HEART

Editorial

Physical activity and the triggering of myocardial infarction: the case for regular exercise

Exercise can both prevent and cause acute myocardial infarction and sudden cardiac death. This paradox has led to uncertainty about clinical recommendations and to a need for further research on the mechanisms of these opposing effects.

Though it has been difficult to obtain conclusive evidence in a single study that exercise prevents acute cardiovascular disease, prospective studies have shown an association between increasing levels of regular physical exertion and decreasing cardiovascular event rate. The weight of evidence of a beneficial effect in both men and women is such that a sedentary lifestyle has recently been identified as a risk factor as important as hypertension, hypercholesterolaemia, or cigarette smoking.[1] Physical activity favourably influences several risk factors, such as total cholesterol, HDL cholesterol, and triglycerides.[2] In addition, physical activity is associated with reduced blood pressure, improved glucose tolerance, increased insulin sensitivity, and reduced blood coagulability.[3] In conjunction with dietary changes, exercise has been shown to aid in weight loss. Exercise training has also been associated with an increase in heart rate variability and baroreflex sensitivity, markers of vagal activity and responsiveness. Vagal activity has been shown to have an antifibrillatory effect.[4] As Tunstall Pedoe has already pointed out, it is negative to think of exercise purely as an insurance policy against possible future coronary events.[5] "Exercise should be a pleasure and bring its own immediate rewards. Fortunately, exercise, after the initial breaking in period, is usually enjoyable, improves the exerciser's self image and has a large number of other health benefits."[5]

Does physical exertion trigger myocardial infarction?

Whereas data indicating that regular exercise is protective are convincing, numerous anecdotal cases, from the first marathon runner onwards, have linked physical exertion to precipitation of infarction and sudden death. Interest in the triggering hypothesis has been renewed by observations that myocardial infarction, sudden cardiac death, stroke, and transient myocardial ischaemia all show a prominent circadian variation characterised by a morning peak in incidence.[6] These findings have led to examination of the frequencies with which possible triggers are reported by patients. Almost half (48%) of 849 patients from the Multicenter Investigation of Limitation of Infarct Size (MILIS) indicated exposure to one or more possible triggers, including moderate physical activity (14%) and heavy physical activity (9%).[7] Although this study, and others like it,[8] support the role of triggering, they are limited by a lack of appropriate control data to calculate relative risks of potential triggers. This need for control data shaped the design of the Myocardial Infarction Onset Study (MIOS), an ongoing multicentre investigation to identify and characterise triggering of onset of acute myocardial infarction.[9] The study uses a new epidemiological technique, called the case-crossover design. Patients undergo an extensive interview covering the 26 hour interval before the infarction to determine the frequency and level of physical activity and other potential triggers. Data for a "hazard period" immediately before infarction onset, are compared with either a "control period" at the same time on the prior day or the usual frequency of the activity.

In MIOS 4·4% of subjects reported heavy exertion within an hour before the start of infarction. Heavy exertion was classified as 6 METS or more, and was regarded as at least vigorous, with panting and sweating. The range of activities included jogging, speed walking, shovelling snow, heavy gardening, and overhead work.[9] The case-crossover method indicated that the relative risk of infarction onset in the hour after strenuous exertion was 5·9 (95% CI 4·6 to 7·7). Among sedentary individuals who usually exercised less than once a week, the relative risk was 107 (65 to 171). The relative risk fell markedly with increasing frequency of exertion: one to two times per week 19·4 (9·9 to 38·1), three to four 8·6 (3·6 to 20·5), and five times or more per week 2·4 (1·5 to 3·7). There was a non-significant trend ($P = 0·11$) toward an increased relative risk of infarction after exertion among patients over 70 years of age, in part, because they had a lower prevalence of regular exercise. There was, however, no increase in relative risk among patients who had a past history of angina or infarction. Similar findings to MIOS were published concurrently from Germany by Willich and colleagues.[10]

Although sexual activity is associated with an average energy expenditure of 3–4 METS, a lower level than that associated with triggering the onset of myocardial infarction, preliminary data from MIOS study indicate that sexual activity can trigger infarction. Among the 761 subjects who reported that they were sexually active in the year preceding infarction, 22 (3%) reported sexual activity in the 24 hours preceding MI, whereas according to their reported usual annual frequency only 10·5 would have been expected to have reported sexual activity in this period. This case-crossover analysis yielded a relative risk of 2·1 (95% CI 1·3 to 3·3) for infarction within two hours after sexual activity.[11]

Physical exertion may trigger infarction in several ways. First, haemodynamic stress may trigger the disruption of a vulnerable, but not necessarily stenotic atherosclerotic plaque. Second, in the presence of endothelial dysfunction, vasoconstriction rather than dilatation may occur with physical as well as emotional stress. Narrowing of stenotic segments may lead to increased shear forces and platelet deposition. Third, in patients with coronary artery disease, exercise may induce a prothrombotic state char-

acterised by platelet activation and a reduced fibrinolytic response and reduced prostacyclin release.[12 13]

What advice should patients be given?

A common initial reaction to recognition of a possible triggering activity is to assume that efforts should be made to urge patients to avoid such activity. In most cases, this is not appropriate. First, many potential triggers such as an unexpected physical and psychological stress cannot be avoided. Second, avoidance is often recommended because the difference between relative and absolute risk has not been considered. While relative risk may transiently increase to an enormous extent with a potential trigger (as noted above, heavy exertion increases relative risk over 100-fold in a sedentary individual) absolute risk increases only a small amount, because the baseline risk of an event occurring in any given hour is extremely low. The absolute risk of sudden cardiac death also remains low, although it is much higher in cardiac patients than in apparently healthy people (1:60 000 *v* 1:565 000 person-hours of vigorous exercise).[14] However, when viewed again from the perspective of relative risk, the likelihood of a cardiac arrest was sixfold higher during the exertion in the rehabilitation programme and 164-fold higher during exercise tests. These large increases in relative risk, which seem to rise with increased levels of exertion, highlight the difficulty in determining the proper level of exertion to recommend. Because of the increased and variable baseline risk in patients with known cardiovascular disease, the risks and benefits of heavy physical exertion must be assessed by the patient's own physician.

Several comments regarding clinical implications can be made. First, when a sedentary individual decides to start an exercise programme, consultation and assessment of cardiovascular risk by a physician is helpful. Risk stratification will provide an invaluable insight into recommendations. Second, individuals will lessen the hazards of physical exertion by starting an exercise regimen gradually, using warmup procedures, avoiding overexertion, and seeking medical attention promptly if symptoms develop on exertion. Too many patients are reluctant to seek attention for warning symptoms. Third, it seems reasonable to provide patients taking anti-ischaemic and antihypertensive therapy with adequate pharmacological coverage during the morning and other times of increased risk of infarction onset. Fourth, patients with unstable angina or infarction should avoid vigorous exertion until the results of a further workup and risk stratification are known.

The optimal amount and intensity of exercise remains a subject of ongoing debate and shifting guidelines.[15 16] Among healthy subjects with no history of coronary artery disease, the training effect provided by vigorous exercise seems to provide added benefit. For most people with known coronary disease, walking daily provides a low risk initial activity. In patients undergoing rehabilitation after myocardial infarction, Goble and colleagues found that a low intensity group exercise programme was almost as effective in the short term as aerobic exercise training and was as effective at one year.[17] Although dynamic exercise is necessary to improve cardiovascular endurance, moderate intensity resistance training increases strength and muscular endurance. While supervised resistance training using a specified programme of light to moderate intensity workloads can be undertaken by low risk patients, its safety in high risk patients has not been well evaluated. A recent American College of Cardiology task force, chaired by Dr Paul Thompson, provided specific guidelines for activity level and intensity and emphasised the importance of initial risk stratification.[18] The value of individuals finding an exercise programme that they can perform consistently is supported by evidence that the protective effect of regular exertion persists only during the months or years that the individual engages in regular exertion. Thus the protective effect of exercise requires continued exertion.

The finding that more infarcts occur in the morning raises questions about the desirability of exercise in the morning. At present, although theoretical concerns can be raised, there is no evidence that exercise in the morning induces a higher relative risk than exercise at other times of the day. Murray and colleagues found no difference in risk between individuals who attended cardiac rehabilitation programmes in the morning and those who attended in the afternoon.[19]

As well as these practical applications, recognition that triggering occurs opens up several research avenues. First, studies are needed to determine whether the identification of exaggerated haemodynamic, prothrombotic, or vasoconstrictor responses to stressors can improve the current prediction of acute myocardial infarction.[20] Second, whereas exercise testing may identify patients with significant obstructive coronary artery disease, the future challenge is to identify the plaque that is vulnerable to rupture—hypothesised to be lipid rich with a thin fibrous cap and increased macrophage activity. Third, we need to identify treatments that can interrupt the link between the stressors and disease onset. β Adrenergic blocking agents, which attenuate the increased morning risk of ischaemia and infarction,[21 22] may inhibit the stressor response more effectively than other antihypertensive or anti-ischaemic agents.

A renewed focus on prevention is needed because with treatment alone there can be no major gains against a disease that often causes sudden death outside hospital. For example, despite the enormous and continuing effort thrombolytic therapy is unlikely to prevent more than 5% of the annual deaths from infarction and sudden cardiac death. From the public health perspective, the protection against triggering of myocardial infarction afforded by regular exercise, provides further evidence for encouraging regular physical activity. An exercise programme will lower the baseline risk, and also decrease the relative risk that an episode of heavy physical exertion will trigger a myocardial infarction.

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