High aerobic fitness in late adolescence is associated with a reduced risk of myocardial infarction later in life: a nationwide cohort study in men

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Aims	Cardiovascular disease is the leading cause of morbidity and mortality worldwide, and signs of atherosclerosis are present in all large arteries already in adolescence. We investigated the association between high physical fitness in late adolescence and myocardial infarction (MI) later in life.
Methods and results	The study cohort comprised 743 498 Swedish men examined at the age of 18 years during conscription 1969–84. Aerobic fitness (W_{max}) and muscle strength at conscription were measured using standardized methods. Myocardial infarctions occurring in the cohort were tracked through national registers. During a median follow-up period of 34 years, 11 526 MIs were registered in the cohort. After adjusting for age, body mass index (BMI), diseases, education, blood pressure, and socio-economic factors, one standard deviation increase in the level of physical fitness (W_{max}) was associated with an 18% decreased risk of later MI [hazard ratio (HR) 0.82, 95% confidence interval (CI) 0.80–0.85]. The beneficial effects of W_{max} were significant across all recognized BMI groups, ranging from lean (BMI < 18.5) to obese (BMI > 30) ($P < 0.05$ for all). However, obese men (BMI > 30) in the highest fourth of W_{max} had a higher risk of MI than did lean men (BMI < 18.5) in the highest (HR 4.6, 95% CI 1.9–11.2), and lowest (HR 1.7, 95% CI 1.2–2.6) fourth of W_{max}.
Conclusions	We report a significant graded association between aerobic fitness in late adolescence and MI later in life in men. However, obese men with a high aerobic fitness had a higher risk of MI than lean men with a low aerobic fitness.
Keywords	Myocardial infarction • Physical fitness • Adolescent men

Introduction

Cardiovascular disease (CVD) is the leading global cause of death, and ischaemic heart disease accounted for 12.8% of all deaths worldwide and 15.6% of all deaths in high-income countries in 2008.[1] The great burden of CVD on health-care systems worldwide necessitates the identification of modifiable risk factors, enabling the implementation of early preventive measures.

Several prospective studies have linked leisure-time physical activity or aerobic fitness to the incidence of CVD.[2–4] The association between aerobic fitness and CVD seems to be independent of, and stronger than that of reported physical activity.[5,6] These findings could have been influenced by the assessment of physical activity using questionnaires, which increases the risk of recall bias.

Most prospective studies that have examined the association between aerobic fitness and/or physical activity and the risk of CVD have used cohorts of middle-aged subjects,[7,8] resulting in relatively short follow-up periods and the risk that subclinical CVD influenced reported physical activity or aerobic fitness. Nevertheless, some recent studies have indicated that selected cohorts of obese adult subjects with high physical fitness may have similar or even lower risk of CVD or death from CVD than do non-obese subjects

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with low physical fitness.[9–11] Given that the signs of atherosclerosis are already present in large arteries in adolescence,[12] the evaluation of whether physical fitness in adolescence is associated with CVD later in life, and whether high physical fitness protects obese young subjects from later CVD, would be of interest. Therefore, in the present study, the association of objectively measured physical fitness at the age of 18 years with the later incidence of myocardial infarction (MI) was investigated in a nationwide cohort of men.

Methods

Study population

The study cohort comprised all Swedish men conscripted into compulsory military service between 1969 and 1984, and only 2–3% of all men were relieved from conscription due to severe chronic medical illness. Age and anthropometric data (weight, height) were available for a total of 752 811 men. All these men participated in a 2-day, standardized, baseline intelligence, and physical examination regimen. All conscripts were also examined by a medical doctor, who, based on self-reports, diagnosed any medical disorder according to the International Classification of Disease (ICD) 8th edition. Blood pressure was measured using a mercury sphygmomanometer with subjects in supine position.

An electrically braked ergometer cycle test was used to ascertain conscripts' aerobic fitness. Briefly, each conscript underwent resting electrocardiography and, if results were normal, continued with the exercise test. Following a warm-up period, the resistance was increased linearly at a rate of 25 W/min until the participant had to discontinue the test due to fatigue; the final work rate (W_{max}) was recorded and used in further analysis.

Isometric muscle strength for knee extension, grip, and elbow flexion was measured in Newton (N) using dynamometers. Each test was repeated three times unless the final value was highest; in such cases, the test was repeated until the value stopped increasing. Testing equipment was calibrated daily. The knee extension test was performed on the right knee with the subject in a seated position with crossed arms. The dynamometer strap was placed on the malleolus of the ankle and the test began with the knee bent at 90°; the leg was then extended with maximal force. Elbow flexion was assessed on the right arm with the conscript in a seated position with the left hand on the left knee to ensure a straight shoulder position. The subject then flexed the arm to 90° with the forearm held vertically. Grip strength was assessed in the subject's dominant hand in a standing position with the arm held vertically and the forearm positioned at 90°.

Data on subjects' education, incomes, and disability pensions at 20 years after conscription were collected from Statistics Sweden (Statistiska Centralbyrån). Education was classified using four levels: <9 years of elementary school, completion of elementary school (9 years), high school (2–4 years), and university education. Data were missing for education and income in 0.8 and 0.4% of the subjects, respectively. Information regarding deaths in the cohort was acquired from the National Board of Health and Welfare. This study was approved by the regional ethics board in Umeå.

Inclusion criteria and sub-cohorts

Conscripts were included in the study cohort if they met the following criteria: age at baseline ≥17 years, bodyweight ≥40 or ≤170 kg, and height ≥140 or ≤215 cm. Men who died or emigrated before 1987 were excluded. A total of 743 498 subjects were included in the present study. Because no aerobic fitness testing was conducted

between 1969 and 1972, 620 089 men were included in analyses involving W_{max}. Data on smoking were registered only in a sub-cohort of men ($n = 23\ 602$) conscripted in 1969–78, 23 489 of whom were conscripted in 1969–70. Finally, haematocrit values were available for 119 011 men in the cohort.

Assessment of myocardial infarction

Information on diagnosis of MI in the cohort was collected via record linkage using the unique personal identification number given to all Swedish citizens and the National Hospital Discharge Register (HDR), superintended by the National Board of Health and Welfare. Subjects were diagnosed during the follow-up period according to the ICD 9th (1987–96) and 10th (1997–2009) editions.

A validation study of the HDR conducted on 713 patients diagnosed with MI between 1987 and 1995 found that 86% of patients fulfilled the present criteria for MI diagnosis, 9% were likely to have had an MI, and the remaining 5% did not have an MI.[13] The authors of that study found that the consistency between clinical diagnosis and diagnostic criteria made the Swedish MI statistics applicable in epidemiological studies. Potential risk factors for MI were selected based on risk factors found in previous studies and the most common diagnoses found in the cohort studied at conscription.

Statistical analysis

The associations of independent variables at baseline with MI risk after the age of 40 years were analysed using Cox's proportional hazard models. In the first model, the risks [hazard ratios (HRs)] of MI per standard deviation (SD) change in W_{max}, knee extension, elbow flexion, and grip strength values were investigated after adjusting for age, year and place of conscription, and body mass index (BMI). The same analyses were repeated with additional adjustment for socio-economic factors, education, the 12 most commonly diagnosed conditions at baseline, and systolic and diastolic blood pressure. The inclusion of BMI and some other factors constituted adjustment for factors that could be potential confounders as well as mediators of associations. By also entering the quadratic compound of each exposure, we found that no exposure showed evidence of a non-linear association with MI (data not shown). In a second model, HRs for MIs were estimated for fifth of W_{max} and the different measures of muscle strength. In a third model, the joint effect of the different exposures, BMI, and the risk of later MI were further analysed. In this model, BMI was classified based on the World Health Organization's (WHO's) definitions of underweight/lean (BMI < 18.5 kg/m^2), normal weight (BMI ≥ 18.5 and <25 kg/m^2), overweight (BMI 25–30 kg/m^2), and obese (BMI > 30 kg/m^2), and physical fitness (W_{max} and knee extension strength) were divided into ranked fourth. These procedures created 16 sub-cohorts for the combinations of exposures that were entered into the Cox regression models together with all confounders specified above. The study endpoint for all Cox regression analyses was the date of MI, date of death, or 1 January 2011, whichever came first. The hazard proportional assumption was evaluated graphically using a Kaplan–Meier curve. SPSS software (ver. 20.0; SPSS, Inc., Chicago, IL, USA) was used for all statistical calculations, with $P < 0.05$ considered significant. Unless stated otherwise, all data are presented as means ± SDs.

Results

Baseline examinations

The cohort considered for inclusion in this study consisted of 743 498 men with a mean age of 18.5 ± 0.8 years at conscription.

W_{max}, knee extension strength, and BMI data acquired at conscription are shown in *Figure 1*. The median follow-up period was 34 (range 5–41) years, during which 11 526 men were diagnosed with MI. Anthropometrics, blood pressure, and diagnoses at conscription, as well as socio-economic factors and education levels at 20 years after conscription, are presented in *Tables 1* and *2* for fifth of aerobic fitness and knee extension strength. When comparing low and high fifth of aerobic fitness (*Table 1*), the most prominent differences included higher BMI, higher incidence of most diagnosed diseases, and lower total income and education 20 years after conscription. Similar results were found when comparing the extreme fifth of muscle strength, but the differences were generally less pronounced (*Table 2*).

Aerobic fitness, strength, and myocardial infarction during follow-up

The number of MIs increased with decreasing fifth of aerobic fitness (*P* for trend <0.001, *Figure 2*). The relationship between increasing muscle strength and the risk of MIs later in life was less clear (*Figure 2*).
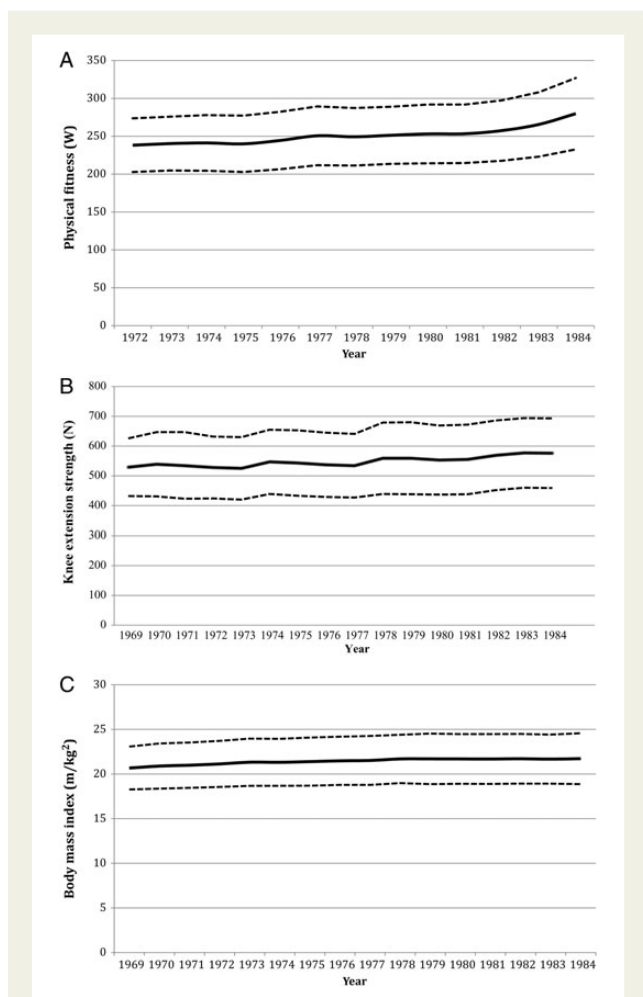

Figure 1 Means and standard deviations of aerobic fitness (W_{max}; *A*), knee extension strength (*B*), and BMI (*C*) during the years of conscription.

After adjusting for age, BMI, and year and place of conscription, each SD increase in W_{max} was associated with a decreased risk of MI during the follow-up period [HR 0.76, 95% confidence interval (CI) 0.74–0.78; *Table 3*]. All measurements of muscle strength were also associated with a decreased risk of MI during follow-up, but the associations were weaker than for W_{max} (HRs 0.91–0.96, 95% CIs 0.89–0.98 per SD increase; *Table 3*). Further adjustment for education, socio-economic factors, the 12 most common diagnosed conditions at baseline, and blood pressure reduced the strength of associations between W_{max} and MI (HR 0.82), whereas the risk associated with muscle strength measurements remained largely unchanged (HRs 0.91–0.95, *P* < 0.001 for all; *Table 3*). Further adjustments for also haematocrit in the sub-cohort where such data were available (*n* = 119 011) changed all HRs <0.001.

Using the highest fifth of aerobic fitness as a reference, men in the lowest fifth had a 2.1-fold increased risk of MI during follow-up (95% CI 2.0–2.3, *P* for trend <0.001) after adjustment for BMI, age, and place and year of conscription. Men in the lowest fifth of muscle strength also showed a higher risk of MI during follow-up compared with the highest fifth (HRs 1.1–1.3, *P* < 0.01 for all), but the associations were significantly weaker.

Because aerobic fitness was associated with the different estimates of muscle strength (*r* = 0.27–0.38, *P* < 0.001 for all), fifth of aerobic fitness and knee extension strength were included in the final model together with all covariates. The association between fifth of aerobic fitness and the risk of MI remained (HR 1.69, 95% CI 1.55–1.85), whereas knee extension strength and MI was not significantly associated (HR 1.01, 95% CI 0.93–1.09).

The joint and independent effects of physical performance and body mass index

HRs for the later risk of MI based on W_{max} fourth and the WHO's BMI groups, adjusted for age, BMI, and year and place of conscription, blood pressure, education, socio-economic factors, and diagnosed conditions at baseline, are presented in *Figure 3*. The risk of later MI increased significantly when comparing the highest and lowest W_{max} fourth for all BMI groups (HRs 1.34–2.57, *P* < 0.05 for all). Similarly, the risk of MI increased when comparing obese (BMI > 30) and lean (BMI < 18.5) men for all groups of aerobic fitness (HRs 2.44–4.65, *P* < 0.01 for all). In a separate analysis, obese men (BMI > 30) in the highest fourth of W_{max} had a higher risk of MI during follow-up than did lean men (BMI < 18.5) in the lowest (HR 1.71, 95% CI 1.15–2.56) and highest (HR 4.6, 95% CI 1.9–11.2) fourth of W_{max}, after adjustment for all available covariates. Furthermore, overweight men (BMI ≥ 25–30) in the highest fourth of aerobic fitness were found to have a higher risk of MI (HR 1.31, 95% CI 1.13–1.51) than normal-weight men (BMI ≥ 18.5 and <25) in the lowest fourth of aerobic fitness.

Smoking and myocardial infarction later in life

In the sub-cohort with data on smoking (*n* = 23 602), knee extension strength was associated with a decrease in the risk of MI (*n* = 893) after adjusting for BMI, age at baseline, and year and place of conscription (HR 0.90, 95% CI 0.84–0.97 per SD increase in knee extension strength value). Further adjustment for smoking only marginally

Table 1 Baseline characteristics of subjects who performed aerobic fitness (*n* = 620 089) testing at conscription, according to fifth of physical fitness, with the first fifth representing men with the highest physical fitness

	Total (*n* = 620 089)	Fifth of aerobic fitness				
		1st >282 W	2nd 255–282 W	3rd 237–254 W	4th 216–236 W	5th <216 W
Age (years)	18.3 ± 0.8	18.2 ± 0.6	18.3 ± 0.7	18.3 ± 0.9	18.3 ± 0.9	18.4 ± 1.0
Weight (kg)	69.1 ± 10.0	73.8 ± 8.8	71.5 ± 9.5	69.7 ± 9.5	67.3 ± 9.5	63.3 ± 9.5
Height (cm)	179 ± 7	181 ± 6	180 ± 6	179 ± 6	178 ± 6	176 ± 7
BMI (kg/m^2)	21.5 ± 2.7	22.4 ± 2.3	22.1 ± 2.6	21.7 ± 2.7	21.2 ± 2.8	20.3 ± 2.8
Haematocrit (%)	45.5 ± 6.5	45.5 ± 6.6	45.5 ± 6.5	45.5 ± 6.6	45.5 ± 6.5	45.5 ± 6.5
Income (1000 euro/year)[a]	18.0 ± 11.2	20.7 ± 15.6	18.7 ± 10.3	17.8 ± 9.8	17.0 ± 9.5	16.0 ± 9
Disability pension (%)[a]	1.0	0.5	0.7	0.9	1.2	1.7
Elementary school (%)						
<9 years	0.9	0.2	0.6	0.9	1.2	1.7
9 years	18.5	8.8	14.2	18.8	22.6	27.9
High school	53.3	49.2	54.0	54.8	54.9	53.6
University education	27.2	41.7	31.1	25.5	21.4	16.7
Blood pressure (mmHg)						
Systolic	129 ± 11	130 ± 11	129 ± 11	129 ± 11	128 ± 11	127 ± 11
Diastolic	68 ± 10	67 ± 10	68 ± 10	68 ± 10	69 ± 10	69 ± 10
Diagnosis (%)						
Impaired hearing	10.0	8.6	9.4	9.8	10.6	11.6
Allergic rhinitis	7.6	8.6	7.5	7.5	7.5	7.3
Lumbago	6.8	4.1	5.9	6.9	7.8	9.1
Neurosis	3.1	0.8	1.6	2.6	3.9	6.6
Asthma	2.6	1.8	2.3	2.5	3.1	3.4
Upper resp. infection	1.5	0.8	1.3	1.7	1.7	1.9
Gastritis	1.3	0.6	1.0	1.2	1.6	2.0
Personal disorder	0.8	0.1	0.4	0.7	1.1	1.9
Atopic dermatitis	1.0	0.9	1.0	0.9	1.0	1.0
Drug dependence	0.4	0.06	0.2	0.4	0.6	1.1
Alcoholism	0.3	0.04	0.1	0.2	0.4	0.7
Diabetes	0.07	0.04	0.05	0.08	0.09	0.08

Cut-off limits for the fifth of aerobic fitness (Watt, W) and knee extension strength (Newton, N) are shown.
[a]Assessed at 38 years of age.

attenuated this risk (HR 0.91, 95% CI 0.85−0.97). The risk of later MI was increased two-fold among smokers compared with non-smokers (HR 2.31, 95% CI 1.98−2.67).

Discussion

In the present study, aerobic fitness in late adolescence was associated with the later risk of MI in a nationwide cohort of men. The association between aerobic fitness and MI was consistent in all BMI groups, ranging from lean to obese. However, obese and overweight fit men had a higher risk of MI than did lean or normal-weight unfit men. In contrast, the association between muscle strength and the risk of MI was weaker and dependent of aerobic fitness and BMI. Overall, these findings suggest that high aerobic fitness in late adolescence may reduce the risk of MI later in life, although high

cardiovascular fitness appears not to fully compensate for overweight or obesity with respect to this risk.

To our knowledge, the present study is the first to investigate associations between objective measures of physical performance in late adolescence and later MI in a population-based cohort. The clinical relevance of such findings could be further evaluated in the present cohort. Previous exercise intervention trials have found that endurance training may increase aerobic fitness by about 30%.[14] In the present study, we found that a 15% (1 SD) increase in aerobic fitness was associated with a ∼18% lower risk of MI 30 years later, after adjustment for multiple confounders including BMI. Thus, our results indicate that regular cardiovascular training in late adolescence is independently associated with a ∼35% reduced risk of early MI in men. Given the pronounced effects found, the low cost and easy accessibility of cardiovascular training, and the role of

Table 2 Baseline characteristics of knee extension strength (n = 743 313) testing at conscription, according to fifth of physical fitness, with the first fifth representing men with the highest physical fitness

	Total (n = 743 313)	Fifth of knee extension strength				
		1st >639 N	2nd 570–639 N	3rd 511–569 N	4th 451–510 N	5th >451 N
Age (years)	18.4 ± 0.8	18.4 ± 0.8	18.4 ± 0.8	18.4 ± 0.8	18.4 ± 0.8	18.4 ± 0.8
Weight (kg)	68.7 ± 10.0	74.7 ± 10.5	70.7 ± 9.3	68.6 ± 8.8	66.4 ± 8.5	63.2 ± 8.6
Height (cm)	179 ± 6	180 ± 6	179 ± 6	179 ± 6	179 ± 6	178 ± 7
BMI (kg/m^2)	21.5 ± 2.7	23.0 ± 2.9	21.4 ± 2.5	21.4 ± 2.4	20.8 ± 2.3	20.0 ± 2.4
Current smoker	59	56	59	59	61	61
Haematocrit	45.5 ± 6.5	45.5 ± 6.7	45.6 ± 6.4	45.5 ± 6.6	45.5 ± 6.6	45.5 ± 6.6
Income (thousand euro/year)[a]	18.2 ± 11.0	19.0 ± 13.9	18.6 ± 10.6	18.3 ± 10.5	17.9 ± 10.5	17.0 ± 9.4
Disability pension (%)[a]	1.1	0.8	0.9	1.0	1.1	1.6
Elementary school (%)						
<9 years	0.9	0.2	0.6	0.9	1.2	1.7
9 years	18.5	8.8	14.2	18.8	22.6	27.9
High school	53.3	49.2	54.0	54.8	54.9	53.6
University education	27.2	41.7	31.1	25.5	21.4	16.7
Blood pressure (mmHg)						
Systolic	128 ± 11	130 ± 11	129 ± 11	128 ± 11	128 ± 11	127 ± 11
Diastolic	69 ± 10	69 ± 10	69 ± 10	69 ± 10	69 ± 10	68 ± 10
Diagnosis (%)						
Impaired hearing	9.4	9.0	9.1	9.2	9.4	10.3
Allergic rhinitis	6.9	7.0	6.9	6.9	6.7	7.0
Lumbago	6.9	6.0	6.4	6.7	7.2	8.3
Neurosis	3.6	2.5	3.0	3.1	3.8	5.4
Asthma	2.5	2.4	2.4	2.5	2.5	2.8
Upper resp. infection	1.6	1.3	1.4	1.6	1.8	2.1
Gastritis	1.3	1.1	1.2	1.3	1.3	1.6
Personal disorder	1.2	0.7	0.8	1.1	1.4	2.2
Atopic dermatitis	0.9	0.9	0.9	0.9	0.8	0.9
Drug dependence	0.5	0.3	0.5	0.5	0.5	0.8
Alcoholism	0.4	0.3	0.3	0.4	0.4	0.5
Diabetes	0.07	0.05	0.06	0.07	0.06	0.09

Cut-off limits for the fifth of aerobic fitness (Watt, W) and knee extension strength (Newton, N) are shown.
[a]Assessed at 38 years of age.

CVD as a major cause of mortality and morbidity worldwide,[1] these results are of interest with respect to public health. However, it should be noted that the relationship between aerobic fitness and myocardial infarction is complex, and probably influenced by confounders not investigated in the present study. This could include a genetic predisposition to both a high physical fitness and a low risk of CVD. We have recently found in a Swedish twin cohort that 78% of the variation in aerobic fitness at conscription is associated with genetic factors.[15]

Given that obesity is a key risk factor for MI,[16] and that atherosclerosis is found in arteries already early in life,[12,17] it would be of great value if high physical fitness in adolescence could neutralize the negative effects of obesity with respect to MI later in life. In the present study, high aerobic fitness was significantly associated with a graded

reduced MI risk within any group of BMI, supporting the results of some previous studies in older subjects.[5,18] For example, Lakka et al.[18] found a graded association between higher levels of cardiorespiratory fitness and subsequent acute MI in middle-aged men. However, our results do not support studies in middle-aged and elderly individuals suggesting that obese subjects with high physical fitness may have similar or even lower risk of CVD, or death from CVD, as normal-weight unfit subjects.[9–11,19] Thus, in our cohort, obese and overweight fit men had a significantly higher risk of MI during follow-up than unfit lean or normal-weight men. The different results compared with the studies above could be related to many factors, for example differences in age at baseline and follow-up, and different statistical powers. Furthermore, we investigated a young nationwide unselected cohort of men, in contrast to selected

cohorts of patients with CVD,[9,10] or middle-aged subjects that were well educated and self-selected in many cases.[11]

Several possible mechanisms may link a high level of aerobic fitness in late adolescence to a lower risk of MI. Aerobic fitness has been associated with several established cardiovascular risk factors, including blood pressure, insulin, obesity, and blood lipids.[20,21] Other suggested mechanisms through which greater aerobic fitness may influence the development of CVD include reduced vascular inflammation, reduced thrombogenesis, increased resting fibrinolytic activity, decreased blood clotting, and decreased platelet aggregation.[22–27]

Limitations

Several limitations of the present study should be considered. The nationwide cohort investigated in this study included only young men; hence, the results may not be applicable to women or the elderly. Given that the present study was observational the associations found between physical fitness and MI is no indication of a cause-effect relationship. The effects of smoking could be evaluated only in a sub-cohort of 23 000 men, although adjusting for the effects of smoking in this cohort had no significant effect on the association between muscle strength and MI. Furthermore, the strength of the associations in the sub-cohort with smoking data was very similar to those obtained in the total cohort. However, we could not investigate any effects of smoking on the association between aerobic fitness and the risk of MI. No data were available for some covariates such as cholesterol levels, which could influence the independent association between physical fitness and MI. However, as discussed above, risk factors for CVD, such as cholesterol levels, BMI, and blood pressure, are most likely mediating some of the effects of physical fitness with respect to the risk of CVD rather than being only
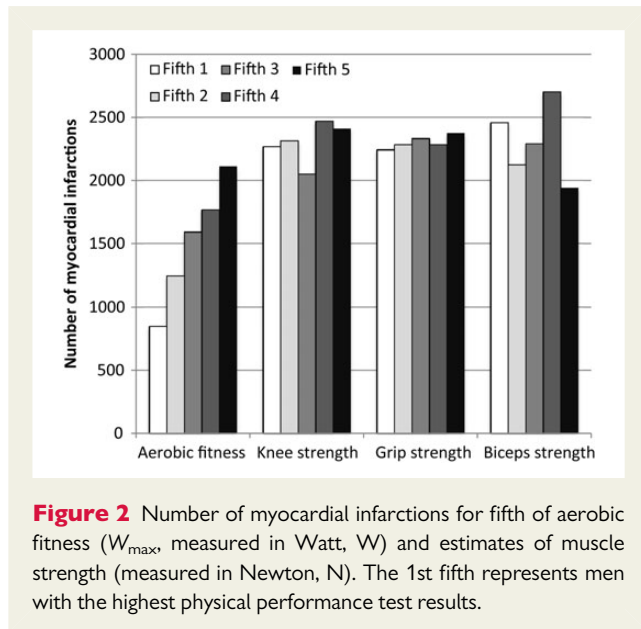

Figure 2 Number of myocardial infarctions for fifth of aerobic fitness (W_{max}, measured in Watt, W) and estimates of muscle strength (measured in Newton, N). The 1st fifth represents men with the highest physical performance test results.

Table 3 Associations between aerobic fitness and estimates of muscle strength and the risk of myocardial infarction during follow-up

Model 1	per SD increase		1st fifth		2nd fifth		3rd fifth		4th fifth		5th fifth		P for trend
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Aerobic fitness (W)	0.76	0.74–0.78	1.00	–	1.27	1.17–1.39	1.55	1.43–1.69	1.66	1.53–1.80	2.15	1.98–2.33	<0.001
Aerobic fitness/weight (W/kg)	0.83	0.80–0.85	1.00	–	1.23	1.13–1.35	1.45	1.33–1.58	1.52	1.39–1.65	1.72	1.57–1.87	<0.001
Knee extension (N)	0.92	0.90–0.94	1.00	–	1.07	1.01–1.13	1.07	1.01–1.14	1.18	1.12–1.26	1.24	1.17–1.32	<0.001
Grip strength (N)	0.91	0.89–0.93	1.00	–	1.09	1.03–1.15	1.09	1.03–1.16	1.27	1.19–1.34	1.29	1.21–1.37	<0.001
Biceps strength (N)	0.96	0.94–0.98	1.00	–	0.99	0.94–1.05	1.06	1.00–1.12	1.07	1.01–1.14	1.07	1.01–1.14	0.002
Model 2													
Aerobic fitness (W)	0.82	0.80–0.85	1.00	–	1.16	1.06–1.27	1.34	1.23–1.47	1.39	1.27–1.51	1.69	1.55–1.85	<0.001
Aerobic fitness/ weight (W/kg)	0.89	0.86–0.93	1.00	–	1.18	1.07–1.29	1.34	1.22–1.46	1.37	1.25–1.49	1.45	1.32–1.59	<0.001
Knee extension (N)	0.95	0.93–0.97	1.00	–	1.04	0.98–1.11	1.04	0.98–1.11	1.13	1.07–1.20	1.13	1.06–1.20	<0.001
Grip strength (N)	0.91	0.89–0.93	1.00	–	1.11	1.04–1.17	1.12	1.06–1.19	1.30	1.22–1.38	1.30	1.22–1.38	<0.001
Biceps strength (N)	0.95	0.93–0.97	1.00	–	1.02	0.96–1.08	1.09	1.03–1.16	1.12	1.06–1.19	1.12	1.05–1.19	<0.001

The different exposures were analysed per standard deviation increase and for fifth, with the 1st fifth representing men with the highest performance. Two Cox regression models are presented: Model 1 was adjusted for age, BMI, and place and year of conscription, and Model 2 was also adjusted for education, socio-economic factors, blood pressure, and the 12 most common diagnoses at conscription (see Table 1).
Aerobic fitness: 1st fifth >282 W, 2nd fifth 255–282 W, 3rd fifth 237–254 W, 4th fifth 216–236 W, 5th fifth <216 W.
Knee extension strength: 1st fifth >639 N, 2nd fifth 570–639 N, 3rd fifth 511–569 N, 4th fifth 451–510 N, 5th fifth <451 N.
Grip strength: 1st fifth >699 N, 2nd fifth 640–699 N, 3rd fifth 590–639 N, 4th fifth 540–589 N, 5th fifth <540 N.
Biceps strength: 1st fifth >440 N, 2nd fifth 391–440 N, 3rd fifth 351–390 N, 4th fifth 310–350 N, 5th fifth <310 N.
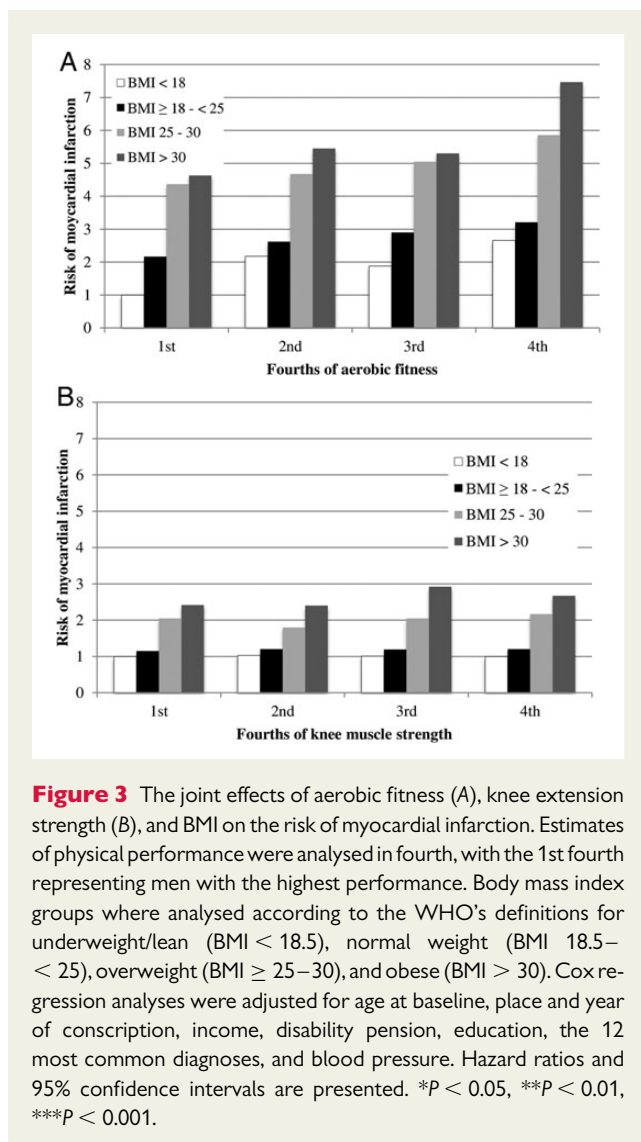SD, standard deviation; HR, hazard ratio; CI, confidence interval; W, Watt; N, Newton.

Figure 3 The joint effects of aerobic fitness (*A*), knee extension strength (*B*), and BMI on the risk of myocardial infarction. Estimates of physical performance were analysed in fourth, with the 1st fourth representing men with the highest performance. Body mass index groups where analysed according to the WHO's definitions for underweight/lean (BMI < 18.5), normal weight (BMI 18.5– < 25), overweight (BMI ≥ 25–30), and obese (BMI > 30). Cox regression analyses were adjusted for age at baseline, place and year of conscription, income, disability pension, education, the 12 most common diagnoses, and blood pressure. Hazard ratios and 95% confidence intervals are presented. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

confounders. Finally, we did not have access to any follow-up data concerning the covariates evaluated in the present study, e.g. physical fitness, blood pressure, and BMI. Adjusting for changes in these covariates during follow-up would most likely strengthen the associations between physical fitness and MI. The strengths of the present study include a large unselected study cohort comprising of Swedish men born predominantly in 1950–66 with objectively measured physical fitness, careful baseline examinations for disease, a total of 24.5 million follow-up years and more than 11 000 MIs.

Conclusions

The present study found a graded association between aerobic fitness in late adolescence and MI several decades later in men. The estimated associations of aerobic fitness with MI risk were consistent in all BMI groups, ranging from underweight to obese. However, the risk of MI remained higher in overweight and obese fit men than in lean and normal-weight men with poor aerobic fitness, suggesting

that high physical fitness cannot compensate for the cardiovascular risk associated with obesity.

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CARDIOVASCULAR FLASHLIGHT

Chest pain 9 months after interventional atrial septal defect occlusion: do not forget the worst!

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Nine months after interventional occlusion of a 27 mm atrial septal defect (ASD) with an Amplatzer 32 mm septal occluder (ASO; AGA Medical), a 45-year-old man presented with chest pain. On transthoracic echocardiography, a pericardial effusion of 5–7 mm could be demonstrated.

Transoesophageal echocardiography showed fluid at the roof of the left atrium (arrow on *Panel A*) towards the posterior aortic wall (*Panel A*: LA, left atrium; RA, right atrium; AO, Aorta; *, ASO). Under the suspicion of an erosion of the LA by ASO, a CT scan was done demonstrating the density of blood in the retroartic fluid (*Panel B*: arrow, retroaortic fluid, LA, left atrium; RA, right atrium; AO, Aorta; *, ASO). The indication for a surgical intervention was established after proof of haemopericardium. Through a midline sternotomy, the chest was opened and 500 mL of blood was removed. From outside the heart, two fibrotic erosions of the LA (*Panel C*: *) and on the posterior aortic wall (*Panel C*: #) could be seen macroscopically. Inside the heart, a white strain of fibrotic tissue on the right atrial side of the ASO could be seen (*Panel D*: arrow). The device was explanted and the ASD closed with a patch.
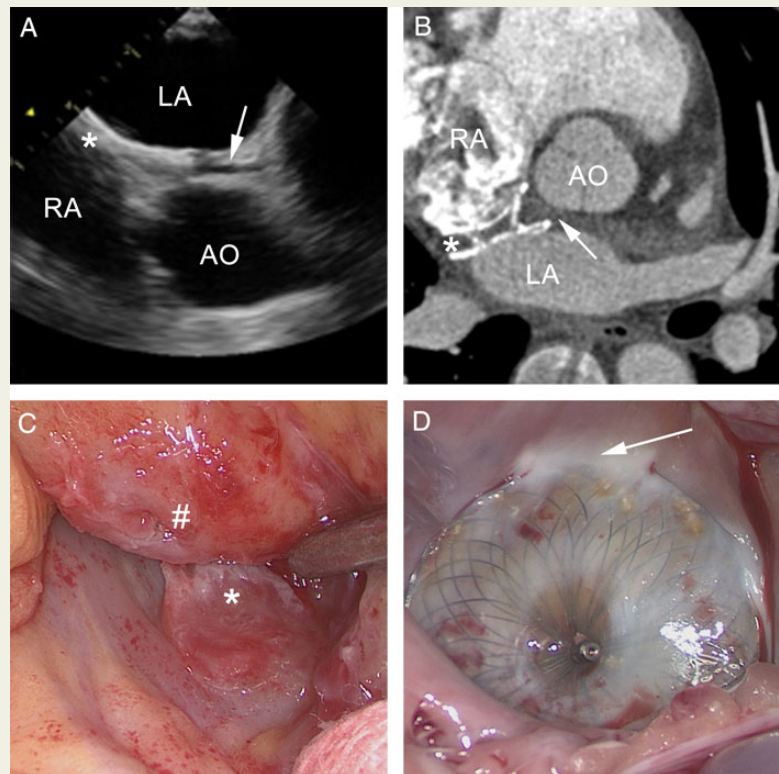
Erosion of the LA roof and posterior aortic wall are possible lethal complications after ASD device occlusion with ASO. As there might be a long interval between implantation and appearance of symptoms the diagnosis might be missed. Deficient anterior superior rims and the use of oversized devices are known as risk factors. Any fluid around the heart even months/years after ASO should be a striking warning not to miss a haemopericardium.