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Physical activity and risk of peripheral arterial disease in the general population: Edinburgh Artery Study

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Abstract

***Study objective*—To determine associations between physical activity at age 35–45 years with peripheral arterial disease and cardiovascular risk factors at age 55–74 years.**

***Design*—Cross sectional survey of the general population—Edinburgh Artery Study. The presence of peripheral arterial disease was determined using the WHO/Rose questionnaire on intermittent claudication, and the ankle brachial pressure index at rest and during reactive hyperaemia. Levels of physical activity undertaken at the time of the survey and at the times the subjects were aged 35–45 years were measured by self administered recall questionnaire.**

***Setting*—City of Edinburgh, Scotland.**

***Participants*—Altogether 1592 men and women aged 55 to 74 years, selected from the age-sex registers of 10 general practices spread geographically and socioeconomically throughout the city.**

***Main results*—Participation in moderate or strenuous activity when aged 35–45 years was reported by 66% of men and 40% of women. In men, but not in women, less peripheral arterial disease (measured by an increasing trend in the ankle brachial pressure index) was found with increasing amounts of exercise at age 35–45 years ($p<0{\cdot}001$). Higher levels of exercise at age 35–45 years were associated with lower blood viscosity ($p<0{\cdot}05$) and plasma fibrinogen levels ($p<0{\cdot}05$) in men and women aged 55–74 years, and also with higher current alcohol intake ($p<0{\cdot}001$) and high density lipoprotein cholesterol concentrations ($p<0{\cdot}01$) in women aged 55–74 years. After adjustment for age, sex, life-time smoking, social class, body mass index, and alcohol intake, the association between leisure activity aged 35–45 years and the ankle brachial pressure index aged 55–74 years remained highly significant in men who had at some time smoked ($p<0{\cdot}001$) but not in men or women who had never smoked ($p>0{\cdot}05$)**

***Conclusion*—The risk of peripheral arterial disease, particularly among male smokers, is inversely related to previous physical activity in early middle age, suggesting a protective effect of exercise.**

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The relationship between physical activity and ischaemic heart disease has been widely investigated, with most studies showing that exercise is associated with a lower rate of heart disease in later life.[1 7] The protective effect of exercise was first identified by Morris *et al* who compared London bus drivers with bus conductors, and postmen with Post Office supervisors, and found lower mortality from heart disease in those doing more active work.[1] Similar findings were reported by Khan, who compared letter carriers with mail clerks,[2] and by Paffenbarger *et al* who compared San Francisco cargo handlers with sedentary longshoremen.[3] With the general decline in physically strenuous occupations, more recent studies[4 5] have concentrated on leisure time activity as a protective factor for ischaemic heart disease. In 1973, Morris *et al* investigated the reported leisure activities of London civil servants, and showed that the death rate from ischaemic heart disease over an eight year follow up period was appreciably reduced in those who had taken physical exercise.[4] Leren *et al* made the interesting observation that the most favourable coronary risk profile occurred in men who did sedentary work but took vigorous leisure activity.[5]

The relationship between physical exercise and the risk of peripheral arterial disease has been investigated only in studies where the main concern was heart disease. In the Framingham Study, an association was found between low levels of physical activity and the development of intermittent claudication, but the association was not statistically significant after adjustment for age.[8] In the Finnish cohort of the Seven Countries Study, however, "claudication was clearly associated with sedentary habits" at the 10 year follow up.[9] The role of physical activity in protecting against peripheral arterial disease might be expected to be similar to that for ischaemic heart disease, but differences may arise because of variations in the relative importance of certain risk factors, particularly smoking,[10 11] and because the leg is directly involved in most forms of exercise.

The Edinburgh Artery Study[12] is the first population survey in which physical activity has been measured in subjects examined for symptomatic and asymptomatic peripheral arterial disease. The objectives were to determine associations between physical activity at age 35–45 years with peripheral arterial disease and cardiovascular risk factors at age 55–74 years.

Methods

STUDY POPULATION

The Edinburgh Artery Study is a cross sectional survey of 1592 men and women aged 55 to 74 years, slected from the age-sex registers of 10 general practices with catchment populations spread geographically and socioeconomically throughout the city. The sample was selected at random within sex specific, five year age bands to produce equal numbers in each group. Subjects attended a university clinic to complete a questionnaire and to have a comprehensive medical examination. The response rate was 65%, and follow up of a sample of non-responders did not show any substantial bias. Details of the study population, recruitment, and prevalence of peripheral arterial disease have been described previously.[12] Ethics committe approval was given for this study, and informed consent was obtained from each patient.

ASSESSMENT OF PHYSICAL ACTIVITY

Levels of physical activity were determined using a self administered questionnaire (Appendix) adapted from the Welsh Heart Health Study questionnaire,[13] previously validated against measures of cardiovascular fitness.[14] Respondents were asked to assess the amount of activity undertaken during the last year, and when aged 35–45 years old; this last category was important in order to obtain a measure of previous physical activity which could be related to present disease status.

MEASUREMENT OF PERIPHERAL ARTERIAL DISEASE

Symptomatic peripheral arterial disease was identified using the WHO/Rose questionnaire on intermittent claudication,[15] and asymptomatic disease was detected by measuring the ankle brachial systolic pressure index at rest, and the change in ankle systolic pressure during reactive hyperaemia. Systolic and diastolic (phase V) blood pressures were taken in the right arm after 10 minutes rest in the supine position, using a random zero sphygmomanometer. Ankle systolic blood pressures were taken first in the right, then in the left leg using the random zero sphygmomanometer and a Doppler probe. Where possible, blood flow was detected at the ankle in the posterior tibial artery. In the reactive hyperaemia test, ankle systolic pressure was measured in the right and left legs 15 seconds after the release of a cuff occluding arterial flow above the knee for four minutes at approximately 50mmHg above systolic pressure. The timing was standardised using an electronic timer.

For descriptive purposes, the population was divided into four categories of peripheral arterial disease: (i) intermittent claudication (WHO questionnaire positive); (ii) major asymptomatic disease (ankle brachial pressure index ≤0·9 and >20% drop in ankle systolic presure after occlusion *or* ankle brachial pressure index ≤0·7 *or* >35% drop following occlusion); (iii) minor asymptomatic disease (ankle brachial pressure index ≤0·9 *or* >20% drop following occlusion); and (iv) normal values (none of the above). Since these categories have not been used in other studies the validities were unknown, but results of studies comparing the ankle brachial pressure index and the reactive hyperaemia response with angiography suggest that the classification had adequate face validity.[16] The main analysis, however, concentrated on the ankle brachial pressure index because it was almost completely recorded and is a continuous measure, thus giving greater power to detect associations. In addition, the ankle brachial pressure index seems to be a good measure of peripheral arterial disease in population surveys, because decreasing levels have been shown to be associated both with disease severity detected on duplex scanning[17] and with the prevalence of other markers of artherosclerosis such as angina and conventional cardiovascular risk factors.[10]

STATISTICAL ANALYSIS

Data were analysed on the Edinburgh University mainframe computer using the BMDP statistical package.[18]

Physical activity was classified into none, light, moderate, and strenuous for both leisure and occupational activity independently, according to the maximum amount of activity recorded in either summer or winter: no activity=0; maximum of light activity=1; maximum of moderate activity=2; maximum of strenuous activity=3. Current occupational activity was excluded from the analysis because many subjects were no longer in paid employment. Present activity was also excluded from the main analysis because symptomatic arterial disease inevitably produces low levels of activity, distorting any possible causal association between activity and the development of atherosclerosis.

Spearman rank correlation coefficients were calculated to show the relationship between physical activity at aged 35–45 years and activity at the time of the survey, the ankle brachial pressure index, and risk factors for peripheral arterial disease. The χ^2 test was used to examine the relationship between the four categories of peripheral arterial disease and the categories of leisure activity. A linear test for trend was performed for mean ankle brachial pressure index levels, and risk factors, across different categories of leisure activity. The distribution of the ankle brachial pressure index throughout the population was approximately normal .

The independent relationship between leisure activity at aged 35–45 years and disease was determined using multiple linear regression with the ankle brachial pressure index as the dependent variable. A significant leisure activity by sex and by smoking (ever *v* never) interaction was found (p=0·02), and therefore twelve dummy variables were created representing each of the leisure activity categories, relative to no activity in men and women, and ever and never smokers. Tests for interaction between additional risk factors were also carried out. The regression analysis adjusted for age, sex, social class, body mass index, alcohol, and smoking as measured by pack years (average number of packs of 20 cigarettes per day × number of years as a smoker). Square root transformations were used for smoking and alcohol consumption because of positive skewness.

Results

Forty eight per cent of men recalled taking part in some form of moderate leisure activity when aged 35–45 years, and an additional 18% were undertaking strenuous leisure activity. Thirty seven per cent of women were taking some moderate physical exercise at this age, but only 3% were undertaking any strenuous activity. Eight per cent of

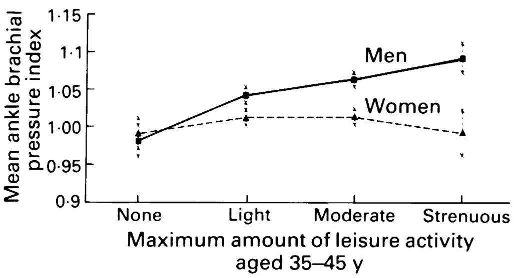
Table I Leisure activity age 35–44 years in relation to severity of peripheral arterial disease at age 55–74 years

Leisure activity*	Subjects taking leisure activity (%) Intermittent claudication (n=72)	Major asymptomatic disease (n=106)	Minor asymptomatic disease (n=228)	No disease (n=1071)
None	12·5	10·4	10·5	8·7
Light	43·1	39·6	39·5	35·4
Moderate	38·9	41·5	39·5	44·4
Strenuous	5·6	8·5	10·5	11·6

χ^2=24·55, p=0·02
*Grade of leisure activity is the maximum reported
114 subjects could not be classified for disease status

men and 12% of women were taking no leisure activity of note at this age. The amount of leisure activity undertaken when aged 35–45 years showed good correlation with the amount of leisure activity undertaken at the time of the survey (r=0·56, p<0·001), although activity was slightly less at age 55 to 74 years.

Table I shows the proportion of subjects taking different levels of leisure activity when aged 35–45 years, for each category of arterial disease. There was a significant association between increasing disease and lower levels of exercise in the population as a whole (p<0·05) and in men (p<0·05), but not in women. An increasing trend in the proportions who undertook light or no activity was observed across the normal to the severe disease categories; a reverse trend of increasing strenuous exercise occurred from diseased categories to normal subjects. In men, but not in women, an increasing trend in ankle brachial pressure was found with greater amounts of exercise at age 35–45 years (p<0·001), (figure).



Ankle brachial pressure index (ABPI) (mean ±2SEM) in 809 men and 782 women aged 55–74 years in relation to leisure activity at age 35–45 years

The amount of occupational activity undertaken at age 35–45 years was also significantly associated with the different categories of peripheral arterial disease present at the time of the survey (p<0·05) but, unlike leisure activity, no association was found with the ankle brachial pressure index in either men or women. There was a highly significant association between occupational activity and leisure activity at age 35–45 years (p<0·001).

The amount of leisure activity undertaken at age 35–45 years was also significantly associated with several well established risk factors for peripheral arterial disease, measured at the time of the survey (table II). In women, higher levels of exercise at age 35–45 years were associated with higher current alcohol intake and high density lipoprotein cholesterol concentrations aged 55–74 years, and with lower levels of plasma fibrinogen and blood viscosity aged 55–74 years. In men there was a similar association between previous high leisure activity and low blood vicosity, low plasma fibrinogen levels, and lower consumption of cigarettes at the time of the survey. Similar findings occurred on testing for linear trend. In both men and women, higher levels of leisure activity at age 35–45 years were associated with higher social class aged 55–74 years.

Table III shows the effect of correcting for age, sex, life-time smoking, social class, body mass index and alcohol intake, on the association between previous exercise and the ankle brachial pressure index separately in smokers and non-smokers. In men who had ever smoked, there was a significant association between leisure activity at age 35–45 years and change in mean ankle brachial pressure index after adjustment for other risk factors, which increased with increasing amounts of exercise. In women, however, and in men who had never smoked, there was no significant association between leisure activity and the change in mean ankle brachial pressure index after correcting for the other risk factors.

Discussion

Physical activity is the process which promotes physical fitness, a biological marker of the body's ability to perform exercise. Studies examining both physical activity and fitness have shown them to be closely correlated,[19] although fitness may be a more powerful predictor of disease,[20] and more closely related to risk factors for coronary heart disease.[19] Most population surveys have measured activity rather than fitness, primarily because it can be readily determined by questionnaire, and also because it has been shown to be protective against coronary heart disease.[21 22] In addition, physical activity measured by recall questionnaires has shown good correlation with treadmill estimation of oxygen uptake,[23] body composition,[23] and forced expiratory volume,[14] suggesting that it is a reasonably valid method.

Fewer women than men (41 *v* 66%) reported moderate or strenuous activity when aged 35–45 years. This is consistent with other findings,[24] but may also have been exaggerated by the emphasis in the questionnaire on competitive sport, especially in the strenuous category, which may have been more relevant to men than women. In addition, some activities in the light category such as horse riding or sailing could, depending on their intensity and duration, actually be moderate or strenuous. Another potential problem was recall bias, which it was not feasible to assess. However, a recent study has shown the validity of recall of previous exercise over a 10 year period to be satisfactory, independent of recall interval and age.[25]

Table II Spearman rank correlation coefficients of leisure activity at age 35–45 years with risk factors for peripheral arterial disease at age 55–74 years

Risk factor	Leisure activity at age 35–45 years Women (n=782)	Men (n=809)
Body mass index	−0·06†	−0·006
Smoking (pack years)*	−0·004	−0·11‡
Alcohol intake*	0·15§	0·05
Social class	−0·32§	−0·23§
HDL cholesterol	0·12‡	0·06
Fibrinogen	−0·08†	−0·07†
Blood viscosity	−0·15§	−0·08†

*Square root transformation
†=p<0·05; ‡=p<0·01; §=p<0·001

Table III Multiple regression of leisure activity at age 35–45 years on the ankle brachial pressure index (ABPI) at age 55–74 years by sex and cigarette smoking

	Changes in mean (SEM) ABPI*			
	Women		Men	
Maximum leisure activity (relative to none)	Ever smoked (=386)	Never smoked (n=382)	Ever smoked (n=568)	Never smoked (n=224)
Light	0·04 (0·03)	0·01 (0·03)	0·06† (0·03)	0·05 (0·04)
Modeate	0·03 (0·03)	0·01 (0·03)	0·08‡ (0·03)	0·03 (0·04)
Strenuous	0·07 (0·05)	–0·07 (0·06)	0·10‡ (0·03)	0·05 (0·04)

*Adjusted for age, sex, life-time smoking, social class, body mass index, alcohol
†=p<0·05; ‡=p<0·001

The recall of physical activity undertaken at the time of the survey, would undoubtedly have been more accurate than that for activities undertaken up to 30 years earlier, but because any relationship between current physical inactivity and increased prevelance of disease was less likely to be causal, current activity was excluded from the main analysis. Indeed, an association between low current physical activity and arterial disease in those with intermittent claudication would be inevitable, because of its restriction on exercise capacity. In addition, intermittent claudication often coexists with angina, which could further restrict physical activity; in this study there was a significant decrease in current leisure activity with increasing angina (p<0·05). In contrast, a relationship between previous physical activity and present arterial disease would be more suggestive of a causal relationship, because it is highly unlikely that any significant amount of arterial disease would have restricted physical activity in subjects aged between 35–45 years. Activity at age 35–45 years was, however, strongly correlated with present day levels of activity, suggesting that exercise habits were established early in life and remained relatively unchanged, in the absence of any intervening illness. Surprisingly, at age 35–45 years, occupational activity was positively correlated with leisure activity, although less leisure activity might have been expected in those who were very active at work.

A highly significant linear increase in the mean ankle brachial pressure index was found with increasing leisure activity in men, but not in women. A similar dose-response relationship at all levels of exercise has been shown in physiological studies investigating the effects of exercise on other known risk factors, such as a high low density and low high density lipoprotein cholesterol concentration.[26] Epidemiological studies have also shown reduced cardiovascular mortality at all levels of exercise, suggesting that even low levels are worthwhile, although there is little change in other risk factors.[3 27]

Multiple regression analysis showed that the increase in the ankle brachial pressure index with exercise was most noticeable in men who had at some time in their lives smoked. Similar multiple regression analyses for ischaemic heart disease[8 26 28] and stroke[29] have shown physical activity to be an independent risk factor in men, but not women,[30] although they have not identified that this occurred only in smokers, possibly because smoking is relatively less important in the aetiology of ischaemic heart disease than in peripheral arterial disease.[31]

The mechanism through which exercise protects against arterial disease has not been clearly established, but could operate via changes in blood lipid levels[26] or rheological factors,[32] both of which were shown to be associated with exercise in this study. Alternative mechanisms may include improvement of glucose intolerance and hyperinsulinaemia,[33] reduction of blood pressure,[34] plus the indirect benefit of maintaining body weight. Whatever the mechanism, increased levels of physical activity in earlier life seem to be beneficial in preventing cardiovascular disease. Our results suggest that physical activity is particularly important in men who smoke.

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Appendix

PHYSICAL ACTIVITY

The following section gives examples of the sort of activities you might do or may have done *regularly.*

Light activity	*Moderate activity*	*Strenuous activity*
Ballroom dancing	Badminton	Basketball
Bowling	Cricket	Competitive cycling
Light do-it-yourself	Cycling (include to and from work, to shops etc)	Competitive swimming
Light gardening	Heavy do-it-yourself	Competitive running
Horse riding	Golf	Field sports (such as rugby, soccer, hockey)
Sailing	Jogging	Training for strenuous sport
Walking (including to and from work to shops etc)	Swimming	Squash
Yoga	Tennis	
And other activities of similar intensity. Please specify others you have done.	And other activities of similar intensity. Please specify others you have done.	And other activities of similar intensity. Please specify others you have done.
....	....	....
....	....	....

(1) In a typical week during the past year, on how many occasions would you take part, for more than 20 minutes each time:

	Insert "none" if appropriate	
In *light* physical activity?	in summer	times
	in winter........................	times
In *moderate* physical activity?	in summer	times
	in winter........................	times
In *strenuous* physical activity?	in summer	times
	in winter........................	times

(2) In a typical week, when you were 35–45 years old, on how many occasions would you take part, for more than 20 minutes each time:

	Insert "none" if appropriate	
In *light* physical activity?	in summer	times
	in winter........................	times
In *moderate* physical activity?	in summer	times
	in winter........................	times
In *strenuous* physical activity?	in summer	times
	in winter........................	times

Which of the following best describes your daily work or other daytime activity at the present time?

Please tick one box only.

I am usually sitting during the day and do not walk about much	☐	eg office workers, drivers
I stand or walk about quite a lot during the day but do not have to carry or lift things very often	☐	eg housewives, shop assistants
I usually lift or carry light loads and have to climb stairs and/or hills often.	☐	eg postmen, packers
I do heavy work and carry heavy loads	☐	eg building, mining and agricultural workers

Which of the following best described your daily work or other daytime activity when you were 35–45 years old?

I usually sat during the day and did not walk about much	☐	eg office workers, drivers
I stood or walked about quite a lot during the day but did not have to carry or lift things very often	☐	eg housewives, shop assistants
I usually lifted or carried light loads and had to climb stairs and/or hills often.	☐	eg postmen, packers
I did heavy work and carried heavy loads	☐	eg building, mining and agricultural workers

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