SCIENTIFIC LETTER

Increased carotid intima-media thickness in healthy young subjects with a parental history of hypertension (parental hypertension and vascular health)

Sergio Cuomo, Giovanni Gaeta, Pasquale Guarini, Georgio Tudisca, Mario De Michele, M Gene Bond, Maurizio Trevisan

Heart 2007;93:368–369. doi: 10.1136/hrt.2006.091769

Preclinical abnormalities are detectable in young normotensive individuals with a positive parental history of hypertension (PHH).¹ Increased carotid intima-media thickness (IMT) is considered an early and valuable predictor of atherosclerotic disease; however, information on the effect of PHH on potential vascular structural abnormalities in young normotensive healthy subjects is limited.

The aim of this study was to evaluate the presence of carotid structural differences in normotensive young adults and children with and without PHH.

METHODS

The study population comprised 29 cases (healthy subjects with PHH, 45% males, mean (SD) age 23 (5) years) consecutively recruited among the offspring (age 11–30 years) of patients with essential hypertension who had been followed at the Hypertension Outpatient Clinic of the Department of Cardiology, Cardarelli Hospital of Naples, Italy. Parental hypertension was defined as a blood pressure of at least 140/90 mm Hg, measured on three different days in the supine position by sphygmomanometry. The control group consisted of 29 age-matched (+1 year) and sex-matched healthy subjects without PHH (parents not on antihypertensive drugs and blood pressure values <140/90 mm Hg at repeated examinations); they were offspring of patients admitted to the same hospital for a wide spectrum of acute illnesses unrelated to essential hypertension or hospital workers.

To minimise the confounding effects of other known cardiovascular risk factors, we excluded individuals with a parental history of coronary, cerebral or peripheral arterial disease and/or diabetes mellitus. The study protocol was approved by the local ethics committee and written informed consent was obtained from each subject and/or their parents. All participants were given a questionnaire to obtain information about smoking, history of diabetes, hypertension, family history of vascular disease and diabetes. Body mass index (BMI) was calculated as the ratio of weight in kilograms to height in metres squared. Blood pressure in the offspring was measured twice, 1 min apart, after sitting quietly for 5 min.

Venous blood samples were collected after 14 h of fasting to determine concentrations of total HDL and LDL cholesterol, triglycerides, Apo A-I, Apo-B and lipoprotein(a).

High-resolution carotid ultrasonographic studies were performed with a Hewlett Packard Sonos 2000, with a 7.5-MHz transducer (Hewlett-Packard, Seattle, USA). The study protocol involved scanning the far wall of common carotid arteries in the distal 1.0 cm. The crest at the origin of the bifurcation was used as an anatomical landmark to identify the segment to be visualised. In each examination, the sonographer used three

different scanning angles (anterior, lateral and posterior) to record the greatest IMT. One expert reader, unaware of the subject's family history, reviewed the scans and performed IMT quantitative measurements using the digital caliper of the ultrasound machine. For each side, three different end-diastolic frames that contained the maximum IMT were selected.

The three calculated values were averaged to give the mean common carotid IMT for each side and both sides combined. The mean (SD) absolute difference in IMT in 25 healthy young subjects in whom the same observer performed two carotid artery examinations 7 days apart was 0.02 (0.03) mm (coefficient of variation, 2.6%).

Values are expressed as mean (SD). Comparisons were made using paired Student's *t* tests and χ^2 analysis for continuous and categorical variables. Pearson's correlation coefficients were calculated to assess the univariate association between variables. Odds ratios (with 95% confidence intervals) for PHH were determined by conditional logistic regression analysis.

RESULTS

As expected, age and sex were comparable between subjects with and without PHH. There was no significant difference in blood pressure, lipids, apolipoproteins, lipoprotein (a), smoking and BMI between the two groups. Subjects with PHH had a greater IMT of the right (0.48 (0.1) mm vs 0.42 (0.072) mm; *p* = 0.011) and left common carotid artery (0.49 (0.108) mm vs 0.42 (0.089) mm; *p* = 0.024) than subjects without PHH. No difference was observed for carotid lumen diameter.

Table 1 summarises the results of the logistic regression analyses with PHH as dependent variable: two models are presented, with and without BMI; additional variables were included because of their established association with carotid IMT and coronary heart disease. Mean carotid IMT was significantly associated with PHH, independent of Apo-B, lipoprotein (a), blood pressure and smoking; BMI, while slightly reducing the statistical significance, does not account for the observed differences in carotid IMT between participants with and without PHH.

DISCUSSION

Our results show that healthy young offspring of parents with arterial hypertension have significantly increased carotid IMT compared with the offspring of normotensive parents. Statistical significance is retained even after adjustment for a range of confounders, suggesting an independent association between PHH and carotid thickening.

Abbreviations: BMI, body mass index; IMT, intima-media thickness; Lp(a), lipoprotein(a); PHH, parental history of hypertension

Table 1 Odds ratios from conditional logistic regression analysis for parental history of hypertension

Independent variable	OR (95% CI)	p Value
Multivariate model		
Mean carotid IMT	2.48 (1.05 to 5.83)	0.038
Apo-B	1.04 (0.46 to 2.35)	0.931
Systolic blood pressure	1.90 (0.75 to 4.78)	0.175
Log Lp(a)	1.52 (0.76 to 3.03)	0.232
Smoking	1.02 (0.17 to 6.16)	0.987
Multivariate model		
Mean carotid IMT	2.43 (1.02 to 5.83)	0.046
Apo-B	0.97 (0.41 to 2.27)	0.943
Systolic blood pressure	1.99 (0.74 to 5.36)	0.173
Log Lp(a)	1.84 (0.85 to 4.01)	0.123
Smoking	0.74 (0.10 to 5.56)	0.768
BMI	2.39 (0.58 to 9.89)	0.231

BMI, body mass index; IMT, intima-media thickness; Lp(a), lipoprotein (a).

One unit is a change of one standard deviation. The mean value of combined sides was used for carotid IMT.

The role of genes and shared environment in determining the observed differences needs to be clarified. Two previously published studies^{2,3} have shown the heritability of carotid IMT. The study by Xiang *et al*² showed that (in Latino families with a hypertensive proband) heritability was particularly evident in younger rather than in older family members; these authors interpreted their findings as an indication that acquired factors contribute progressively more to IMT variability with the advancement of age. The Erasmus Rucphen Family Study has recently confirmed the heritability of carotid IMT in 930 individuals connected in a single pedigree from an isolated population.³

The temporal sequence between the observed vascular and cardiac differences and blood pressure in individuals with predisposition to hypertension remains to be fully clarified. Traditionally, it has been considered that these abnormalities were the result of an early action of raised blood pressure and other risk factors. Our findings support the notion that arterial involvement may precede the increase in blood pressure; this notion is supported by findings from other investigations that have indicated that cardiac abnormalities observed in individuals with PHH may as well precede a considerable increase in blood pressure.^{4,5} The important question is whether these observed vascular abnormalities are the result of subtle differences in blood pressure and other factors or whether the vascular abnormalities observed are an integral part of the mechanisms responsible for the increase in blood pressure and increased cardiovascular risk.

The small number of individuals included in our study and the hospital-based nature of our sample are potential important limitations. In addition, we did not measure ambulatory blood pressure or glucose and insulin metabolism, and therefore cannot exclude the possibility that these factors (or other factors not included in our study design) may be linked to the observed differences in carotid IMT between the two groups of participants.

Our data show that PHH is associated with a modest but considerable increase in carotid IMT in healthy young individuals. Further studies are needed to elucidate the biological mechanisms underlying this association and the possible implications for preventive measures.

Authors' affiliations

Sergio Cuomo, Department of Cardiology, SUN, Monaldi Hospital, and Cardiology, Cardarelli Hospital, Napoli, Italy

Giovanni Gaeta, Giorgio Tudisca, Department of Cardiology and Clinical Analysis Laboratory, Cardarelli Hospital, Napoli, Italy

Pasquale Guarini, Department of Cardiology, Clinica Villa dei Fiori, Acerra, Italy

Mario De Michele, Department of Cardiology, S G Moscati Hospital, Aversa, Italy

M Gene Bond, Division of Vascular Ultrasound Research, Wake Forest University, Winston Salem, North Carolina, USA

Maurizio Trevisan, University at Buffalo, School of Public Health and Health Professions, Buffalo, New York, USA

Funding: None.

Competing interests: None.

Disclaimers: None.

The study protocol was approved by the local committee on ethical practice (Antonio Cardarelli Hospital Ethics Committee, Azienda Ospedaliera di Rilievo Nazionale A Cardarelli, Via A Cardarelli 9, 80131 Napoli, Italy). Written informed consent was obtained from each subject and/or their parents.

Correspondence to: Dr M Trevisan, University at Buffalo, School of Public Health and Health Professions, Kimball Tower, Room 435, 3435 Main Street, Buffalo, NY 14214-2034, USA; trevisan@buffalo.edu

Accepted 5 July 2006

REFERENCES

- Dependence of morphological changes of the carotid arteries on essential hypertension and accompanying risk factors. *Int Angiol* 2002;**21**:70-7.
- Xiang AH, Azen SP, Buchanan TA, *et al*. Heritability of subclinical atherosclerosis in Latino families ascertained through a hypertensive parent. *Arterioscler Thromb Vasc Biol* 2002;**22**:843-8.
- Sayed-Tabatabaei FA, van Rijn MJE, Schut AFC, *et al*. Heritability of the function and structure of the arterial wall. Findings of the Erasmus Rucphen Family (ERF) Study. *Stroke* 2005;**36**:2351-6.
- Mo R, Nordrehaug JE, Omvik P, *et al*. The Bergen Blood Pressure Study: prehypertensive changes in cardiac structure and function in offspring of hypertensive families. *Blood Press* 1995;**4**:16-22.
- Grandi AM, Poletti L, Tettamanti F, *et al*. Left ventricular anatomy and function in normotensive young adults with hypertensive parents. Study at rest and during handgrip. *Am J Hypertens* 1995;**8**:154-9.