic stiffness index.

was higher, but aortic distensibility and strain were lower in offspring of hypertensive parents than offspring of hypertensive parents. Similarly, Yasmin et al[23] have shown that the large-artery abnormalities may be present early in offspring of hypertensive parents. However, their study population was different from ours. In the study of Yasmin et al, systolic, diastolic, mean arterial pressures, as well as homocysteine, creatinine, and glucose levels, were higher in offspring of hypertensive parents compared with offspring of hypertensive parents, whereas in our study, groups were very homogeneous and these parameters were similar between groups. In another study, McVeigh et al[24] also demonstrated increased arterial stiffness in young adults (mean age 23.5 years) with persistent high normal blood pressure using the pulse contour analysis technique measured non-invasively. Kucerova et al[25] in a recent study reported that large-artery properties are altered in offspring of hypertensive parents compared with offspring of hypertensive parents, but their findings from that cross-sectional study suggest that the alterations in arterial function in offspring of hypertensive parents are determined mainly by an increased blood pressure and age-related haemodynamic changes.

A reduction in aortic distensibility may worsen the burden of a weakened heart through change in blood pressure. The consequences of aortic stiffening during the ageing process with preserved left ventricular systolic function are higher systolic blood pressure and lower diastolic blood pressure.[26] Aortic stiffness leads to an increased systolic blood pressure and simultaneously a decreased diastolic blood pressure, resulting in wide pulse pressure.[27] Iris et al's[28] study, which demonstrated that elevated systolic and diastolic blood pressure throughout the day and night in offspring of hypertensive parents (mean age 32.8 years) obtained by two 24-hour ambulatory blood pressure sessions (one work day and one off work day), may explain the difference in aortic elastic properties in the two groups despite having similar parameters.

The elastic properties of the aorta and endothelial functions can be affected by risk factors for coronary artery disease, such as hypercholesterolaemia, hypertension, diabetes mellitus, sex, age, and smoking habit. In the present study, all these coronary artery disease risk factors were similar between our groups. However, the findings were retested after adjustment for all coronary artery disease risk factors, considering their possible effects. In conclusion, the level of significance did not change, indicating that our results occurred independently of these risk factors.

Limitations of the study include the relatively small size of study population and limited resolution of the B-mode ultrasonography, which may complicate reliable detection of the diameter changes and measurements of the aortic diameters. Another potential limitation is the fact that this study is a cross-sectional hypothesis-generating study rather than a prospective study; thus, clinical implications of the present study can only be hypothetical.

To conclude with, we observed blunted endothelium-dependent dilatation and aortic stiffness in offspring of hypertensive parents compared with offspring of hypertensive parents. This is evident in the absence of overt hypertension and other diseases, suggesting that parental history of hypertension is a risk for subclinical atherosclerosis and it may contribute to the progression to hypertension and overt atherosclerosis in later life.

References

1. Meaney E, Samaniego V, Alva F, et al. Increased arterial stiffness in children with parental history of hypertension. Pediatr Cardiol 1999; 20: 203–205.
2. Celentano A, Galderisi M, Garofalo M, et al. Blood pressure and cardiac morphology in young children of hypertensive subjects. J Hypertens 1998; 6: 107–109.
3. Widgren BR, Berglund G, Wikstrand J, Anderson OK. Reduced venous compliance in normotensive men with positive family histories of hypertension. J Hypertens 1992; 10: 459–465.

https://doi.org/10.1017/S104795111200008X Published online by Cambridge University Press

4. Blankenhorn DH, Kramsch DM. Reversal of atherosis and sclerosis. The two components of atherosclerosis. Circulation 1989; 79: 1–7.
5. Frohlich ED. Target organ involvement in hypertension: a realistic promise of prevention and reversal. Med Clin North Am 2004; 88: 209–221.
6. Laurent S, Boutouyrie P, Asmar R, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension 2001; 37: 1236–1241.
7. Blacher J, Guerin A, Marchais SJ, et al. Impact of aortic stiffness on survival in end-stage renal disease. Circulation 1999; 99: 2434–2439.
8. Meaume S, Benetos A, Henry OF, et al. Aortic pulse wave velocity predicts cardiovascular mortality in subjects >70 years of age. Arterioscler Thromb Vasc Biol 2001; 21: 2046–2050.
9. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet 1992; 340: 1111–1115.
10. Stout M. Flow-mediated dilatation: a review of techniques and applications. Echocardiography 2009; 26: 832–841.
11. Celermajer DS, Sorensen KE, Georgakopoulos D, et al. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. Circulation 1993; 88: 2149–2155.
12. Stefanadis C, Stratos C, Boudoulas H, et al. Distensibility of the ascending aorta: comparison of invasive and non-invasive techniques in healthy men and in men with coronary artery disease. Eur Heart J 1990; 11: 990–996.
13. Joannides R, Haefeli WE, Linder L, et al. Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries in vivo. Circulation 1995; 91: 1314–1319.
14. Ludmer PL, Selwyn AP, Shook TL. Paradoxical vasoconstriction induced by acetylcholine in atherosclerotic coronary arteries. N Engl J Med 1986; 315: 1046–1051.
15. Busse R, Fleming I. Regulation and functional consequences of endothelial nitric oxide formation. Ann Med 1995; 27: 331–340.
16. Teragawa H, Kato M, Kurokawa J, et al. Usefulness of flow-mediated dilation of the brachial artery and/or the intima-media thickness of the carotid artery in predicting coronary narrowing in patients suspected of having coronary artery disease. Am J Cardiol 2001; 88: 1147–1151.
17. Hashimoto M, Eto M, Akishita M, et al. Correlation between flow-mediated vasodilatation of the brachial artery and intima-media thickness in the carotid artery in men. Arterioscler Thromb Vasc Biol 1999; 19: 2795–2800.
18. Stefanadis C, Wooley CF, Bush CA, et al. Aortic distensibility abnormalities in coronary artery disease. Am J Cardiol 1987; 59: 1300–1304.
19. Pitsavos C, Toutouzas K, Dernellis J, et al. Aortic stiffness in young patients with heterozygous familial hypercholesterolemia. Am Heart J 1998; 135: 604–648.
20. Lehmann ED, Gosling RG, Sonksen PH. Arterial wall compliance in diabetes. Diabet Med 1992; 9: 114–119.
21. Stefanadis C, Tsiamis E, Vlachopoulos C, et al. Unfavorable effect of smoking on the elastic properties of the human aorta. Circulation 1997; 95: 31–38.
22. Nurnberger J, Keflioglu-Scheiber A, Opazo Saez AM, et al. Augmentation index is associated with cardiovascular risk. J Hypertens 2002; 20: 2407–2414.
23. Yasmin, Falzone R, Brown MJ. Determinants of arterial stiffness in offspring of families with essential hypertension. Am J Hypertens 2004; 17 4: 292–298.
24. McVeigh GE, Donahue RP, Prineas RJ, et al. Young adults with persistent high-normal BP have decreased arterial compliance (Abstr). Circulation 1995; 92: 3577.
25. Kucerová J, Filipovský J, Staessen JA, et al. Arterial characteristics in normotensive offspring of parents with or without a history of hypertension. Am J Hypertens 2006; 19 (3): 264–269.
26. Nichols WW, Orourke MF. Vascular impedance. In: McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles, 4th edn. Edward Arnold, London, UK, 1998, 54–97, 243–283, 347–395.
27. London GM, Guerin AP. Influence of arterial pulse and reflected waves on blood pressure and cardiac function. Am Heart J 1999; 138 (2): 220–224.
28. Goldstein IB, Shapiro D, Guthrie D. Ambulatory blood pressure and family history of hypertension in healthy men and women. Am J Hypertens 2006; 19 (5): 486–491.

https://doi.org/10.1017/S104795111200008X Published online by Cambridge University Press