Physical activity for cardiovascular disease prevention

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Introduction

Cardiovascular disease is the primary cause of death in Italy and across the European Union[1] and health services of the European countries are strongly committed in the research of interventions able to reduce cardiovascular risk. Clear scientific evidence is now available linking regular aerobic physical activity to a significant cardiovascular risk reduction[2-4], while a sedentary lifestyle is currently considered one of the five major risk factors for cardiovascular disease[5]. In Italy, the physical activity habits of the general population have been recently explored and available data indicate that 34 and 46% of Italian men and women, respectively, are not involved in regular aerobic leisure-time physical activity[6], and that 18 and 22% of Italian men and women, respectively, can be classified as obese (body mass index $\geq$ 30 kg/m^2)[6]. Moreover, data from the ISYDE (Italian Survey on Cardiac Rehabilitation) project show that < 50% of patients eligible for cardiac rehabilitation are currently offered this service in Italy[7]. It thus seems reasonable to supply institutions and individuals with information on how to implement effective strategies for the adoption of a physically active lifestyle, so as to help them to effectively incorporate physical activity into their daily life both in the primary and the secondary prevention settings. This paper summarizes the available scientific evidence dealing with the relationship between physical activity and cardiovascular health in primary and secondary prevention, and focuses on the preventive effects of aerobic physical activity, whose health benefits have been extensively documented.

Primary prevention

In healthy subjects, aerobic physical activity and cardiorespiratory fitness are associated with a significant reduction in the risk of all-cause mortality in a dose-response fashion[2-5,8,9]. The preponderance of evidence suggests that the risk of dying during a given period declines progressively with increasing levels of physical activity and cardiorespiratory fitness; this seems to be true both for men and women and across a broad range of ages from childhood to the very elderly. As these conclusions are based on results of observational studies, there may have been a selection bias, linked on the one hand to the existence of subclinical, undiagnosed diseases which might have led some individuals to reduce their physical activity level before the beginning of the study, and on the other hand to the tendency for healthier lifestyle habits (such as smoking avoidance and a healthier diet) to be found more often in physically active individuals. However, studies controlling for these potential confounders still observed an inverse association between physical activity or cardiorespiratory fitness and all-cause mortality. Most of this reduced mortality effect seems to be based on a decrease in cardiovascular and coronary artery disease mortality, and the level of decreased coronary risk attributable to regular aerobic physical activity is similar to that attributable to other lifestyle factors, such as smoking cessation. Available data relative to 2 286 806 person-years for studies of physical activity and to 317 908 person-years for studies of cardiorespiratory fitness[10] indicate that the risk of cardiovascular disease (including coronary artery disease and stroke) or coronary artery disease alone is significantly reduced in more physically active or fit persons, the relative risk reduction being nearly twice as great for cardiorespiratory fitness than for an increase in physical activity at all percentiles > 25th. A possible explanation for the stronger dose-response gradient for fitness than for physical activity is that fitness is measured objectively, whereas physical activity is assessed by self-reports that may lead to misclassification and a consequent bias toward weaker physical activity/health benefits associations[11].

The reduction in cardiovascular and coronary artery disease mortality in physically active or fit individuals finds its biological rationale in the effects of aerobic exercise on the cardiovascular system and cardiovascular risk factors. Regular aerobic physical activity results in improved exercise performance, which depends on an increased ability to use oxygen to derive energy for work. An improvement in both maximal cardiac output and peripheral oxygen extraction contributes to such an increase in maximal oxygen uptake. These effects are attained for regular aerobic physical activity intensities which range between 40 and 85% of heart rate or VO_2 reserve, with higher intensity levels being necessary the higher the initial level of fitness, and vice versa[12-14]. Aerobic exercise also results in decreased myocardial oxygen demands for the same level of external work performed, as demonstrated by a decrease in the product of heart rate and systolic blood pressure, so reducing the likelihood of myocardial ischemia[4,13]. Moreover, animal studies have demonstrated that the coronary circulation may also be modified by aerobic exercise, with an increase in the interior diameter of major coronary arteries and formation of new myocardial capillaries and arterioles[15]. Additional reported effects of aerobic exercise are an antithrombotic effect through a decrease in platelet adhesiveness, a reduction in the arrhythmic risk via a favorable modulation of the autonomic balance[16], and an improvement in endothelial function[17]. Physical activity also has a positive effect on many of the established risk factors for cardiovascular diseases, preventing or delaying the development of high blood pressure in normotensive subjects and reducing blood pressure in individuals with hypertension, increasing HDL cholesterol levels, helping to control body weight, and lowering the risk of developing non-insulin-dependent diabetes mellitus[4,13]. Overall, the above-mentioned effects tend to ameliorate the coronary risk profile and curtail the development of atherosclerosis, so reducing the risk of cardiovascular and coronary artery disease mortality.

Available data and guidelines suggest that a volume of moderate intensity aerobic physical activity of about 1000 kcal/week is sufficient to yield a reduction in the risk of all-cause and cardiovascular mortality by about 20-30%[2-5,18,19], and that higher volumes of physical activity may translate into greater health benefits. An energy expenditure of 1000 kcal/week is achievable with ≥ 30 min of moderate intensity aerobic physical activity performed most, and preferably all, days of the week. The minutes of daily activity may be performed in a single session or accumulated in multiple bouts each lasting at least 8-10 min. Examples of aerobic physical activity involve not only sport-related activities such as hiking, running or jogging, skating, bicycling, rowing, swimming, cross-country skiing, and taking part in aerobic classes, but also common lifestyle activities such as walking briskly, climbing stairs, doing more house- and yard-work, and engaging in active recreational pursuits. However, it should be pointed out that the concept of moderate intensity physical activity is potentially misleading in that what constitutes moderate intensity activity for a middle-aged man would be low intensity for a young man and high intensity for an 80-year-old. Hence moderate intensity aerobic activity would be better expressed in terms of its relative, not absolute, intensity as an activity performed at 45-60% of the heart rate or VO_2 reserve and/or 50-70% of the maximal predicted heart rate and/or at a rate of perceived exertion of 11-13 on the 6-20 Borg scale[4,20,21]. This would correspond to an energy expenditure of about 4.8-7.1 METs in the young, 4.5-5.9 METs in the middle-aged, 3.6-4.7 METs in the elderly, and 2.3-3 METs in the very elderly (Table I)[4,20-22]. However, recent data suggest that the volume of physical activity needed to obtain significant cardiovascular benefits may be < 1000 kcal/week in subjects with a low physical fitness (i.e. older persons), provided that their effort be perceived as moderate intensity[23].

In summary, healthy individuals of both sexes and of all ages should perform moderate intensity aerobic physical activity for at least 30 min per day most, but preferably all, days of the week, in order to achieve a weekly energy expenditure of about 1000 kcal. Such a physical activity-related energy consumption will translate into a reduction of about 20-30% of the all-cause, cardiovascular and coronary artery disease mortality, and higher volumes of physical activity are likely to produce even greater benefits. On the basis of the available evidence, the target of 1000 kcal/week may be divided into several short bouts of exercise, which highlights the value of incidental physical activity (i.e. climbing stairs instead of taking the elevator and walking instead of going by car). The term "moderate intensity physical activity" should be intended as relative to the individual's maximal aerobic power, i.e. a physical activity of a progressively lower intensity will be required with increasing age and/or decreasing cardiovascular fitness.

Secondary prevention

In the secondary prevention setting, aerobic physical activity is considered as an exercise training intervention within a structured and comprehensive cardiac rehabilitation program. For this reason, available data

Table I. Moderate intensity leisure-time physical activities for healthy subjects as related to age (45-60% of heart rate and/or VO_2 reserve).

	Young (20-39 years) 4.8-7.1 METs	Middle-aged (40-64 years) 4.5-5.9 METs	Old (65-79 years) 3.6-4.7 METs	Very old (≥ 80 years) 2.3-3 METs
Bicycling	18-20 km/hour 100-125 W	16-18 km/hour 75-100 W	14-16 km/hour 50-75 W	– ≤ 50 W
Home activities	Moving furniture, household Carpentry, outside house	Cleaning, vigorous effort Carpentry, finishing furniture Laying or removing carpet Planting, inside or outside house Playing with children, vigorous	Cleaning, moderate effort Food shopping, grocery cart Playing with children, moderate Child care, standing	Cleaning, light effort Sweeping floors Playing with children, light Child care, sitting Wash dishes, cooking
Lawn and garden	Gardening with heavy power tools Mowing lawn, walk, hand mower Shoveling, snow, by hand Chopping wood	Digging, spading, filling garden Mowing lawn, walk, power mower Planting trees Carrying, stacking wood	Raking lawn Sacking grass, leaves Trimming shrubs or trees	Mowing lawn, riding mower Seeding a lawn
Running	Jogging, general	–	–	–
Sports	Basketball, non-game, general Tennis, general Skating, roller Soccer, non-game, general	Softball or baseball, general Children's games Volleyball, game, general	Golf, general Coaching (soccer, basketball, etc.) Table tennis Horseback riding, general	Billiards Bowling
Walking	Walking, 5-6 km/hour, uphill Carrying 7-10 kg, upstairs Hiking, cross country Climbing hills with 0-5 kg load	Walking, grass track Carrying 1-6 kg, upstairs Walking, 7 km/hour, level	Carrying infant or 5 kg load, level Walking, 5-6 km/hour, level Walking the dog	Pushing stroller with child Walking, 2-4 km/hour, level

From Ainsworth et al.[22], modified.

deal almost exclusively with cardiovascular fitness measurements and not with habitual physical activity level evaluation. This is due to the need of both a formal evaluation of the exercise-associated risk and a lifestyle behavioral change in patients with established cardiac, and especially coronary, disease. Cardiac rehabilitation has thus been defined as the coordinated sum of the interventions required to ensure the best possible physical, psychological and social conditions so that patients with chronic or post-acute cardiovascular disease may, by their own efforts, preserve or resume optimal functioning in society and, through improved health behaviors, slow or reverse the progression of disease[24-27]. According to the recently published position paper on secondary prevention through cardiac rehabilitation of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology[28], cardiac rehabilitation interventions should be integrated in a multifactor, comprehensive long-term program including: clinical assistance and optimized medical or interventional treatment, appropriate cardiovascular risk evaluation, education and counseling, adequate follow-up, and exercise training. In this context, the effects of physical activity alone on cardiovascular risk may not be easily discernible. However, a recent meta-analysis[29] of 8440 patients (mainly middle-aged males), most with a previous acute myocardial infarction, the remaining being previous coronary artery bypass or percutaneous transluminal coronary angioplasty (PTCA) patients or subjects with stable angina pectoris, showed a 31 and 26% reduction in the total cardiac mortality for exercise only and comprehensive rehabilitation programs, respectively; these percentages rose to 35 and 28% respectively when only the mortality due to coronary artery disease was considered. Neither exercise alone nor comprehensive rehabilitation interventions were found to have any effect on the occurrence of non-fatal myocardial infarction, whereas insufficient data were available as to the effects of physical activity alone and cardiac rehabilitation on revascularization rates. The reason for the apparent absence of any difference between exercise alone and comprehensive rehabilitation programs on the cardiac mortality rate reduction is not clear. The extreme heterogeneity between the available secondary prevention trials in terms of study design, quality, type and length of exercise and non-exercise interventions, and study populations must be considered. In addition, the mean follow-up of the available trials was limited to 2.4 years; as physical exercise is a type of human activity highly affected by socio-psychological factors and, since compliance with exercise programs is usually poor and strictly dependent on appropriate counseling and educational interventions[26], it seems likely that follow-ups of longer duration would better underscore the utility of the comprehensive rehabilitation approach. It must also be considered that the ever more extensive use of thrombolysis, the improvements in myocardial revascularization techniques, and aggressive pharmacological treatments during the past 15 years have progressively resulted in a relatively low-risk general population of cardiac patients, in which significant survival improvements are less likely to occur as a result of any added intervention. In this clinical setting, mortality and reinfarction should probably not be the only endpoints to evaluate in determining the effectiveness of physical activity interventions, but also other descriptors focused on quality of life, functional independence, and performance of daily activities assessment should be part of the standard outcome measures for all cardiac patients. In any case, recent data confirm the existence of an inverse dose-response relationship between cardiovascular fitness (evaluated by treadmill stress testing and expressed in METs) and all-cause mortality in a population of 3679 cardiovascular patients, defined as subjects with a history of angiographically documented coronary artery disease, myocardial infarction, coronary bypass surgery, PTCA, congestive heart failure, peripheral vascular disease, or signs or symptoms suggestive of coronary artery disease during an exercise test; the results were the same irrespective of the use of beta-blocking agents[30].

The mechanisms proposed to justify the positive effects of aerobic physical activity in secondary prevention are the same as those for primary prevention, i.e. decreased myocardial oxygen demands for the same level of external work, a favorable modulation of the autonomic and coronary endothelial functions, an improved cardiovascular risk factor profile, an improved cardiovascular fitness, and an increased patient surveillance[26]. This, together with technological advances leading to an ever earlier detection of atherosclerosis in asymptomatic individuals, tends to weaken the dividing line between primary and secondary prevention. Indeed, recent clinical indications for inpatient and outpatient cardiac rehabilitation programs from the American College of Sports Medicine[20] include both established cardiac disease and the presence of coronary risk factors in otherwise healthy subjects.

In the secondary prevention setting, exercise prescription is strongly conditioned by the exercise-related risk, estimated on the basis of established risk stratification criteria[13,19,24,25,31]. Low-risk patients may be assigned an exercise prescription similar to that of apparently healthy individuals, i.e. a volume of moderate intensity activity of about 1000 kcal/week, with the frequency, duration, and supervision of the physical activity sessions individualized on the basis of their clinical characteristics. Moderate-to-high-risk patients should follow a strictly individualized exercise prescription, the volume of which may or may not reach the abovementioned threshold of 1000 kcal/week depending on the metabolic load that is known to evoke abnormal signs or symptoms. However, even in patients with more severe pathology, small amounts of properly supervised physical activity are beneficial in that they help to maintain an independent lifestyle and counteract disease-related depression.

In summary, all patients who have suffered cardiac, in particular coronary, events or who are known to be affected by any asymptomatic cardiac disease should undergo exercise-related risk stratification and be offered a cardiovascular rehabilitation comprehensive program. Low-risk male middle-aged patients who have suffered myocardial infarction should perform moderate intensity aerobic physical activity for at least 30 min per day most, if not all, days of the week in order to achieve a weekly energy expenditure of about 1000 kcal, which will yield a cardiac mortality reduction of about 20-30%. As for the primary prevention setting, incidental physical activity may be promoted as a useful way for patients to achieve their scheduled volume of weekly energy expenditure. Even though there seems to be no biological reason why patients who are older or female or who have undergone myocardial revascularization procedures should not obtain the same benefit from physical activity interventions, clear scientific evidence regarding this aspect is still unavailable to date. Moderate-to-high-risk cardiac patients must be given an individualized exercise program and receive an exercise prescription within the limits imposed by their disease.

Conclusions

In the year 2000, 64 555 Italians suffered from acute myocardial infarction and were discharged alive from hospital; in the same year, 55 568 Italians underwent PTCA procedures, 28 267 coronary artery bypass grafting, 17 439 cardiac valvular surgery, and 290 heart transplantation[32]. Had physical activity been adequately promoted by the Italian institutions responsible for primary prevention, the above cited number of events would have probably been much lower, with a significant economic and social gain. Unfortunately, policies for a population-wide approach to primary cardiovascular prevention are lacking, and only limited local experiences regarding the implementation of primary prevention programs are currently available in Italy[33]. Moreover, the Italian Survey on Cardiac Rehabilitation[7] reported an involvement in cardiac rehabilitation programs of 17, 6, 76, and 51% of patients with a recent acute myocardial infarction, PTCA, coronary artery bypass graft, and cardiac valvular surgery, respectively, underlining both the heterogeneity and quantitative inadequacy of the secondary prevention program availability in our country.

In conclusion, in Italy a large gap seems to exist between the required and actually existing primary and secondary cardiovascular prevention interventions. In an era of paramount attention to the cost of any intervention in the health sector, physical activity appears to be a simple tool for large-scale cardiovascular disease prevention with an extremely favorable cost-effectiveness profile. The Italian government and Healthcare Service should be aware of the unique opportunity that physical activity offers to significantly improve the health and quality of life of their population and significantly reduce healthcare costs.

Terminology

Physical activity. Any bodily movement produced by contraction of skeletal muscles and resulting in energy expenditure above the basal level[21,34]. A distinction may be drawn between leisure-time physical activity (with sports, recreational, and exercise/training as subcategories) performed during free time and based on personal interests and needs, and occupational physical activity, associated with the performance of a job. Moreover, physical activity may be classified as aerobic or anaerobic depending on the metabolic pathways predominantly involved in the energy production for the particular type of activity. Physical activity is usually measured by questionnaires or interviews which may yield a quantitative or semi-quantitative estimate of the energy expenditure associated with leisure-time and/or occupational physical activities performed by an individual over a given period of time.

Exercise (or exercise training). A subcategory of leisure-time (and possibly occupational) physical activity in which planned, structured, and repetitive bodily movements are performed to maintain or improve one or more attributes of physical fitness.

Physical fitness. The ability to carry out daily tasks with vigor and alacrity, without undue fatigue and with ample energy remaining to enjoy leisure-time pursuits and meet unforeseen emergencies[21,34]. Physical fitness involves a set of attributes (i.e. cardiorespiratory endurance or fitness, skeletal muscle endurance, skeletal muscle strength and power, flexibility, agility, balance, reaction time, body composition) related to the ability to perform physical activity. Physical fitness may be differentiated into performance- (or skill-) related fitness and health-related fitness, linked to those attributes that favor morbidity and mortality risk reduction and quality of life improvement (i.e. cardiorespiratory endurance, muscular strength and endurance, body composition, and flexibility). Cardiorespiratory endurance or fitness is a component of physical fitness defined as the ability of the cardiovascular and respiratory systems to supply oxygen to the working muscles during dynamic exercise, and is usually measured as maximal oxygen uptake.

Volume of physical activity. Total energy expenditure associated with a physical activity and equal to the product of its intensity (expressed as oxygen uptake in ml/kg/min or METs or as kcal), frequency and duration[35]. Energy expenditure can be estimated by indirect calorimetry measuring respiratory gases; oxygen uptake is converted to kcal using a constant of 5 kcal/l.

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