Habitual Exercise and Blood Pressure: Age Dependency and Underlying Mechanisms

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BACKGROUND
Regular exercise is associated with a reduction in cardiovascular risk, but the precise mechanisms responsible are unknown. The aim of the current study was to examine the relationship between regular exercise, aortic stiffness, and wave reflections, and to determine whether this relationship differs by age.

METHODS
Younger (<30 years) and older (>50 years) individuals, who were either sedentary or undertook regular aerobic exercise, were drawn from the Anglo-Cardiff Collaborative Trial population. This yielded 1,036 individuals, all of whom were nonsmokers, and were free of cardiovascular disease and medication. All individuals undertook a detailed lifestyle and medical history questionnaire including details of physical activity. Brachial and central blood pressure, together with aortic stiffness, wave reflections, cardiac output, and peripheral vascular resistance were assessed in all individuals.

RESULTS
In younger individuals, regular exercise was associated with lower diastolic blood pressure but elevated pulse pressure. In contrast, both systolic and pulse pressure were lower in older active individuals, compared with their sedentary counterparts. Moreover, regular exercise was associated with lower wave reflections and peripheral vascular resistance in younger individuals, but lower large artery stiffness in older individuals.

CONCLUSIONS
These data suggest that regular exercise is associated with a beneficial vascular profile. However, this differs between younger and older individuals such that the smaller preresistance and resistance vessels are involved in younger individuals whereas the large elastic arteries are involved in older individuals. Despite these differential findings, the current data provide support for strategies that increase habitual physical activity levels in the general population.

Keywords: age; blood pressure; hypertension; large artery stiffness; exercise.

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Lack of physical activity is an independent risk factor for cardiovascular disease (CVD)1 and increased physical activity and physical fitness are associated with a decreased incidence of coronary artery disease (CAD) events.2-3 The mechanisms whereby exercise reduces cardiovascular (CV) risk are unclear but may involve an improvement in traditional cardiovascular risk factors such as hypertension, hyperglycemia, and hypercholesterolemia.4 However, recent evidence suggests that the cardiovascular protective effect is still evident after adjusting for such factors.5

Although the importance of blood pressure in CV risk prediction is firmly established,6 recently, aortic stiffness and wave reflections have emerged as important, independent risk factors for CV events.7-10 Moreover, increased aortic stiffness may underlie the development of hypertension.11 While the relationship between exercise and indices such as pulse wave velocity (PWV) and augmentation index (AIx) have been investigated previously,12-21 the results have been conflicting, owing to differences between populations, type of exercise, and variations in methods used to assess arterial stiffness. Moreover, chronic exercise tends to decrease blood pressure,22 making it difficult to assess whether any observed changes in arterial stiffness are independent of reductions in blood pressure. Furthermore, indices such as AIx and aortic PWV (aPWV) are differentially affected by aging,23 and whether aging influences the relationship between regular exercise and arterial properties is unclear.

The aim of the current study was to examine the relationship between regular exercise, aortic stiffness, and wave reflections, in a large group of healthy individuals across a wide age range. Specifically, we wished to determine whether the relationship between regular exercise and cardiovascular hemodynamics differs between younger and older individuals.

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METHODS

Study population

Participants were drawn from the ACCT study population, which consists of more than 12,000 individuals, selected at random from local General Practice lists and open-access Cardiovascular Risk Assessment Clinics, across East Anglia and Wales. To examine the influence of age, we elected to study two groups of individuals: those <30 years (younger) and those >50 years (older). Within each group, comparisons were made between sedentary and active individuals, who were matched for age using frequency matching. This approach yielded 1,036 healthy nonsmokers, who were free from cardiovascular disease and medication, and who had undertaken a detailed lifestyle and medical history questionnaire that included questions concerning physical activity (see below). Ethical approval was obtained from the local research ethics committees and written informed consent provided by all participants.

Protocol

Height and weight were assessed and a medical history questionnaire, including details of medication and physical activity completed. Following 15 minutes of supine rest, brachial blood pressure (BP) and radial artery waveforms were recorded, and aPWV was determined. Ten milliliters of blood were then drawn from the antecubital fossa into plain tubes. The samples were centrifuged at 4°C, and the serum separated and stored at –80°C for subsequent analysis. Cholesterol, triglycerides, and glucose were determined using standard methodology in an accredited laboratory.

Assessment of physical activity

The International Physical Activity Questionnaire (October 2002) was used to assess each individual’s physical activity levels over the previous 12 months. Based on the questionnaire data, those individuals who did not participate in any structured physical activity throughout their average week were deemed sedentary. The active group consisted of subjects who reported that they participated in moderate to high-intensity aerobic exercise (e.g., running, cycling, swimming), ≥3 times per week and for at least 1 hour duration (American College of Sports Medicine guidelines, 1998). To ensure a clear separation of the groups in terms of the amount of physical activity undertaken, individuals who undertook regular resistance training and/or low-intensity physical activity were excluded from the analyses. Individuals who took part in a mixture of resistance and aerobic physical activity were also excluded.

Hemodynamic measurements

Brachial blood pressure was measured with the subject resting supine, using a validated semiautomated oscillometric device24 (HEM-705CP, Omron Corporation), according to British Hypertension Society guidelines. All measurements were taken in duplicate and mean values used in the subsequent analyses. Pulse wave analysis was performed using the SphygmoCor system (SphygmoCor, Atcor Medical, Sydney, Australia) as previously described.25 This method allows noninvasive generation of a central (ascending aortic) waveform from that recorded at the radial artery, using a validated generalized transfer function.26 Using the integral software, augmentation pressure was calculated as the difference between the second and first systolic peaks, and AIX (a measure of wave reflection) as the augmentation pressure expressed as a percentage of the pulse pressure. Nonaugmented systolic pressure was identified as the first systolic peak. Heart rate was determined from the aortic waveform and mean arterial pressure (MAP) was obtained by integration of the waveform. Aortic PWV was measured using the same device by sequentially recording electrocardiography-gated carotid and femoral artery waveforms, as previously described in detail.27 Path length for the determination of aPWV was measured as the surface distance between the suprasternal notch and femoral site minus the distance between the suprasternal notch and carotid site, using a tape measure.

Cardiac output and stroke volume were assessed with the subject resting supine, using a validated,28 noninvasive, inert gas rebreathing technique. In brief, while resting, subjects continuously rebreathed a gas mixture (1% SF6, 5% N20, and 94% O2) over 20 seconds, with a breathing rate of 15 breaths per minute. Expired gases were sampled continuously and analyzed by an infrared photoacoustic gas analyzer (InnoCor, Innovision A/S, Denmark), for the determination of cardiac output and stroke volume. Peripheral vascular resistance (PVR) was calculated using the equation \[ \text{PVR} = \frac{(80 \times \text{MAP})}{\text{CO}} \].

Statistical analysis

All data were analyzed using SPSS (version 17.0) software for windows. Unpaired 2 tailed t tests were used to determine differences between groups. Unless otherwise stated, results are expressed as mean (SD). A P value of <0.05 was used to determine significance.

RESULTS

Younger and older participants were stratified according to their level of habitual physical activity. This yielded a total of 487 young (194 sedentary and 293 active) and 549 older (320 sedentary and 229 active) participants in whom complete data were available for the current analyses. The data presented here are for males and females, since separate analyses based on gender showed the same trends throughout.

Anthropometric characteristics

Anthropometric characteristics for the two groups are presented in Table 1. The sedentary vs. active subjects within each group were matched for age. In younger individuals, there were no differences in weight, body mass index (BMI), or waist circumference between active and sedentary individuals. However, in older individuals, regular exercise was associated with significantly lower body weight, BMI, and waist circumference. A comparison of younger and older subjects within the sedentary and active groups revealed that although body weight, BMI, and waist circumference were
Hemodynamic indices

Haemodynamic indices are presented in Table 2 and Figures 1 and 2. Regular exercise was associated with lower diastolic pressure and lower central, but not brachial systolic pressure in younger individuals. In contrast, in older individuals, regular exercise was associated with lower brachial and central systolic pressures. Interestingly, regular exercise was associated with lower brachial and aortic pulse pressures in older individuals, but higher brachial and aortic pulse pressures in younger individuals (Figure 1). Regular exercise was also associated with significantly higher stroke volume in both age groups; however, cardiac output and cardiac index were significantly higher only in older active vs. sedentary individuals. AIx was significantly lower in younger active vs. sedentary individuals, even after adjustment for confounders (Figure 2), and this was accompanied by a significantly lower PVR in active subjects. In contrast, aPWV was significantly lower in older active vs. sedentary individuals, which persisted after adjustment for age and MAP (Figure 2). All trends persisted following adjustment for differences in BMI between the older groups (data not shown).

As expected, all indices of blood pressure were higher in older individuals, regardless of physical activity level. However, the magnitude of the differences in brachial and aortic pulse pressures between age groups was considerably lower in active individuals (Supplementary Table 1). Similarly, AIx and aPWV were higher in older subjects. However, whereas the age-related difference in AIx was similar between sedentary and active subjects, the difference in aPWV in the active individuals was of a smaller magnitude.

Biochemical indices

Overall, regular exercise was associated with a favorable biochemical profile in both younger and older individuals, although the magnitude of the differences between sedentary and active younger individuals was small (Table 3). After performing multiple regression analyses on younger and older groups, these data illustrated that no biochemical parameter had any impact on vascular hemodynamic parameters studied.
Exercise, Aging, and Arterial Function

**DISCUSSION**

This is the largest study describing the influence of age on the relationship between regular exercise and blood pressure, and provides a comprehensive insight into the underlying hemodynamic mechanisms. Our major, novel finding was that the relationship between regular exercise and blood pressure, wave reflections, and arterial stiffness...
Table 3. Biochemical profile of sedentary and active younger and older individuals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&lt;30 years</th>
<th></th>
<th>&gt;50 years</th>
<th></th>
<th>P value</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sedentary (n = 194)</td>
<td></td>
<td>Active (n = 293)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>4.1 ± 0.9</td>
<td></td>
<td>4.0 ± 0.7</td>
<td></td>
<td>NS</td>
<td>5.7 ± 1.1</td>
</tr>
<tr>
<td>LDL (mmol/l)</td>
<td>2.3 ± 0.8</td>
<td></td>
<td>2.2 ± 0.6</td>
<td></td>
<td>NS</td>
<td>3.5 ± 1.0</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.4 ± 0.4</td>
<td></td>
<td>1.5 ± 0.4</td>
<td></td>
<td>0.01</td>
<td>1.4 ± 0.4</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.1 ± 0.7</td>
<td></td>
<td>0.9 ± 0.5</td>
<td></td>
<td>0.002</td>
<td>1.9 ± 1.0</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>4.9 ± 0.9</td>
<td></td>
<td>4.7 ± 0.7</td>
<td></td>
<td>0.01</td>
<td>5.5 ± 2.1</td>
</tr>
</tbody>
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Data are mean ± SD.
Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant.

differed significantly between younger and older individuals. In younger individuals, regular exercise was associated with lower diastolic blood pressure, but elevated pulse pressure. In contrast, both systolic and pulse pressure were lower in older active individuals. Moreover, regular exercise was associated with lower wave reflections and PVR in younger individuals, but lower large artery stiffness in older individuals. These data suggest that regular exercise is associated with a beneficial vascular profile, involving the smaller preresistance and resistance vessels in younger individuals, whereas the large elastic arteries are involved in older individuals. Despite these differential age-related findings, the current data provide further support for strategies which increase habitual physical activity levels in the general population.

A recent meta-analysis emphasised the well-accepted view that regular exercise confers beneficial effects on brachial systolic and diastolic blood pressure, although the authors did not distinguish between younger and older individuals. To our knowledge, the current study is the first to demonstrate that the relationship between regular exercise and blood pressure may be dependent on age, where exercise is associated with lower brachial diastolic pressure in younger individuals, but systolic pressure in older individuals. Interestingly, diastolic blood pressure is more predictive of cardiovascular risk in younger subjects. Whereas in older individuals it is systolic and pulse pressure which have superior predictive value. Therefore, the relationships between regular exercise and blood pressure observed in the current study appear to be consistent with a longer-term reduction in cardiovascular risk.

Pulse pressure, the difference between systolic and diastolic pressure, is often considered a surrogate of large artery stiffness, and has even greater predictive value for cardiovascular events than either systolic or diastolic pressure alone, in older individuals. Interestingly, regular exercise was associated with opposite patterns of pulse pressure in younger and older individuals. Both brachial and central pulse pressures were elevated in younger individuals who undertook regular exercise. However, in older active individuals, both brachial and central pulse pressures were significantly lower relative to sedentary controls. Physiologically, the major determinants of pulse pressure, and, in particular, nonaugmented pulse pressure, are the stroke volume and aortic stiffness, representing the volume of blood flowing into the aorta, and the ability of the aorta to buffer this volume and thus minimize any rise in intra-arterial pressure. As expected, regular exercise was associated with a higher stroke volume in both younger and older individuals, an adaptation which has been described previously. However, despite the higher stroke volume, there were no differences in brachial or nonaugmented central systolic pressures between active and sedentary younger individuals. Instead, the widened pulse pressure in younger active individuals was associated with a significantly lower diastolic pressure.

The lower diastolic blood pressure is likely to involve exercise-related adaptations of the smaller, preresistance and resistance vessels, which have a greater influence on diastolic, rather than systolic, pressure. Indeed, in younger individuals, regular exercise was associated with a lower PVR, and a lower AIX, indicating diminished wave reflections, which is also likely to explain the lower central systolic pressure observed in younger active individuals. These data are in agreement with other studies showing that increased habitual physical activity is associated with a lower AIX in young female twins, in competitive, endurance trained athletes vs. recreationally active controls, and in patients with systemic lupus erythematosus. Although the mechanisms underlying the lower PVR and AIX cannot be confirmed in the current study, likely candidates include altered insulin sensitivity, shear stress, nitric oxide bioavailability and decreased sympathetic activity, as a result of regular exercise.

In older individuals, the lower brachial and central pulse pressures observed in active subjects were due predominantly to lower systolic pressures in these individuals, with a much more modest influence of diastolic pressure. Since stroke volume was significantly increased in active individuals, the lower systolic pressures observed in this age group are likely to be due, at least in part, to a lower level of large artery stiffness. Indeed, aPWV was significantly lower in active than sedentary individuals. Previous data describing the influence of exercise on arterial stiffness remain difficult to interpret, in part due to the wide variety of methods used to measure arterial properties, and differences in age ranges and exercise modalities. Nevertheless, cross-sectional and interventional studies have previously demonstrated that regular exercise is associated with beneficial effects on large artery stiffness in older individuals, although others have shown only modest or no effects of regular exercise.

In contrast to the situation in older individuals, there were no differences in aPWV between younger active and sedentary individuals in the current study, despite the higher pulse pressures observed in active individuals. This illustrates that...
pulsed pressure may not be a reliable surrogate of large artery stiffness in younger individuals. Previous cross-sectional studies in younger subjects showed an inverse association between cardiorespiratory fitness and aPWV and between regular physical activity and measures of carotid artery stiffness. However, intervention studies have failed to detect an effect of aerobic exercise training on aPWV in young rats or carotid stiffness in young humans. In addition, and in keeping with previous cross-sectional data, we did not observe any differences in AIx between older sedentary and active individuals, although previous intervention studies have demonstrated significant reductions in AIx during acute dynamic exercise and during exercise training in older healthy subjects and those with coronary artery disease. Aging exerts one of the most potent effects on the cardiovascular system. Indeed, previous data from the ACCT study suggest that aging exerts a differential effect on arterial stiffness and wave reflections, and that associations between traditional cardiovascular risk factors and AIx are stronger in older individuals, whereas risk factors are more strongly related to aPWV in older individuals. The findings of the current study are in keeping with these previous observations, particularly with regard to the lower AIx observed in younger active individuals, but lower aPWV observed in older active individuals, compared with sedentary subjects. Unfortunately we cannot clarify the mechanisms underlying the apparent beneficial effects of regular exercise on aPWV in older individuals. However, it is possible that life-course exposure to regular exercise may retard the process of large artery stiffening, which is prevalent in this age group, whereas the smaller, more muscular vessels appear to be less affected by the longer-term benefits of regular exercise in older individuals.

The current findings also support the concept that lifestyle factors such as physical activity levels may affect the relationship between age and markers of cardiovascular health, such as blood pressure. Indeed, age-related differences in blood pressure and large artery stiffness were blunted in individuals who undertook regular exercise. Irrespective of whether age affects the relationship between regular exercise and the cardiovascular system or whether undertaking regular exercise influences “cardiovascular aging” per se, the current data suggest that the beneficial effects of regular exercise on the cardiovascular system are consistent with longer-term age-specific reductions in cardiovascular risk. Finally, body weight, BMI, and waist circumference were all significantly reduced in older active individuals compared with their sedentary counterparts, demonstrating that undertaking regular exercise had a more favorable anthropometric profile and therefore, lower cardiovascular risk.

The current study has a number of limitations. The classification of “physically active” vs. “sedentary” was based on self-report, using a questionnaire administered at the time hemodynamic measurements were undertaken. Moreover, although the same criteria were applied to define levels of regular exercise in each age group, the average level of exercise undertaken by each of the “active” groups may have differed. Nevertheless, every effort was made to include only those individuals undertaking regular moderate-to-high intensity exercise, in order to minimise heterogeneity between the groups. Moreover, the major comparisons focussed on differences between active and sedentary individuals within each age group, although it is apparent from our data that age-related differences in hemodynamic variables also varied according to the level of physical activity undertaken. In addition, we did not record the number of years over which an individual has exercised at their current level and therefore we cannot quantify life-course exposure to physical activity, which is bound to differ between younger and older individuals. Finally, because of the cross-sectional nature of these analyses, we cannot examine causal relationships. For example, as alluded to above, it may be the case that exercise induces beneficial age-related changes in cardiovascular hemodynamics, or simply that healthier individuals are more likely to undertake regular exercise, especially later in life.

Blood pressure is a major risk factor for cardiovascular events. However, it is now widely recognised that aging influences the association between blood pressure and cardiovascular risk, such that elevated diastolic pressure is associated with increased risk in younger individuals, whereas systolic and pulse pressures hold greater predictive value in older individuals. Interestingly, in the current study, the relationship between regular exercise and blood pressure was also age-dependent, where diastolic pressure and wave reflections were lower in the young but systolic and pulse pressures, together with large artery stiffness, were lower in older individuals. Therefore, the current data support the concept that strategies designed to increase habitual physical activity levels in the general population may have considerable benefits in reducing cardiovascular risk, regardless of age.

SUPPLEMENTARY MATERIAL

Supplementary materials are available at the American Journal of Hypertension online (http://www.oxfordjournals.org/our_journals/ajh/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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DISCLOSURE

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