

## SCIENTIFIC LETTER

## Carotid intima–media thickness in post-coarctectomy patients with exercise induced hypertension

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The significance of exercise blood pressure in post-coarctectomy patients and its relation to clinical outcome and organ damage is still unknown. Several authors have suggested that patients with exercise induced hypertension might be amenable to antihypertensive medication or limitation of strenuous physical activity.<sup>1</sup> However, recently Swan and colleagues<sup>2</sup> discouraged the use of exercise testing for the assessment of blood pressure profiles in these patients. Intima–media thickness (IMT) is nowadays considered a validated and reproducible end point for atherosclerosis.<sup>3</sup> The aim of the present study was to investigate the relation between exercise induced hypertension and carotid IMT in adult post-coarctectomy patients.

## METHODS

From 2001 until 2002, all 137 consecutive adult post-coarctectomy patients (89 male) from our tertiary referral centre participated in this study. The protocol was approved by the institutional review committee and informed consent was obtained from all participants. In all patients significant residual aortic stenosis or re-coarctation had been ruled out by magnetic resonance imaging within two years of the start of this study. Risk factors for atherosclerosis, such as smoking and serum lipids, were assessed. All patients underwent 24 hour ambulatory blood pressure monitoring in the right arm. Patients were considered hypertensive when mean daytime systolic blood pressure was  $\geq 140$  mm Hg and/or diastolic blood pressure was  $\geq 90$  mm Hg. B mode ultrasound images of the right and left common carotid arteries were acquired according to a standardised protocol. Measurements were summarised in one variable. All patients underwent a maximal, symptom limited, standardised treadmill exercise test following the Bruce protocol. Blood pressure was measured in the right arm at regular intervals of three minutes by conventional sphygmomanometry. Patients were considered to have exercise induced hypertension when mean daytime systolic blood pressure was  $< 140$  mm Hg and peak exercise systolic blood pressure  $\geq 200$  mm Hg.

Comparisons between groups of continuous variables were made by two sided Student's *t* test or the Mann-Whitney *U* test when applicable. Multivariate stepwise regression analyses were used to identify independent predictors of common carotid IMT. Variables included in this analysis were: body mass index (BMI), age, age at repair, sex, mean daytime systolic pressure, exercise induced hypertension (dichotomous variable), cholesterol, and history of smoking. Multivariate regression analyses were performed separately for the non-hypertensive post-coarctectomy patients, and for all subjects combined, with a dummy variable for a history of hypertension. Differences were considered significant at  $p < 0.05$ . Data analysis was performed using the SPSS 10.1 statistical package.

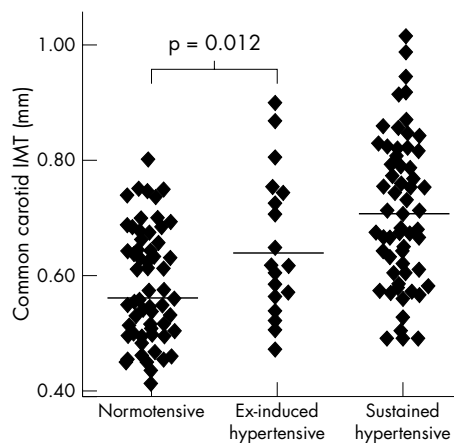


Figure 1 Common carotid artery intima–media thickness (IMT) in post-coarctectomy patients.

## RESULTS

Mean age of the study subjects was 31.0 years (range 17–74 years) and mean age at repair 7.8 years (range 0.01–46 years). Twenty of the 137 adult post-coarctectomy patients were repaired before the age of 1 year. Seven patients had coarctation repair before the age of 1 month. Repair was performed by resection and end-to-end anastomosis in 100 patients (73%). None of the patients had major co-existing congenital cardiac anomalies.

Of the 137 patients, 59 (43%) patients had hypertension. Twenty eight patients had a history of hypertension and received antihypertensive medication. Eighteen patients (13%) had exercise induced hypertension. BMI, age, age at surgery, lipids, and history of smoking of the patients with exercise induced hypertension, were not significantly different from the normotensive patients. Patients with exercise-induced hypertension had significantly higher mean daytime systolic blood pressure compared to normotensive patients (mean (SD) 136 (6) mm Hg *v* 128 (7) mm Hg,  $p = 0.006$ ).

IMT of the common carotid artery was significantly increased in the exercise induced hypertensive patients compared to the normotensive patients (0.564 (0.095) mm *v* 0.635 (0.124) mm;  $p = 0.012$ ) (fig 1). The sustained hypertensive patients were significantly older than the other patients. IMT of the common carotid artery was significantly increased in patients with sustained hypertension compared to normotensive patients (0.700 (0.131) mm *v* 0.564 (0.095) mm;  $p < 0.001$ ). There was no significant difference in common carotid IMT between the sustained and exercise induced hypertensive patients (0.700 (0.131) mm *v* 0.635 (0.124) mm;  $p = 0.063$ ).

The variables associated with common carotid IMT in the univariate analysis were compared using multivariate

stepwise regression analysis for all subjects combined. Age ( $p < 0.0001$ ) and history of hypertension ( $p = 0.020$ ) were independently associated with common carotid artery IMT. In the 78 patients with normal ambulatory blood pressure readings, BMI ( $p = 0.041$ ), age ( $p = 0.012$ ), and the presence of exercise induced hypertension ( $p = 0.014$ ) were all independent clinical predictors of common carotid IMT. Age at repair in this population, which had a small number of patients with neonatal repair, was not a significant predictor of common carotid IMT.

## DISCUSSION

Our results demonstrate that exercise induced hypertension in post-coarctectomy patients is an independent predictor of common carotid IMT. Structural vascular abnormalities and alterations in vascular reactivity are thought to be causative factors in the development of raised blood pressure in post-coarctectomy patients at rest and during exercise.<sup>4</sup> These abnormalities are probably caused by a developmental defect of the aortic wall and by the damaging effects of pre- and postoperative hypertension.

Studies in normal individuals with exercise induced hypertension or high to normal blood pressures have shown an increased risk of developing established hypertension in later years. Our group has demonstrated a clear association between exercise systolic blood pressure and systolic ambulatory blood pressure in post-coarctectomy patients,<sup>5</sup> which suggests that these patients are also at increased risk of future sustained hypertension. Hypertension functions as cause and effect; untreated high blood pressure contributes to increased arterial stiffness, whereas arterial stiffness, in turn, increases systolic blood pressure. The increased carotid IMT in post-coarctectomy patients with exercise induced hypertension may be the cause and result of the higher

ambulatory blood pressures. These findings probably indicate an additional risk of exercise induced hypertension in post-coarctectomy patients, who already have a high burden of vascular and myocardial damage. Medical treatment might prevent additional damage and delay the onset of sustained hypertension in these patients; however, a large intervention trial is needed to confirm the benefit of medical treatment on the long term outcome of post-coarctectomy patients.

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## REFERENCES

- 1 Sigurdardottir LY, Helgason H. Exercise-induced hypertension after corrective surgery for coarctation of the aorta. *Pediatr Cardiol* 1996;**17**:301-7.
- 2 Swan L, Goyal S, Hsia C, et al. Exercise systolic blood pressure are of questionable value in the assessment of the adult with a previous coarctation repair. *Heart* 2003;**89**:189-92.
- 3 De Groot E, Hovingh GK, Wiegman A, et al. Measurement of arterial wall thickness as a surrogate marker for atherosclerosis. *Circulation* 2004;**109**(suppl III):33-8.
- 4 De Divitiis M, Pilla C, Kattenhorn M, et al. Vascular dysfunction after repair of coarctation of the aorta. Impact of early surgery. *Circulation* 2001;**104**(suppl I):165-70.
- 5 Vriend JWJ, Van Montfrans GA, Romkes HH, et al. Relation between exercise-induced hypertension and sustained hypertension in adult patients after successful repair of aortic coarctation. *J Hypertens* 2004;**22**:501-9.

## FROM BMJ JOURNALS

### Work related stressful life events and the risk of myocardial infarction. Case-control and case-crossover analyses within the Stockholm heart epidemiology programme (SHEEP)

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Please visit the Heart website [www.heartjnl.com] for a link to the full text of this article.

**Study objectives:** Recent changes in labour market conditions and in the organisation of work in developed societies have increased exposure to work related stress. The question is whether this also implies an increased risk of myocardial infarction, either through the triggering effect of acute stress, or through accumulation of stress over several months.

**Design:** A case-control and a case-crossover study design was applied.

**Setting:** The Stockholm heart epidemiology programme (SHEEP), in Stockholm County during 1992 to 1994.

**Participants:** Patients with a first episode of non-fatal acute myocardial infarction, a total of 1381 men and women, responded to questionnaires and participated in interviews and health examinations.

**Main results:** The case-crossover analysis showed triggering effects of sudden, short term situations of increased work load or work competition. Having "had a high pressure deadline at work" entailed a sixfold increase in risk of myocardial infarction (OR = 6.0 95% CI (1.8 to 20.4)) during the next 24 hours. The importance of work related life events as risk factors for myocardial infarction was supported by the case-control analysis. However, no support was found for the hypothesis that an accumulation of stressful life events over a period of 12 months increases the risk of myocardial infarction.

**Conclusion:** Specific work related stressful life events seem to be potential triggers of the onset of myocardial infarction.

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