Cardiorespiratory Fitness, Physical Activity, and Arterial Stiffness

The Northern Ireland Young Hearts Project

Colin A. Boreham, Isabel Ferreira, Jos W. Twisk, Alison M. Gallagher, Maurice J. Savage, Liam J. Murray

Abstract—Poor cardiorespiratory fitness and low physical activity have been identified as determinants of greater arterial stiffness, a mechanism that can partially explain the association of both variables with increased cardiovascular disease. However, the nature of these associations are not clear because cardiorespiratory fitness and physical activity can both mediate and confound the associations of one another with arterial stiffness. This issue was therefore examined in a population-based cohort of young adults. Subjects included 405 young men and women participating in an ongoing longitudinal study, the Northern Ireland Young Hearts Project. Pulse wave velocity was used to determine arterial stiffness in 2 arterial segments (aortoiliac and aortodorsalis pedis) using a noninvasive optical method. Cardiovascular fitness was estimated with a submaximal cycle test of physical work capacity and physical activity was estimated using a modified Baecke questionnaire. Associations were investigated with the use of multiple linear regression models with adjustment for potential confounders and/or intermediate variables. Cardiorespiratory fitness and sports-related physical activity (but not leisure- and work-related physical activity) were inversely associated with arterial stiffness in young adults. The associations between sports-related physical activity and arterial stiffness were strongly mediated by cardiorespiratory fitness, whereas physical activity levels did not disturb the associations between cardiopulmonary fitness and arterial stiffness. These findings suggest that arterial stiffness-related benefits of exercise are most likely to accrue if exercise prescription in young adults targets improvements in cardiorespiratory fitness. (Hypertension. 2004; 44:721-726.)

Key Words: young adults ■ exercise ■ cross-sectional studies ■ epidemiology ■ arteriosclerosis ■ hypertension, arterial

The arterial system is a network of vessels designed to convert the intermittent flow of blood from the heart to a continuous and steady flow across the arterial tree, thereby reducing the afterload imposed to the heart. Alterations to this cushioning function, because of increases in arterial stiffness, lead to systolic hypertension, left ventricular hypertrophy, and impaired coronary perfusion,1–3 thereby increasing cardiovascular risk.4–6 Several risk factors such as aging, obesity, diabetes, dyslipidemia, have been identified as determinants of arterial stiffness.7–14 Other such risk factors include poor cardiorespiratory fitness15–20 and low physical activity.21,22 However, the nature of the associations between cardiorespiratory fitness and physical activity on the one hand and arterial stiffness on the other is not well known. They could both confound and/or mediate the relationships between each other and arterial stiffness or, as has been suggested, physical activity could favorably influence arterial stiffness independently of cardiorespiratory fitness.15,18 In addition, cardiorespiratory fitness and/or physical activity may affect arterial stiffness through a beneficial impact on body composition (ie, less body fat),23–25 which itself is a strong determinant of arterial stiffness in young individuals.7–9

In view of these considerations, we investigated, in a population-based cohort of young adults from Northern Ireland, the associations between cardiorespiratory fitness, physical activity, and arterial stiffness. Associations with stiffness (as estimated by pulse wave velocity [PWV]) of 2 arterial segments (the elastic aortoiliac and the muscular aortodorsalis pedis segments) were investigated.

Methods

Study Population

This study was conducted as part of an ongoing longitudinal study, The Young Hearts (YH) Project, which initially examined the...
prevalence of coronary risk factors in a random sample of young people (n=1015; aged either 12 years or 15 years) in Northern Ireland. Sampling procedures, study design, and response rates of the first 2 screening phases (YH1 and YH2) are described in detail elsewhere.26,27 All subjects in the original cohort were invited to participate in a third screening phase (YH3: October 1997–October 1999) when aged 20 to 25 years. Two hundred and fifty-one men (48.7% of the original male cohort) and 238 women (51.3% of the original female cohort) attended the third phase of the study.28 The present analyses involved 405 subjects (203 women) for whom complete data on arterial stiffness, cardiorespiratory fitness, and physical activity were available at this time point. Table 1 shows the main characteristics of the study population. Each subject provided written informed consent, and the study was approved by the Medical Ethical Committee of the Queen’s University of Belfast.

Cardiorespiratory Fitness and Physical Activity
Cardiorespiratory fitness was measured using a submaximal cycle ergometer test described in detail elsewhere.27 In brief, subjects were seated on a pedal at a steady pace of 70 pedal revolutions/min for the duration of the test, which normally lasted 15 minutes. The workload was increased after each 3-minute period until a heart rate of approximately 170 bpm was achieved. Heart rate was averaged over the last 15 sec of each workload (Polar Vantage heart rate monitor, Polar, Finland). Oxygen uptake was monitored throughout the test using an on-line respiratory gas analyzer (Quinton QMC) and maximal oxygen uptake (VO2max) predicted by extrapolation of VO2 at 170 bpm to the age-adjusted maximal heart rate, and expressed in mL/kg per minute.

Data on frequency, duration, and type of physical activities habitually undertaken were obtained using a modification of the Bauece questionnaire of habitual physical activity which was designed to quantify work, sports, and nonsports leisure activity.29 Work, sports, and nonsports leisure activity scores were calculated based on 5-point Likert scales; these 3 scores were then added to provide a total physical activity score.

Arterial Stiffness
We used a noninvasive optical method to estimate PWV, by determining the transit time (TT) that the wave of dilatation, propagating in the arterial wall as a result of the pressure wave generated by contraction of the left ventricle, took to arrive at a distal site over a known distance.30,31 TT measurements were performed with a photoplethysmographic probe and were triggered by the R-wave of the ECG (in milliseconds). The distance between the sternal notch to the femoral artery and between the sternal notch to the aortoiliac segment was now significant. No significant associations were found between (nonsports) leisure-related physical activity and PWV of the aortodorsalis pedis segment. These associations were only slightly stronger with the muscular segment and were independent of (ie, not confounded nor mediated by) lifestyle variables, body fatness, and physical activity (Table 2).

Potential Confounders/Intermediate Variables
Assessment of body height, weight and skinfolds, blood pressure, lipids and glucose levels, smoking behavior, alcohol consumption, and nutrient intake have been described in detail previously.25,26,28,30

Statistical Analysis
We used multiple linear regression models to investigate the relationship between VO2max and physical activity scores on the one hand (determinants) and PWV of 2 different arterial segments on the other (outcomes). The analyses were performed in several steps based on an initial model which included adjustments for age, sex, mean arterial pressure, and body height and weight (model 1); further adjustments for potential confounders such as smoking status (non-, light-, and heavy-smoker, as determined by the sex-specific median number of cigarettes smoked per day among smokers), alcohol consumption (non-, moderate-, and heavy-drinker, as determined by the sex-specific median number of grams of alcohol consumed per day among drinkers), and intake of fat (as % of total energy intake), and/or intermediate (ie, in the pathway between the determinants and the outcome) variables, such as body fatness (as expressed by the sum of 4 skinfolds) were investigated. Mutual adjustments between VO2max and physical activity were also performed to assess not only the strength of the relationships with arterial stiffness independently of one another, but also their potential confounding/intermediate role in the associations investigated.

After we assessed the main effects, we added interaction terms between our main determinants and sex to the linear regression models. When the probability value of the interaction term was significant (ie, <0.05), stratified analyses were performed and results presented separately for men and women. All analyses were performed with the Statistical Package of Social Sciences, 10.1 for Windows (SPSS Inc).

Results
Cardiorespiratory Fitness and Arterial Stiffness
VO2max was inversely and significantly associated with PWV of both the elastic aortoiliac segment and the muscular aortodorsalis pedis segment. These associations were only slightly stronger with the muscular segment and were independent of (ie, not confounded nor mediated by) lifestyle variables, body fatness, and physical activity (Table 2).

Physical Activity and Arterial Stiffness
Sports-related physical activity score was inversely and significantly associated with PWV of the aortodorsalis pedis segment only (Table 3). Adjustment for other lifestyle variables and body fatness did not attenuate the strength of the latter association, which, however, decreased considerably (≈40%) after further adjustment for VO2max.

Conversely, and in the men only, positive associations were found between (nonsports) leisure-related physical activity and PWV of both arterial segments, though more strongly and significantly with the PWV of the aortoiliac segment only (P=0.001 and P=0.021 for interaction with sex in the associations between leisure-related physical activity and PWV of the aortoiliac and the aortodorsalis pedis segments, respectively). Again, these associations were not attenuated after adjustment for other lifestyle variables and body fatness. Further adjustment for VO2max, however, strengthened the associations so that the association between leisure physical activity and PWV of the aortodorsalis pedis segment was now significant. No significant associations were found between work-related activity and PWV of both segments.

Discussion
The main findings of our study were that cardiorespiratory fitness was inversely associated with arterial stiffness (as measured by PWV). With regard to physical activity levels, only sports-related physical activities were favorably (ie, inversely) associated with arterial stiffness (a phenomenon that was mediated by cardiorespiratory fitness), whereas leisure physical activities, in men only, were adversely (ie, positively) associated with arterial stiffness. All these asso-
ciations were independent of other lifestyle variables and body fatness. This is the first population-based study to report the associations of cardiorespiratory fitness and physical activity (investigating the confounding and/or mediating role of each other in the relationships) with arterial stiffness in the same population. This has eliminated the possibility that differences in results thus obtained, as compared with previous reports, could be attributed to different study design and/or methodologies for measuring arterial properties.

The strong associations between cardiorespiratory fitness and arterial stiffness largely mirror those reported in other population-based studies relating VO2max levels and arterial stiffness in younger\textsuperscript{32} and older adults\textsuperscript{17} as well as in smaller scale studies.\textsuperscript{15,18,19} In addition, several exercise-training studies have shown that improvements in cardiorespiratory fitness are accompanied by beneficial changes in arterial stiffness, both in healthy individuals\textsuperscript{15,18,33} and in heart patients.\textsuperscript{34} However, such exercise needs to be cardiovascular in nature (ie, aerobic, involving large muscle groups) because compelling evidence exists showing that strength (or resistance) training is associated with greater arterial stiffness.\textsuperscript{35–37}

Whether aerobic physical activity has to lead to increases in VO2max to be favorably associated with arterial adaptations is, however, not clear.\textsuperscript{15,18,21,33} Two recent intervention studies have indicated that a 3-month aerobic exercise training program significantly decreased arterial stiffness, arguing that this decrease in arterial stiffness was independent of concomitant increases in VO2max (and beneficial changes in other risk factors).\textsuperscript{15,18} These increases were indeed present in both and were even significant in one of the studies,\textsuperscript{15} but the data to sustain such an argument (ie, the role of increases in physical activity independently of VO2max) were, unfortunately, not shown. In the present study, our statistical analyses models specifically addressed this question. We found that only sports-related activities (eg, jogging, swimming, tennis), which by definition are of higher intensity than those performed in leisure-time (eg, walking, bicycling), were favorably associated with arterial stiffness, an association that

<table>
<thead>
<tr>
<th>Study Variable</th>
<th>Men (n = 202)</th>
<th>Women (n = 203)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td>22.4 (1.6)</td>
<td>22.8 (1.7)</td>
<td>0.034</td>
</tr>
<tr>
<td><strong>Height, cm</strong></td>
<td>178.2 (6.6)</td>
<td>164.5 (6.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>75.6 (11.8)</td>
<td>64.6 (12.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Body mass index, kg/m(^2)</strong></td>
<td>23.8 (3.2)</td>
<td>23.9 (4.3)</td>
<td>NS</td>
</tr>
<tr>
<td><em><em>Sum of 4 skinfolds,</em> mm</em>*</td>
<td>44.5 (18.8)</td>
<td>58.8 (20.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Systolic pressure, mm Hg</strong></td>
<td>118.7 (11.5)</td>
<td>106.7 (10.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Diastolic pressure, mm Hg</strong></td>
<td>76.6 (9.2)</td>
<td>71.1 (9.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Mean arterial pressure, mm Hg</strong></td>
<td>90.6 (8.7)</td>
<td>83.0 (9.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Total cholesterol, mmol/L†</strong></td>
<td>4.49 (0.88)</td>
<td>4.75 (0.88)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>LDL-cholesterol, mmol/L†</strong></td>
<td>2.85 (0.82)</td>
<td>2.92 (0.79)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>HDL-cholesterol, mmol/L†</strong></td>
<td>1.28 (0.29)</td>
<td>1.47 (0.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Triglycerides, mmol/L†</strong></td>
<td>0.82 (0.43)</td>
<td>0.77 (0.42)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Fasting plasma glucose, mmol/L‡</strong></td>
<td>4.47 (0.54)</td>
<td>4.31 (0.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Heart-rate, bpm</strong></td>
<td>71.1 (11.4)</td>
<td>73.8 (10.6)</td>
<td>0.016</td>
</tr>
<tr>
<td><strong>Total energy intake, kcal</strong></td>
<td>3146 (824)</td>
<td>1985 (581)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Fat intake, % total energy intake</strong></td>
<td>32.7 (5.8)</td>
<td>33.1 (6.1)</td>
<td>0.526</td>
</tr>
<tr>
<td><strong>Alcohol drinkers, %</strong></td>
<td>85.6</td>
<td>76.4</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>Alcohol consumption among drinkers, g/day</strong></td>
<td>43 (28–72)</td>
<td>16 (8–26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Smokers, %</strong></td>
<td>36.1</td>
<td>36.0</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Tobacco consumption among smokers, cigarettes/day</strong></td>
<td>10 (10–20)</td>
<td>10 (5–13.5)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>VO2max, mL/kg per minute</strong></td>
<td>38.3 (8.3)</td>
<td>26.9 (5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Sports physical activity score</strong></td>
<td>2.73 (0.81)</td>
<td>2.44 (0.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Works physical activity score</strong></td>
<td>2.81 (0.63)</td>
<td>2.57 (0.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Leisure physical activity score</strong></td>
<td>2.37 (0.67)</td>
<td>2.38 (0.55)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Total physical activity score</strong></td>
<td>7.90 (1.34)</td>
<td>7.40 (1.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>PWV aortoiliac segment, m/s</strong></td>
<td>3.26 (0.49)</td>
<td>2.91 (0.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>PWV aortodorsalis pedis, m/s</strong></td>
<td>5.19 (0.53)</td>
<td>4.74 (0.47)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are means (standard deviations) or medians (interquartile ranges). PWV indicates pulse wave velocity; VO2max, predicted maximal oxygen uptake.

*The 4 skinfolds are biceps, triceps, suprailiac and subscapular.
†Data available on 189 men and 166 women and ‡159 men and 155 women only. Differences between males and females were determined by Student t test for independent samples or $\chi^2$ tests.
TABLE 2. Associations Between Cardiorespiratory Fitness and Pulse Wave Velocity in 2 Arterial Segments

<table>
<thead>
<tr>
<th>Main Determinant</th>
<th>Model</th>
<th>Aortoiliac Segment</th>
<th>Aortodorsalis Pedis Segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{VO}_2\text{max})</td>
<td>1</td>
<td>-0.14 (0.018)</td>
<td>-0.20 (&lt;0.001)</td>
</tr>
<tr>
<td>2*</td>
<td>-0.19 (0.003)</td>
<td>-0.21 (&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-0.18 (0.004)</td>
<td>-0.21 (0.001)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-0.18 (0.008)</td>
<td>-0.20 (0.002)</td>
<td></td>
</tr>
</tbody>
</table>

Data are standardized regression coefficients (\(P\) values). \(\text{VO}_2\text{max}\) indicates cardiorespiratory fitness.

Model 1: adjusted for age, sex, height, weight and mean arterial pressure; Model 2, model 1 further adjusted for total physical activity score; Model 3, model 2 further adjusted for smoking behavior, alcohol consumption, and total intake of fat; Model 4, model 3 further adjusted for body fatness (as estimated by the sum of 4 skinfolds). *Adjustments for sports-related physical activity resulted in \(\beta = -0.14\) (\(P=0.031\)) and \(\beta = -0.18\) (\(P=0.004\)) for aortoiliac and aortodorsalis pedis pulse wave velocity, respectively.

was highly mediated by concomitant levels of \(\text{VO}_2\text{max}\). This indicates that arterial stiffness-related benefits of exercise are most likely to accrue if exercise prescription in young adults targets improvements in \(\text{VO}_2\text{max}\).

In contrast, an adverse relationship between leisure-related physical activities and arterial stiffness was found, and this was, to a certain extent, sex-specific, in that the men, but not the women, of our sample displayed consistently adverse relationships between these types of activities and PWV. Although an explanation of the mechanisms behind a sex difference in the association between any determinant investigated, and arterial stiffness, could be an estrogen-dependent phenomenon, such explanation in the present cohort is unlikely (as no other sex interactions were found). We therefore hypothesized that a difference in the kind of physical activities undertaken by men as compared with women in their leisure time might explain this sex differentiation. With this in mind, we examined further the 4 items that contribute to the leisure physical activity score: television watching, walking, bicycling, and bicycling to and from work or shopping. We found that television watching contributed significantly (\(P=0.006\)) more in men than in women to the leisure activity score, whereas walking contributed significantly (\(P<0.001\)) more to the leisure activity score of women than men, thus confirming our hypothesis.

The differentiation of the activity scores in work-, leisure-, and sports-related activities was an important feature of our study, which allowed us greater insight into the physical activity-arterial stiffness relationships, which otherwise would have been masked by the use of a general, total habitual activity score (data not shown). The behavior of physical activity is difficult to measure, and self-reported physical activity is subject to recall bias and misclassification (unlike cardiorespiratory fitness, which can be measured objectively, using laboratory techniques, as in the present study). This may explain the relatively weaker associations found between arterial stiffness and (sports-related) physical activity than with cardiorespiratory fitness. Despite this limitation, our study clearly demonstrates that a detailed characterization of physical activities performed by individuals (ie, not only their frequency, duration, and intensity, but also the kind of activity) is essential and needs to be extracted from questionnaires to better understand the relation between physical activity and arterial stiffness.

The associations between cardiorespiratory fitness and arterial stiffness were independent of lifestyle variables and body fatness. Other mechanisms may thus explain the associations observed. Further adjustments for other traditional cardiovascular risk factors (such as fasting LDL, HDL and total cholesterol, triglycerides and plasma glucose levels) did not decrease the strength of the associations reported (data not shown). The only other variable that did so to a considerable extent was resting heart rate (changes from \(\beta = -0.18\), \([P=0.008]\) to \(\beta = -0.15\), \([P=0.028]\), in the aortoiliac segment and \(\beta = -0.20\), \([P=0.002]\) to \(\beta = -0.13\), \([P=0.047]\), in the aortodorsalis pedis segment). Heart rate has been shown to be an important factor in the intraindividual variation of PWV, and therefore could have been an important confounder in the associations investigated.\(^{15,30}\) Alternatively, a reduced resting heart rate is a known adaptation to endurance training, and therefore could constitute, at least partially, one mechanism that links high cardiorespiratory fitness to low arterial stiffness. However, as the associations reported above remained significant, other factors may also be involved. Adaptation to shear stress forces can explain both the acute and chronic adaptations to training-induced improvements of cardiorespiratory fitness in humans.\(^{40}\) During exercise, blood
flow increases leading to higher intraluminal forces, which stimulates the release of vasodilating factors such as nitric oxide (NO) and prostacyclin by the endothelium. For a given exercise intensity, however, such increase in arterial blood flow velocity is considerably higher at the distal than proximal site of the abdominal aorta, which may thus explain the stronger associations between the muscular as compared with the more elastic segment, and cardiopulmonary fitness. In addition, changes in the relative proportions of collagen and elastin within the arterial wall as a consequence of aerobic exercise training (in particular of the arteries irrigating the limbs more involved in exercise) could constitute another mechanism explaining the observed beneficial associations.

Perspectives
Our study has relevant clinical and public health implications. The clinical relevance of our findings lies in the important role that cardiorespiratory fitness can play on the etiology of arterial stiffness-related diseases such left-ventricular hypertrophy, heart-failure, and stroke. Indeed, cardiorespiratory fitness is a strong, independent risk factor for cardiovascular and all-cause mortality. The results of the present study, obtained in a young and apparently healthy adult population, suggest that these beneficial associations have their roots in early life, and support the concept that arterial stiffness may lie in the causal pathway between physical fitness and stiffness-related morbidity. Therefore, and from a public health perspective, the improvement of cardiorespiratory fitness is an important tool for the primary prevention of cardiovascular disease. This may be achieved by engaging in sport activities on a regular basis.

Acknowledgments
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References


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