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Physical Activity and Cardiovascular Disease

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It has been estimated that up to one third of cardiovascular morbidity and mortality are attributable to lack of physical exercise.[1] Increasing physical activity may have substantial health benefits both in the general population and in individuals at high risk such as the elderly and those with known cardiovascular disease. This report reviews evidence that regular exercise reduces cardiovascular risk, describes potential mechanisms for this benefit, and addresses possible hazards of exercise in patients with established cardiac disease.

Epidemiological and cohort studies of exercise and coronary artery disease

In many epidemiological studies, the mortality rate has been lower in physically fit compared with sedentary individuals.[1-5] The differences in risk are substantial. For example, the mortality rate during 16 years of follow-up was approximately four times greater in the least fit compared with the most fit quartile of middle-aged Norwegian men assessed using a bicycle stress test.[4] Substantial differences in risk have also been observed using relatively crude exercise data obtained by questionnaires. In the Nurses' Health Study,[1] there was a stepwise graded reduction in the risk of coronary artery disease according to the reported amount and speed of regular walking. The risk of coronary artery disease was less than half in the most active individuals compared with the most sedentary individuals. Those who increased their usual level of activity by the equivalent of walking briskly for half an hour each day reduced their cardiovascular risk by approximately 40%. This observation suggests that recent levels of physical activity are most important.

In observational studies, regular exercise has also been associated with a lower risk of non-haemorrhagic stroke. In the Nurses' Health Study,[6] walking at an average pace for a total of two hours per week reduced the risk of stroke by 25%, and greater amounts of physical activity were associated with larger reductions in risk. Regular exercise may also reduce non-cardiovascular morbidity and mortality. In the elderly, aerobic exercise and strength training lower the risks of falls and of hip and other fractures, improve physical functioning, and prolong disability-free survival. Improved muscle strength and reduced frailty may increase the ability to cope with illness.[7,8]

Randomised clinical trials of exercise rehabilitation

Clinical trials of cardiac rehabilitation provide evidence that interventions that increase the level of physical activity improve outcomes after myocardial infarction. The Cochrane Collaborators undertook a systematic review of 34 randomised clinical trials of exercise-based cardiac rehabilitation published prior to December 1998.[9] Thirteen were "exercise-only" studies (totalling 2,582 subjects) and 21 compared usual care with "comprehensive cardiac rehabilitation", which included exercise, dietary, lifestyle and stress advice or management (totalling 5,101 subjects). In a pooled estimate, total mortality was reduced by 27% (odds ratio 0.73, 95% confidence interval 0.54-0.98) with exercise-only rehabilitation, and by 13% (odds ratio 0.87, 95% confidence interval 0.71-1.05) with comprehensive cardiac rehabilitation as compared with usual care. The reduction in cardiovascular disease mortality was 31% (odds ratio 0.69, 95% confidence interval 0.51-0.94) with exercise-only rehabilitation and 26% (odds ratio 0.74, 95% confidence interval 0.57-0.96) with comprehensive cardiac rehabilitation. The rate of non-fatal myocardial infarction was not significantly reduced by exercise-only or by comprehensive cardiac rehabilitation. There was insufficient information to reliably assess the effect of the exercise interventions on the rates of coronary artery bypass surgery or coronary angioplasty. The effects on modifiable risk factors such as serum lipids, triglycerides, blood pressure and smoking were small or not statistically significant.

There are, however, weaknesses in the evidence of benefit for exercise-based cardiac rehabilitation. Many individual studies have had methodological limitations. There is heterogeneity between studies in the methods used to screen participants, the timing and duration of the exercise programme, and the types of exercise recommended. There is little evidence regarding the optimal timing of cardiac rehabilitation, its duration and whether certain types of exercise are more beneficial. A further limitation is that the studies predominantly included middle-aged men whose myocardial infarction had occurred at a time when prolonged rest was commonly recommended. There is little information available on the effects of exercise-based cardiac rehabilitation in the elderly, in women, in patients who have undergone cardiac surgery or angioplasty, and in patients with cardiac failure, angina, arrhythmia or heart valve disease. In addition, the relative and absolute benefits of exercise-based rehabilitation are uncertain in patients who receive modern cardiac care such as thrombolysis, statins, angiotensin-converting-enzyme (ACE) inhibitors, angioplasty or coronary artery bypass surgery. The mean follow-up time in the studies included in the Cochrane systematic review was 2.4 years, and there is little evidence of benefit beyond that time.

Exercise and cardiac risk factors

Regular exercise aids in weight reduction and improves insulin sensitivity. The risk of non-insulin-dependent diabetes is reduced by regular exercise in persons at high risk due to obesity, hypertension or a family history of diabetes.[10] Exercise has modest favourable effects on HDL cholesterol levels, triglyceride levels, the coagulation profile, and blood pressure.[11] Although small, in combination these effects may have a moderate impact. In observational studies, about one third of the risk reduction associated with physical activity was explained by adjustment for known cardiovascular risk factors.[1,6] Exercise appears also to reduce risk by other mechanisms.

Exercise and endothelial function

The progression of coronary artery disease, assessed by serial coronary angiography, is greater in individuals with lower levels of leisure time physical activity, and disease regression can occur in those with high levels of physical activity.[12-14] Improvements in exercise capacity and the time to myocardial ischaemia with exercise training are, however, greater than would be expected from the relatively small changes observed at angiography. Regular exercise improves arterial compliance or elasticity, which is a determinant of systolic blood pressure and pulse pressure, and an independent predictor of cardiovascular risk. In addition, recent non-invasive studies have demonstrated that exercise training improves endothelial function.[15] This is likely to be the result of greater synthesis of nitric oxide by endothelial cells in response to repeated shear stress. Flow-mediated release of nitric oxide relaxes vascular smooth muscle and dilates arteries. Nitric oxide may also reduce the progression of atherosclerosis and decrease the likelihood of an acute coronary event by suppressing smooth muscle proliferation, inhibiting platelet aggregation, and reducing adhesion of leucocytes to the vessel wall. Non-specific inflammatory markers such as high-sensitivity C-reactive protein are powerful predictors of cardiovascular risk.[16] It is possible, although not yet established, that an increase in nitric oxide production reduces the inflammatory component of coronary artery disease.

Exercise training improves endothelial function in the coronary arteries of patients with ischaemic heart disease.[17] Diseased segments of the coronary artery may constrict rather than dilate during exercise or with stress, increasing the likelihood of myocardial ischaemia. By improving endothelial function, exercise training reduces this inappropriate vasoconstriction. Exercise training also improves the ability of small coronary vessels to dilate, allowing greater myocardial perfusion in response to increased metabolic demand.[18] Therefore, in addition to any beneficial effect on progression of atherosclerosis, an improvement in endothelial function may increase myocardial blood flow during exercise in patients with inducible myocardial ischaemia. Several studies have demonstrated that exercise training reduces myocardial ischaemia and dyspnoea during exercise.[19]

Exercise and the development of collateral vessels

Although myocardial ischaemia can be hazardous, repeated brief episodes of myocardial ischaemia may be advantageous in patients with stable coronary artery disease by promoting the growth of collateral vessels.[20] Collateral vessels can reduce the size of a myocardial infarction or protect the myocardium from infarction when coronary occlusion occurs on a pre-existing stenosis. Collateral recruitment may also explain "warm-up" or reduced angina after first exercise.[20] Patients with a complete coronary occlusion who have well-developed collateral vessels visible at angiography have a greater "warm-up" response than those with a stenosis and no visible collateral vessels.[20] In animal studies, collateral vessels develop gradually over time in response to myocardial ischaemia. Growth factors that stimulate collateral development and increase collateral flow include vascular endothelial-derived growth factor, which is synthesised in response to hypoxia, and nitric oxide, which is released in response to increased shear stress. The value of exercise training for stimulating development of collateral vessels has, however, been difficult to establish in clinical studies, in part because collateral vessels recruited during the increased metabolic demands of exercise may not be visible at rest. However, recent studies have found evidence of improved myocardial perfusion after exercise training in patients with ischaemic cardiomyopathy.[21]

Risks of exercise

The benefits of exercise need to be balanced against potential hazards, in particular the risk that vigorous exercise can trigger myocardial infarction or sudden death.[22] Myocardial ischaemia and increased sympathetic activity during exercise may induce ventricular arrhythmias. Concerns regarding the risk of exercise training apply particularly to patients with inducible myocardial ischaemia, cardiac failure, or arrhythmias.

The risk of myocardial infarction is on average six times higher during and one hour after vigorous exercise than at rest.[22] The increase in relative risk is greatest in sedentary individuals and lesser in those who exercise regularly. Regular exercise therefore both protects against triggering by vigorous exercise and reduces the risk of myocardial infarction at other times.[22] In contrast, the risk of moderate-intensity exercise is probably very low, even in persons with coronary artery disease. The reported risk of death in cardiac rehabilitation participants is 1 per 784,000 exercise hours, and the risk of myocardial infarction is 1 per 294,000 exercise hours.[23] The risk of myocardial infarction during sexual activity is also very low (approximately 1% of myocardial infarctions), and is even lower in persons who exercise regularly.[22]

Exercise and cardiac failure

In clinical trials, exercise training has improved exercise capacity and wellbeing in patients with cardiac failure.[24,25] Exercise training improves skeletal muscle strength, which is often poor because of physical deconditioning. Muscle weakness is an important contributor to both fatigue and dyspnoea during exercise in patients with cardiac failure. Regular exercise also ameliorates endothelial dysfunction in peripheral arteries, and may decrease peripheral arterial resistance, which is abnormally increased in patients with heart failure.[17] There are limited data to suggest that physical activity may have a favourable effect on left ventricular function.[17,26] Large-scale clinical trials are needed to determine whether exercise training reduces mortality in patients with cardiac failure or poor left ventricular function.

Exercise and the risk of sudden death

The risks and benefits of exercise training in persons at increased risk of sudden death are uncertain. Sudden death is more likely during vigorous exercise than at rest,[27] but regular moderate-intensity exercise may lower the overall risk. In the meta-analysis of randomised trials of cardiac rehabilitation, the risk of sudden death was significantly lower in persons randomised to an exercise programme during the first year (odds ratio 0.63, 95% confidence interval 0.41-0.97), but the risk reduction after three years of follow-up was not statistically significant.[28] The beneficial effects of exercise on the progression of coronary artery disease and myocardial perfusion would be expected to reduce the risk of sudden death. Regular exercise slows the heart rate and improves measures of autonomic imbalance, such as heart rate recovery, which are predictors of mortality after myocardial infarction and in patients with heart failure.[29]

Exercise stress testing

The American College of Sports Medicine[30] and the American Heart Association[31] recommend exercise stress testing prior to exercise training in persons with known or suspected cardiac disease.[32] They also recommend exercise stress testing for asymptomatic persons over 40 years of age who have one or more cardiovascular risk factors and are planning a vigorous exercise programme. These recommendations are based on expert opinion, and reflect concern that vigorous exercise may trigger myocardial infarction or sudden death, a risk which is higher in sedentary individuals who abruptly take up vigorous exercise. However, because of limited resources, these recommendations are difficult to apply in New Zealand. In addition, the benefits of pre-exercise cardiac evaluation in persons with no evidence of cardiovascular disease are not established, and there are limitations to this approach.[33] Myocardial infarction and sudden cardiac death commonly result from abrupt coronary occlusion, triggered by rupture or erosion of a lipid-laden plaque. Because the majority of plaques do not restrict coronary flow, an exercise test is often normal prior to the first coronary event. Furthermore, limited access to exercise testing and specialist advice should not be a barrier to recommending more exercise, because the benefits of moderate regular exercise almost certainly outweigh the risks even in persons with unrecognised coronary artery disease. While a specialist assessment and routine exercise testing may occasionally detect individuals with unsuspected severe coronary artery disease, current evidence suggests that routine stress testing is probably unnecessary for most individuals before beginning exercise training, provided the level of physical activity is gradually increased and unusually vigorous activity is avoided. Prompt assessment by a cardiologist is important when cardiac disease is suspected or if suggestive symptoms occur.

Advice to patients

The American Heart Association recommends 30 minutes of moderate-intensity exercise on most days for all adults.[34] This exercise can be divided into two or three periods of 10-15 minutes each, and can be incorporated into normal daily living.[35] The greatest body of evidence is for aerobic training, but resistance training is also beneficial and safe.[36] A gradual increase in physical activity is important, particularly in patients who are normally sedentary and in those with inducible myocardial ischaemia or poor left ventricular function. Moderate-intensity exercise is safer than vigorous exercise, and is more likely to be maintained in the long term. It is important to take an individual approach and to consider the environment, the social circumstances, other health problems and the need to avoid musculoskeletal injury. A supervised cardiac rehabilitation programme should be considered, if available, for patients with heart failure and for those who have had a myocardial infarction, coronary artery bypass grafting or angioplasty.

The evidence for benefit is compelling: patients at risk or with known cardiovascular disease should be encouraged to exercise for pleasure and for their health.

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