Risk factors, physical activity, and mutual interactions: consolidated knowledge and new frontiers

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There is an inverse relationship, in both men[1] and women[2], between the level of physical activity and the incidence of cardiovascular disease. Among patients with established cardiovascular disease, mortality is lower among those who participate in an exercise program than among those who do not[3].

Physical inactivity is a major risk factor for coronary heart disease (CHD)[4].

Exercise training has a favorable effect on the severity of traditional cardiovascular risk factors such as hypertension, diabetes, hypercholesterolemia, and obesity[5]. However, such influences probably do not account for the overall effect of exercise on cardiovascular disease, since the effect of exercise is independent of the traditional risk factors[1,2,5]. Exercise training also improves myocardial perfusion but has only a limited effect on the extent of atherosclerotic lesions[6], suggesting that morphologic changes in atherosclerotic lesions do not explain the benefits of exercise.

A study with a long-term follow-up[7] demonstrated that subjects participating in sports activities of moderate intensity had a risk of death from any cause 23 to 29% lower than subjects who never engaged in sports. A potential source of bias is that the men who reported participating in sports may have adopted other kinds of health-promoting behavior (such as following a cholesterol-lowering diet) that may have reduced their risk of cardiovascular disease. This is especially true in view of the modest survival advantage (only 9 months of added life) estimated for physically active men, which could readily be explained by confounding variables. Another paper[8] refers to a large cohort of Norwegian men who underwent exercise testing in order to quantify their maximal exercise capacity as a measure of their physical fitness. The relative risk of death from any cause of men in the highest fitness quartile was compared with that of men in the lowest over the subsequent 16 years. Since all the studies were observational in design, no reliable conclusions about cause and effect can be drawn from them. A randomized, controlled trial of physical activity for the primary prevention of cardiovascular disease, which would allow a more rigorous assessment of cause and effect, has never been performed and is probably not feasible because of problems related to compliance and costs. Unfortunately, this leaves a substantial gap in our knowledge that may not be bridged in the near future.

A recent paper[9] investigated the association between leisure-time physical activity and ischemic stroke in a multiethnic population: the Northern Manhattan Stroke Study is a population-based incidence and case-control study. Leisure-time physical activity was significantly protective for stroke after adjustment for cardiac disease, peripheral vascular disease and risk factors. A dose-response relationship was shown for both intensity and duration of physical activity. The Nation Health and Nutrition Examination Survey I (NHANES I)[10], a large epidemiologic follow-up study, demonstrated that the relative risk for stroke (fatal and non-fatal) in white women aged 65-74 years with low non-recreational activity was associated with an increased risk of stroke (relative risk 1.82) after adjusting for the baseline risk factors.

Physical exertion and acute myocardial infarction

Two new reports[11] in the United States[12,13] and in Germany addressed a timely question of special interest: is exercise beneficial or hazardous to your heart?

The authors estimated that the risk of a heart attack during heavy physical exertion (or up to 1 hour after it) was between 2 times greater (in the German study) and 6 times greater (in the US study) than during less strenuous activities or no activity. Heavy physical exertion was again found to be strongly associated with an increased risk of infarction.

It is reasonable to surmise that the increases in blood pressure and heart rate that normally accompany exercise may give rise to hemodynamic shear stresses that, when they act on coronary atherosclerotic plaques, sometimes cause disruption, setting in motion the chain of events which culminate in acute myocardial infarction[11,14-16].

Similar observations were made in marathon runners who were divided according to their marathon running time into three fitness groups: all measured laboratory values such as HDL cholesterol, LDL cholesterol, total cholesterol, triglycerides, blood glucose, and uric acid were superior in the fastest when compared with the slowest runners. These observations corroborated by the findings of Thune et al.[17] suggest the somewhat perplexing possibility of a non-definable upper limit of the dose-response curve between physical activity and risk factors. Specifically, there seems to be no upper limit of exercise level beyond which cardiovascular benefits could not be improved further given that the more the physical activity, the better the risk factors. The only limit to the achievable benefits seems to be the one imposed by the musculoskeletal system. Regular and aerobic physical activity seems as being healthier than other types of activity. Other authors underline that the relation among physical activity is U-shaped when stratifying by age[18].

Physical activity and hypertension

Regular aerobic exercise reduces blood pressure significantly in patients with mild-to-moderate essential hypertension[19] and is now recommended to lower blood pressure in such patients. Even when drug therapy is effective, side effects and cost considerations lead to poor compliance and poorly controlled hypertension. One particular study specifically assessed the effects of regular aerobic exercise on blood pressure and left ventricular hypertrophy in African-American men with severe hypertension[19]. A significant reduction in diastolic blood pressure and regression of left ventricular hypertrophy after 16 weeks of moderately intense aerobic exercise was found, together with a substantial reduction in antihypertensive medication.

Physical activity and smoke

The relationship between sport and smoking habits seems important since subjects who perform maximal aerobic sports do not usually smoke while subjects who play soccer or rugby frequently smoke[20]. It is known that smoking reduces the performance of ventilatory parameters of breathing in proportion to the number of cigarettes: this limitation is particularly evident in subjects who engage in strenuous and/or aerobic activity.

Physical activity and lipids

Irrespective of other confounding variables, each average 100 kcal/day expended in leisure-time physical activity with an intensity > 7 kcal/min during the previous year was associated with an increase of 2.09 mg/dl (0.054 mmol/l) in HDL cholesterol and a decrease of 0.23 in atherogenic index (total/HDL cholesterol). However, only physical activity with an intensity > 9 kcal/min was associated with a decrease in total cholesterol, non-HDL cholesterol, and log (triglycerides). Above the former threshold, the relationship between the amount of physical activity and lipid levels is linear for total cholesterol, HDL cholesterol, non-HDL cholesterol, and atherogenic index and is logarithmic for triglycerides.

Higher insulin sensitivity was also beneficial in subjects with type 2 diabetes and elevated serum cholesterol[21].

Physical activity, fibrinolysis and coagulation

During acute exercise both coagulant and fibrinolytic potentials increase. Since strenuous exertion is associated with an enhanced risk for cardiac events, especially in untrained individuals, it is important to determine whether the initial hemostatic balance is maintained during exercise. During physical activity, while parallel changes in coagulant and fibrinolytic activity occur, this hemostatic balance is not maintained during recovery. This phenomenon could constitute an enhanced risk for coronary artery thrombosis which may contribute to exercise-related cardiovascular events[22,23].

Physical activity and homocysteine

According to a health examination survey by the Norwegian Health Screening Service[24] carried out in 1992 and 1993, total plasma homocysteine levels were positively related to total cholesterol level, blood pressure, and heart rate and inversely related to physical activity. The relations were not substantially changed by multivariate adjustment, including intake of vitamin supplements, fruits, and vegetables. Elevated total plasma homocysteine levels were associated with major components of the cardiovascular risk profile, i.e. male, sex, old age, smoking, high blood pressure, elevated cholesterol levels, and lack of exercise.

Physical activity and genetics

Twin-pairs discordant for CHD can be used to examine the possible contribution of genetic and other familial factors to the relationship between CHD risk factors[25], in particular physical inactivity at leisure, and CHD. Among all men, the age-adjusted relative risk of CHD was 0.52 in men participating in conditioning exercise compared to sedentary men, based on their questionnaire responses. First-degree relatives of female patients with premature CHD are at greater risk for early disease than if the proband is a male patient. To examine coronary risk factors, a sample of healthy offspring of women with documented premature CHD was screened[26]. More than half of the offspring had total and LDL cholesterol levels above the recommended levels for primary prevention, 31% were current smokers, and 56% exercised less than 3 times a week. A high proportion was overweight with a high prevalence of central obesity. A total of 13% had only one major risk factor, a family history of premature CHD, 10% had two risk factors, 23% had three, and 54% had four or more CHD risk factors. Grown-up children of women with premature CHD seem to have a high prevalence of modifiable risk factors and do not consider themselves to be at risk for CHD.

Categories

Females. A large prospective study in females, during an 8-year follow-up[2], indicates that both brisk walking and vigorous exercise are associated with substantial and similar reductions in the incidence of coronary events among women. A moderate-intensity exercise (e.g. brisk walking) for at least 30 min on most (preferably all) days of the week could reduce the risk of coronary events in women by 30 to 40%. Increased walking time or walking with vigorous exercise combined appears to be associated with even greater risk reduction.

Males. In the Copenhagen Male Study[27] the joint effect of fitness and leisure-time activity has been analyzed and followed up for 17 years. In sedentary men, fitness was not a predictor of future risk of ischemic heart disease whatsoever. In medium or highly active men, however, fitness was a strong predictor. The two major new findings of this study were a) that being very fit, provides no protection against ischemic heart disease nor all-cause mortality in sedentary men, and b) that unfit but sedentary men have a higher risk of ischemic heart disease than unfit but active men, i.e. those performing light physical activity, for at least 4 hours per week[28]. In patients with known CHD exercise enables patients to exercise to a higher intensity before reaching their thresholds for myocardial ischemia, including those with exertional angina, regular exercise clearly improves functional work capacity.

Elderly. A randomized placebo-controlled trial[29] demonstrates that a high-intensity, progressive regimen of resistance exercise training improves muscle strength and size in frail elderly people. The aging musculoskeletal system retains its responsiveness to progressive resistance training, and most important, the correction of disuse is accompanied by a significant improvement in the levels of functional mobility and overall activity.

Advantages of physical activity

Endothelial function. According to well-accepted studies[30], physical exertion reduces vasoconstriction and improves blood flow changes in response to acetylcholine, indicating that coronary endothelial function in patients who exercised has improved.

Consequently, improving the production of endothelium-derived nitric oxide by means of exercise training should limit the progression of atherosclerosis. Restoration of nitric oxide-dependent vasodilation in conduit vessels and microvessels should improve myocardial perfusion and limit angina pectoris. Similarly, enhanced endothelial nitric oxide production should limit platelet activation and the risk of thrombus formation, which is an important event in the development of myocardial infarction.

Obesity and insulin sensitivity. A correlation between exercise and serum cholesterol or insulin resistance was studied looking at the change in blood pressure during mild exercise. Changes in diastolic blood pressure, in particular during exercise, are greater in men with type 2 diabetes and with elevated serum cholesterol.

Increased participation in non-vigorous as well as overall and vigorous physical activity was associated with significantly higher insulin sensitivity[21].

Cytokines. Moderate-intensity exercise reduces the secretion of atherogenic cytochines[31].

Anxiety and stress. In addition to the physical benefits of exercise, both short-term exercise and long-term aerobic exercise training are associated with improvements in various indexes of psychological functioning (tests of cognitive functioning, anxiety and depression). Exercise attenuates cardiovascular and neurohumoral responses to mental stress[32,33].

Heart rate. The rise in heart rate during exercise is considered to be due to the combination of parasympathetic withdrawal and sympathetic activation[34]. The fall in heart rate immediately after exercise is considered to be a function of the reactivation of the parasympathetic nervous system.

One problem not completely solved is the design to convince sedentary persons to become active or to increase the activity of less active subjects or patients.

Changing the style of life

After 6 months, the structured program increased cardiorespiratory fitness nearly 3-fold more than the lifestyle program[35].

Recent analyses suggest that the specific stimulus causing adaptations in the cardiorespiratory system may not depend on long duration but on surpassing a threshold of oxygen consumption, perhaps for as little as several minutes[4]. If training is progressive, minimum frequency and duration may be required, thus removing a major barrier to fitness. Emerging evidence indicates that resistance training should also be a core element of such programs[35].

It is more likely for a sedentary person who becomes moderately active to then become vigorously active than it is for a sedentary person to move from being sedentary to vigorously active. If the number of sedentary persons meeting minimal guidelines for activity could be increased from 20 to 30%, then this would be an important public health achievement. There are a wide variety of types, intensities, and patterns of physical activity that provide meaningful health benefits. There is no single best exercise. Depending on initial fitness, health status, personal preferences, and lifestyle, any of several physical activity choices may be the right one for a given individual. To obtain this goal a real and daily interaction among different professional experiences in the field is needed to make the right choices in groups and individuals, to convince them to change their lifestyle and to verify the effects of this action.

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