COMMENTARY

Aerobic physical exercise and arterial de-stiffening: a recipe for vascular rejuvenation?

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Substantial evidence indicates that physical activity, exercise training and overall cardiorespiratory fitness have a favorable impact on cardiovascular health.¹ Over the short term, physical activity exerts multiple beneficial effects on all major modifiable cardiovascular risk factors, including blood pressure (BP), obesity, glucose and lipid levels, and on a variety of other conditions, such as anxiety, depression, cancer and pain control.¹ These short-term benefits translate into significant long-term reductions in the risk of cardiovascular events and mortality.^{2,3}

Chronic dynamic aerobic exercise is an established measure for reducing office and 24-h BP, although its net effects on BP are rather modest. Some postulated mechanisms through which exercise may improve cardiovascular hemodynamics include heart-rate lowering, increased cardiac output and stroke volume and a reduced total peripheral resistance, the latter mediated by a number of different mechanisms including decreased norepinephrine and renin production.⁴

An additional potential mechanism through which aerobic physical exercise may reduce BP is by reducing aortic stiffness. Increased vascular stiffness is increasingly believed to have a key role in cardiovascular disease through amplified pulse pressure, reduced pressure buffering and increased propagation of ventricular tension,⁵ and is a primary marker of cardiovascular disease risk.⁶ A number of observational studies^{7–10} have generally shown an inverse correlation between levels of physical exercise and carotid-femoral pulse wave velocity

(cfPWV) at all ages and for every amount of exercise workload, even after accounting for the effects of several confounders. In a sample of 109 unfit elderly individuals, Gando *et al.*⁹ found that cfPWV had an inverse association with the time spent in light physical activities, such as house work and other unstructured physical exercise. These results suggest that longer time spent in light physical activity is associated with an attenuation of arterial stiffening in unfit people.

Cross-sectional studies, however, demonstrate associations but may not establish cause-and-effect relationships. The proof of a causal link between exercise and arterial de-stiffening relies upon prospective studies. A few intervention studies carried out in small groups of subjects have suggested that aerobic exercise may reduce aortic stiffness^{11–15} (Table 1). In the present issue of *Hypertension Research*, Fantin *et al.*¹⁶ further explore the above area in a prospectively designed study. They evaluated 21 normotensive or hypertensive community-dwelling women aged between 60 and 80 years with no overt cardiovascular disease, who were involved in a light-to-moderate aerobic exercise program for 6 months. Aerobic exercise consisted in a supervised brisk walking at the 75% of maximum heart rate twice a week. At baseline and follow-up, the study subjects underwent a comprehensive clinical evaluation including measurement of aortic (carotid-femoral) and upper-limb (carotid-radial) vascular stiffness with the Complior device, with the time delay between carotid and femoral pulse waves calculated by the foot-to-foot method. A fairly good rate of attendance at walking session was observed throughout the study, with 20% of drop-out rate in the first trimester and a further 15% in the second trimester.

In the whole group, cfPWV was reduced by about 6% at 6 months (12.1 vs. 11.3 m s⁻¹, $P = 0.02$), whereas carotid-radial PWV was not influenced by exercise (9.2 vs. 9.1 m s⁻¹, $P = 0.75$). Exercise was also associated with reduction in waist circumference, abdominal sagittal diameter and serum triglycerides. No significant changes in BP and HR were observed and changes in cfPWV were independent of changes in BP, heart rate and adiposity measures observed between baseline and follow-up. As expected, hypertensive subjects (45% of the total sample) had a higher baseline cfPWV than normotensives (13.2 vs. 11.7, $P = 0.05$). They also showed a more pronounced reduction in cfPWV after training (12.8 vs. 11.9, $P = 0.02$) than normotensives (11.7 vs. 11.3, $P = 0.15$), although the hypothesis of a greater effect of exercise on cfPWV in hypertensive than in normotensive subjects was not tested formally, and the possibility of a 'regression toward the mean' effect was not considered.

The present study adds to a number of investigations, which have consistently shown a reduction in cfPWV over the short term, following different lifestyle interventions, including not only physical exercise^{11–16} but also weight loss, smoking cessation and salt intake restriction^{17–25} (Table 1).

Which potential mechanisms may explain the observed short-time reduction in cfPWV after physical exercise? Arterial stiffness is a measure of the nonlinear relationship between wall stress and deformability, and reflects the increase of arterial pressure at increasing volume. cfPWV is a widely used surrogate measure of arterial stiffness, which expresses the speed of pressure wave along the carotid-to-femoral path and is inversely related to elastic modulus and distensibility. cfPWV increases exponentially with age and

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Table 1 Change in carotid-femoral pulse wave velocity (cfPWV) after non-drug interventions in prospective studies

Population	n	Intervention	Duration	cfPWV change, % (baseline vs. post-intervention, ms^{-1})	Reference
<i>Aerobic exercise</i>					
Young sedentary	10	Aerobic exercise (70% maximal HR)	8 weeks	−5% (5.8 vs. 5.5)*	Kakiyama <i>et al.</i> ¹¹
Pre-HTN or HTN	15	Aerobic exercise (65% maximal HR)	4 weeks	−8% (12.1 vs. 11.1)*	Collier <i>et al.</i> ¹²
ESRD under hemodialysis	19	Aerobic exercise	6 months	−11% (10.2 vs. 9.0)**	Toussaint <i>et al.</i> ¹³
HTN	16	Interval exercise (50–80% HR reserve)	16 weeks	−6% (9.4 vs. 8.9)**	Guimarães <i>et al.</i> ¹⁴
Obese with IGT	12	Aerobic exercise (65% maximal HR)	12 weeks	−8% (9.1 vs. 8.4)*	McNeilly <i>et al.</i> ¹⁵
Elderly women	21	Aerobic exercise (75% maximal HR)	6 months	−6% (12.1 vs. 11.3)*	Fantin <i>et al.</i> ¹⁶
<i>Weight loss</i>					
Obese	28	Diet ($n=16$), bariatric surgery ($n=12$)	1 year	−14% (5.8 vs. 5.0)*	Rider <i>et al.</i> ¹⁷
Overweight or obese	25	Diet	12 weeks	−16% (11.6 vs. 9.7)*	Dengo <i>et al.</i> ¹⁸
Obese	12	Diet	12 weeks	−6% (9.8 vs. 9.2)*	Miyaki <i>et al.</i> ¹⁹
Type 2 diabetes	38	Diet	1 year	−7% (7.4 vs. 6.9)*	Barinas-Mitchell <i>et al.</i> ²⁰
Overweight with HTN	55	Diet	3 months	−16% (7.5 vs. 6.3)*	Clifton <i>et al.</i> ²¹
<i>Smoking cessation</i>					
Smokers	37	Counseling + varenicline	12 weeks	−12% (17.7 vs. 15.6)**	Takami and Saito ²²
<i>Salt intake reduction</i>					
Pre-HTN or HTN	35	High vs. low sodium intake	4 weeks	−6% (7.9 vs. 7.4)**	Todd <i>et al.</i> ²³
Untreated mild HTN	169	Sodium vs. placebo intake	6 weeks	−3% (11.5 vs. 11.1)**	He <i>et al.</i> ²⁴
Pre-HTN or HTN post-menopausal women	35	Dietary sodium restriction	3 months	−13% (8.7 vs. 7.6)*	Seals <i>et al.</i> ²⁵

Abbreviations: ESRD, end-stage renal disease; HR, heart rate; HTN, hypertension; IGT, impaired glucose tolerance.

*Brachial-ankle PWV.

* $P<0.05$.** $P<0.01$.

is a well-known measure of aortic ageing.²⁶ Numerous studies have shown that increased cfPWV is the consequence of structural alterations of the aortic wall, such as elastin fatigue, fracture and fragmentation, and increased deposition and cross-linking of matrix collagen fibers. Thus, short-term changes in cfPWV may reflect structural de-stiffening, with breaking of connective tissue cross-linking.

On the other hand, changes in cfPWV may also reflect favorable changes in the functional determinants of stiffness. Although cfPWV is a relatively straightforward and simple measure of aortic stiffness, it may not fully account for the complexity of the physical mechanisms and interactions involved in the determination of aortic compliance. A number of observations challenge the intuitive concept of stiffness as a static phenomenon, in favor of a more comprehensive dynamic view. Several experimental and epidemiological studies showed that arterial stiffness is critically dependent on distending pressure (expressed as mean arterial pressure),^{27,28} as well as on other determinants subjected to physiological variability, such as heart rate, myocardial geometry and strength of contraction, arterial smooth muscle tone, nitric oxide bioavailability and vascular diameter.^{29,30}

More recently, it has been observed that stiffness of a given segment continuously changes over a single cardiac cycle from diastole to systole because of its dependence on instantaneous distending BP.³¹ Aortic stiffness may act both as a determinant and a consequence of the efficiency of the interaction between the heart and arterial system (named ventricular–vascular coupling), in which the left ventricle and peripheral arteries are functionally coupled with large arteries.³² Indeed, ventricular–vascular interactions have an essential role in the responses of the cardiovascular system to stress demands,³³ and the arterial system undergoes structural and functional adaptations to increased stroke volume in fit individuals, including, for instance, increased conduit artery size and increase in total cross-sectional area of resistance arteries.³⁴ Thus, short-term changes in arterial stiffness may reflect the adaptations of the whole cardiovascular system to the hemodynamic changes induced by physical exercise, which are mirrored only in part by changes in BP and heart rate.

The study by Fantin *et al.*¹⁶ has a number of important limitations, including the lack of data on cardiac and peripheral vascular function and arterial wave reflection. Moreover, the absence of a control group

does not allow the authors to draw conclusions about the net effects of aerobic training on vascular stiffness. Despite these shortcomings, the results of the study, in line with previous observations, further reinforce the view that even light physical activity should be recommended at all ages because of its unequivocal favorable cardiovascular effects. However, only a comprehensive investigation of the relationship between exercise-induced changes in arterial stiffness and changes in cardiac and vascular function will allow researchers to clarify the meaning of short-term changes in cfPWV in this setting.

CONFLICT OF INTEREST

The author declares no conflict of interest

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