PHYSICAL ACTIVITY AND CARDIOVASCULAR DISEASE PREVENTION IN EUROPE: AN UPDATE

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Review
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Abstract:

This paper summarizes the evidence on the relationship between physical activity (PA) and cardiovascular disease (CVD) that has been published mainly during the past 10 years. The primary focus is on aspects related to the primary prevention of the clinical events of coronary heart disease and stroke. The material was collected by conducting a search of the Medline, Embase and Cochrane electronic databases to identify systematic reviews and meta-analyses having been published on the relationship between PA and CVD since 2002. The terms used for the exposure were *physical activity* or *exercise*, and for the outcome the following terms: *cardiovascular disease*, *coronary heart disease*, *coronary artery disease*, *coronary disease*, *myocardial infarction*, *stroke*, *peripheral vascular disease* or *peripheral arterial disease*. In addition, committee reports on the topic were identified through scientific meetings and by personal communication. A large majority of the studies included in the reviews were prospective cohort studies of at-risk populations.

The quantity and quality of scientific data on the cardiovascular and other health-related effects of physical activity has increased greatly during the past decade. The evidence now shows convincingly that insufficient physical activity is one of the key causal risk factors of CVD, particularly of the most prevalent of them, CHD and stroke. The effects of insufficient physical activity are mediated partly through the traditional major risk factors, and partly they are independent. This rather recently shown fact emphasizes the essential, irreplaceable role of PA for cardiovascular health.

Strong epidemiological evidence indicates that a major part of the preventive effect of PA can be attained by activity that is applicable on a large scale in all European populations: moderate-intensity endurance or aerobic activity such as brisk walking on several days during the week, in total approximately 150 minutes per week. Higher, still attainable amounts of moderate-intensity PA would further increase the CV and other health benefits, particularly because PA in all domains, during leisure time, in domestic chores, in transport, and in occupational work has been shown to be effective.

Prevention of CVD through increased PA brings also several other health benefits by decreasing substantially the risk of several of the most common chronic diseases and by improving and maintaining physical, mental, and cognitive functions. PA also decreases, even totally counterbalances in overweight persons the risk of CVD, as well as several other health hazards of being overweight and obese. It is clear that sufficient physical activity is an essential factor in attaining and maintaining health and functional capacity at all ages, and without sufficient physical activity all attempts to improve the health of the Europeans remain deficient.

Key words: *coronary heart disease, stroke, exercise*

Introduction

This paper summarizes the evidence on the relationship between physical activity (PA) and cardiovascular disease (CVD) that has been published mainly during the past 10 years. The primary focus is on aspects related to the primary prevention of the clinical events of coronary heart disease and stroke.

Methods

The paper is mainly a review of reviews. The material was collected by conducting a search of the Medline, Embase and Cochrane electronic databases to identify systematic reviews and meta-analyses having been published on the relationship between PA and CVD since 2002. The terms used for the exposure were *physical activity* or *exercise*, and for the outcome the following terms: *cardiovascular disease, coronary heart disease*, c*oronary artery disease, coronary disease, myocardial infarction, stroke, peripheral vascular disease* or *peripheral arterial disease*. In addition, committee reports on the topic were identified through scientific meetings and by personal communication. In the section *Biological plausibility* selected reviews published in the leading journals of the topic have been used.

The reviews on the relationship between PA and CVD were included if they fulfilled the criteria of a systematic review and included meta-analysis and were written in English. Two reviews in German included the same original studies as the included reviews, and there was no disagreement of the conclusions. A large majority of the studies included in the reviews were prospective cohort studies of at-risk populations, and the quality of the studies was assessed by established procedures in all the included reviews.

Results

Coronary heart disease

The Physical Activity Guidelines Advisory Committee Report (PAGACR, 2008) includes a comprehensive, rigorously conducted systematic review of 16 cohort and 4 case-control studies on men, and 13 cohort and 6 case-cohort studies on women published between 1996 and 2007. In addition 5 cohort and 4 case-control studies reported the results on men and women combined. The studies include approximately 124,000 men aged 15 to 96 years and more than 200,000 women aged 20 to 85 years at baseline. All included studies provide self-report information of the PA of the subjects, a standardized assessment of cardiovascular clinical events, and a comparison of event rates in subjects assigned to 2 or more categories of PA. In all the cited studies, the multivariate adjusted relative risks were recorded and used in all analyses. The adjustments included at a minimum age, body mass index (BMI), cigarette smoking, blood pressure, and blood lipid concentrations. Inclusion of e.g., BMI, blood pressure, and blood lipids may in some cases inappropriately decrease the magnitude of the relation between the PA exposure and the clinical outcome because some of the benefits of PA may be mediated through these “mediating” or “intermediate” variables. In studies where RRs are presented using both limited and multivariate adjustments that accounted for the “intermediate” variables, the RRs for the limited adjustments show about 10% greater effects.

The review revealed that for men the median relative risk (RR) was .81 for moderate intensity or amount of activity versus no or light activity, and .68 for vigorous intensity or high amounts of PA versus no or light activity. The lower CHD event rate for more active men was reported for both nonfatal and fatal CHD with no systematic difference in CHD incidence versus CHD mortality.

In the 13 prospective cohort studies of women the median RR of having a clinical CHD event was .78 for women reporting participation in moderate intensity or amount of PA compared to women reporting no or light intensity activity. The corresponding RR was .62 for women reporting performing vigorous or high amounts of activity as compared to women reporting no or light intensity activity.

The analyses showed no evidence that the effects of PA on CHD are different in men, pre-menopausal and postmenopausal women. The magnitude of the inverse associations between PA and CHD events for men and women older than 65 years were at least as strong as for younger adults.

A few of the prospective studies have reported PA two or more times during the follow-up. The results show that those men or women who reported increased activity during the follow-up had lower relative risk of CVD events compared to the subjects who remained sedentary or at the previous activity level. In these studies the change in activity preceded the clinical events. These findings increase the evidence that links higher levels of physical activity with lower risk of CVD.

A meta-analysis by Nocon, et al. (2008) including 676,605 subjects in 24 cohort studies with at least 5,000 participants provided results that correspond to the findings presented above. Overall, in a fully adjusted model the cardiovascular mortality was 35% (RR, .65; 95% CI, .60-.70) lower in the most active as compared with the least active subjects. Adjusting only for age, the risk reduction was increased to 47% (RR, .53; 95% CI, .46-.61) in all 13 studies that reported both fully adjusted and age-adjusted results. Thus, the reported risk reductions are conservative as in the PAGACR (2008). The risk reduction was larger (RR, .43; 95% CI, .33-.57) in the 8 studies (analyses of 10 groups) in which PA was assessed by a fitness test as compared with those 16 studies (analyses of 20 groups) that assessed PA by questionnaire (RR, .70; 95% CI, .66-.74). Significant risk reduction was found in 26 of the analyses, and in most studies it was 30–50%. The size of the risk reduction was similar in men and women, and the three studies that included also older participants reported a similar decrease in mortality as in the rest of the studies.

Another recent European meta-analysis by Sofi, Capalbo, Cesari, Abbate, & Gensini (2008) included 513,472 individuals in 26 prospective cohort studies with 4-25 years of follow-up. In the included studies the intensity of LTPA had been assessed in at least three categories. The high intensity level of LTPA was associated with 27% lower risk of CHD incidence or mortality (RR, .73; 95% CI, .66-.80) as compared with the low intensity level. The high intensity level of LTPA was determined so that it is attainable by ordinary people. The corresponding decrease of risk associated with moderate intensity level of LTPA was 12% (RR, .88; 95% CI, .83-.93).

Dose-response relationship

The two meta-analyses referred to above (PAGACR, 2008; Sofi, et al., 2008) showed strong evidence for dose-response effect between PA and CHD.

One meta-analysis included studies only on women (Oguma & Shinoda-Tagawa, 2004). In 5 studies out of 30 the relative PA level (amount or volume) was reported for four levels. When these studies were combined, a significant dose-response relationship was found between the relative level of PA and the risk of CHD: RR 1 (Oguma & Shinoda-Tagawa, 2004), .78, .53, .61, p for trend <.0001.

In populations where the reference group is very sedentary even very modest amounts of moderate intensity PA such as 1 to 2 hours walking per week are associated with reduced rates of CHD (Oguma & Shinoda-Tagawa, 2004; PAGACR, 2008). The risk is decreased with increasing the amount or intensity of PA, and much of the benefit is derived when the subjects perform 150 or more minutes per week of moderate-intensity PA. Greater amounts or higher intensity of activity provide increasing benefits. However, the shapes of any dose-response relations have not been well defined, eventually because of the inaccuracy to assess physical activity. The relations are all most closely related to volume, with less information about intensity and none for frequency and duration of sessions. There is very limited and mixed data related to the effects of short bouts (~10 min or less) of PA (accumulation), but they seem to be effective in increasing cardiorespiratory fitness (PAGACR, 2008).

Stroke

Several systematic reviews provide data of the relationship between PA and the risk of a stroke. Lee, Folsom, & Blair (2003) included data on 285,509 men and women from 18 cohort and 5 case-control studies in their meta-analysis. For the cohort studies RR for stroke incidence or mortality for the most active versus the least active individuals was .75 (95% CI, .69-.82) and for the moderately active versus the least active individuals .83 (95% CI, .76-.89). For case-control studies, highly active individuals had 64% lower risk of stroke incidence (RR, .36; 95% CI, .25-.52) and moderately active individuals 48% lower risk (RR, .52; 95% CI, .40-.69) than their least active counterparts. The authors conclude that moderate and high levels of PA are associated with reduced risk of total, ischemic, and haemorrhagic strokes.

The meta-analysis by Wendel-Vos, et al. (2004) included data from 31 studies published in English before 2001, including 24 prospective cohort studies and 7 case-control studies. Persons categorized as most active compared to the least active during their leisure time were at a significantly lower risk for all strokes (RR, .78; 95% CI, .71-.85), ischemic stroke .79 (95% CI, .69-.91), and haemorrhagic stroke .74 (95% CI, .57-.96). When persons categorized as moderately active during their leisure time were compared with those categorized as the least active, the RR of the active persons for all strokes was .85 (95% CI, .78-.93), for ischemic stroke .83 (95% CI, .64-1.09), and for haemorrhagic stroke .76 (95% CI, .55-1.05). Only six studies examined the association of occupational physical activity and the risk of a stroke. Persons categorized as most active in their occupation had (RR, .74; 95% CI, .49-1.12) for total stroke, (RR, .57; 95% CI, .43-.77) for ischemic stroke, and (RR, .31; 95% CI, .13-.76) for haemorrhagic stroke when compared to the least active. Based on four studies, also a moderate amount of occupational activity seemed to protect against total stroke, (RR, .64; 95% CI, .48-.87).

The meta-analysis of Oguma and Shinoda-Tagawa (2004) included 30 articles on women only. The aim of the study was to quantify the dose-response relationship of PA on CVD outcomes including strokes. When the 7 studies reporting three relative levels of PA were combined, the RRs showed a dose-response relationship for a stroke: RR = 1 (Oguma and Shinoda-Tagawa, 2004), .73, .68, p for trend <.0001.

The PAGACR (2008) includes data from studies published between 1996 and 2007, 8 studies on women, 11 studies on men, and 6 studies on men and women combined. For all strokes in men, the median RR was .65 for moderate-intensity versus no or light activity and .72 for high-intensity or amount versus no or light activity. In women, the median RR was .82 for all strokes combined for moderate-intensity activity versus no or light activity, and .72 for high-intensity or amount versus no or light activity.

Reimers, Knapp, & Reimers (2009) analysed 33 prospective cohort studies and 10 case-control studies published up to December 2008. This meta-analysis included the studies of the earlier investigations cited above. LTPA and occupational PA were not differentiated. Two groups were compared: the lowest level of PA as the reference, and the group with the highest level of PA or the one with the greatest risk reduction (in some studies the intermediately active group). The RR for ischemic stroke in 12 cohort studies for the higher activity level as compared with the low level was .75 (95% CI, .67-.84). The corresponding RR for cerebral haemorrhage in 7 studies was .67 (95% CI, .52-.86), and for the undifferentiated type in 23 studies

.71 (95% CI, .64-.80). In most studies in which PA was graded on a scale with three or more levels, the risk of stroke declined with increasing PA. However, a clear dose-response relationship has not yet been demonstrated. In eight studies the risk was lowest in the intermediate PA category, but in five studies the risk was highest in this category. The risk of ischemic stroke was 24% and 27% lower in the more active women and men, respectively, as compared with the least active subjects. The corresponding risk reductions for cerebral haemorrhage were 8% for women and 40% for men, and for the undifferentiated type of stroke 29% and 28%, respectively. The risk reductions were statistically significant only for men, at least partly due to the smaller number of studies on women.

On the basis of the limited amount of data analysed in the cited studies, the inverse association between PA level and stroke risk appears very similar for men and women, and there seems to be no systematic difference in the relationship of LTPA amount to either total or non-haemorrhagic stroke in men or women aged 45 to 64 years versus 65 to 74 years at baseline.

A recent analysis of the follow-up data of the Health Professionals Follow-up Study (43,685 men) and of the Nurses´ Health Study cohorts showed that among men daily PA (assessed several times during the follow-up) decreased the risk of total stroke by 22% and the risk of ischemic stroke by 25%. The corresponding risk reductions for women were 28% and 31%. Of the other risk factors included in the analyses (that were also repeatedly assessed during the follow-up) only "not smoking" decreased the risk more, 40–50% than "daily exercise", while the effect of "optimal weight" on the risk was of the same order as that of "daily exercise" (Chiuve, et al., 2008).

Peripheral arterial disease (PAD)

The relationship between PA and PAD has been reported in a few studies only, and the evidence suggesting the protective effect of PA on PAD is weak (PAGACR, 2008). However, PA particularly as structured supervised exercise training is a powerful secondary preventive measure for those with established PAD with or without claudication symptoms (PAGACR, 2008; McDermott, et al., 2009).

Domain and type of physical activity

Most of the analysed data are related to LTPA, and most forms of LTPA consist mainly of endurance or aerobic activity or at least aerobic activity has been the main component that has been assessed. However, also PA performed in occupational work, domestic chores, or while commuting appears to provide benefit (PAGACR, 2008). A meta-analysis including a total of 173,146 subjects in seven prospective cohort studies and one case-control study analysed the relationship between commuting to work by walking or cycling and several cardiovascular endpoints (mortality, incident coronary heart disease, stroke, hypertension and diabetes) (Hamer & Chida, 2008). The overall meta-analysis revealed a robust protective effect of active commuting on cardiovascular outcomes, integrated (RR, .89; 95% CI, .81-.98). The relationship was stronger among women (RR, .87; 95% CI, .77-.98) than among men (RR, .91; 95% CI, .80-1.04).

Walking is the most common and most feasible type of physical activity. Several recent systematic reviews and meta-analyses have provided consistent evidence of the protective effect of walking on CHD (Zheng, et al., 2009) or CVD (Oguma & Shinoda–Tagawa, 2004; Hamer & Chida, 2008; Boone-Heinonen, Evenson, Taber, & Gordon-Larsen, 2008). The meta-analysis of Oguma and Shinoda-Tagawa (2004) referred to the above included also an analysis of the relationship of walking and risk of CVD. When the included studies were combined by the absolute walking amount, even 1 hour/week walk was associated with reduced risk of CVD outcome. The meta-analysis of Hamer and Chida (2007) included 18 prospective studies and 459,833 subjects. The pooled hazard ratio of CVD mortality in the highest walking category compared with the lowest was .69 (95% CI, .61-.77). The effect was robust among men and women. There was evidence of dose-response relationship across the categories of walking volume, but walking pace was a stronger predictor of risk compared with walking volume. The systematic review of Boone-Heinonen, et al. (2008) including 21 peer-reviewed publications revealed in general dose-dependent reductions in the risk of fatal or non-fatal CVD with higher duration, distance, energy expenditure and pace of walking. Adjustment for clinical CVD risk factors generally attenuated but did not eliminate the associations. Zheng and co-workers (2009) found in their meta-analysis of 11 prospective cohort studies and one controlled randomized trial including 295,177 subjects that an increment of approximately 30 minutes of normal walking a day for 5 days a week was associated with 19% (95% CI 14–23%) CHD risk reduction, and the risk decreased as the walking dose increased. The results were similar in men and women and in different age groups. The findings of all three analyses were consistent with the current physical activity guidelines that recommend at least 150 minutes moderate-intensity aerobic activity per week to attain significant health benefits.

Stair use is one option to integrate PA into everyday life. It is a vigorous activity with oxygen uptake reaching approximately 80% of maximal level in young healthy adults. A short review that summarizes the effects of studies on the biological effects of stair use concludes that climbing stairs is effective in improving aerobic capacity and some CVD risk factors (Meyer, Kayser, & Mach, 2009). For 100–150 climbed floors each week corresponding to 8–12 minutes of daily exercise, the improvement in aerobic capacity may reach, in previously untrained persons, more than 10%, corresponding to an increase of approximately 1 MET. This magnitude of improvement has been associated with a 15% reduction of CHD/CVD mortality in epidemiological studies (Kodama, et al., 2009). Thus, habitual use of stairs seems a promising mode of PA for CVD prevention.

Resistance exercise. Interest in the health-related potential of resistance exercise has gradually increased. The main part of commonly practiced resistance exercise is dynamic as contrasted to static components of the activity, and consequently the effects of resistance exercise refer mainly to those of the dynamic activity. Participation in resistance exercise as a major part of PA practised in fitness studios has increased during the past decades. However, the proportion of resistance exercise of the PA volume at population level remains small. The relationship between resistance exercise and CVD has not been a subject of any major epidemiological study. The eventual role of resistance exercise in CVD prevention is most likely mediated through its effects on some biological risk factors of CVD (Braith & Stewart, 2006; Williams, et al., 2007).

Biological plausibility

PA fulfils well all criteria of a causal risk factor of CHD and stroke. The temporal sequence between the exposure and outcome is correct in a large number of prospective studies, in which PA is measured before the CVD outcomes occur. Furthermore, change of PA during the observation period as revealed by repeated assessments is logically reflected in the outcomes, and is seen as a strengthening of the associations between PA and the outcomes (Andersen, 2004; Stringhini, et al., 2010). In well-conducted epidemiological studies the consistency of the relationship between PA and CVD outcomes is good, and the findings are similar in men and women of different ages as well in populations from a large number of countries. The strength of the associations is significant both statistically and from the public health point of view. The strength of the relationship of PA and CVD is well comparable to that of other cardiovascular risk factors (Stampfer, Hu, Manson, Rimm, & Willett, 2000; Knoops, et al., 2004; Chiuve, McCullough, Sacks, & Rimm, 2006; Chiuve, et al., 2008; McGuire, Janssen, & Ross, 2009). The same applies also for secondary prevention of patients with CHD (Iestra, et al., 2005).

The strength and consistency of the relationship between PA and health outcomes is decreased by the inaccuracy of PA assessment by questionnaires leading to misclassification of the subjects. There is a great need to begin to assess PA also in large epidemiological studies by objective methods such as accelerometers, step counters, heart rate measurements, and various combinations of the new techniques.

The decreased risk of CVD related to PA is partly explained by the effects of PA on other risk factors, and partly it is independent.

Blood pressure. Recent meta-analyses (Fagard & Cornelissen, 2007; PAGACR, 2008) show that aerobic PA decreases resting blood pressure in healthy subjects, a mean reduction of systolic pressure 2.4mmHg, and diastolic pressure 1.6 mmHG (2% / 2%). In prehypertensive subjects the corresponding decrease is 3.1/1.7 mmHG (1% / 2 %), and in hypertensive subjects 6.9/4.9 mmHG (5% / 5%). Changes are independent of changes in body weight. No consistent dose-response relationships between the changes of the blood pressure and characteristics of aerobic PA have been observed. Limited data suggests that also resistance training can have a blood pressure lowering effect.

Blood lipids. Aerobic PA influences favourably the blood lipids. A high amount of PA modestly increases high-density lipoprotein cholesterol and decreases serum triglycerides, most in the subjects with largest baseline abnormalities. The effects of PA on LDL cholesterol are inconsistently demonstrated. The same applies to the effects of resistance exercise on blood lipids (Braith & Stewart, 2006; Kodama, et al., 2007; PAGACR, 2008; Tambalis, Panagiotakos, Kavouras, & Sidosis, 2009).

Impaired glucose tolerance and Type 2 diabetes (T2D). A large number of prospective cohort and cross-sectional studies and several randomized controlled trials show convincingly that increased levels of PA are associated with significantly improved glucose tolerance and decreased risk of T2D (PAGACR, 2008). A key mechanism is the favourable effect of PA on the sensitivity of muscle and other tissues to the action of insulin. Any amount of PA appears to be better than none, but higher intensity and more frequent PA increase the preventive effect. Approximately 30 minutes of moderate-intensity activity at least five days per week decreases the risk of T2D by 25 to 36%, and the findings apply to men and women. Resistance training has shown promise as a mode of PA in the treatment of T2D, but the eventual role of resistance PA in the prevention of T2D has not been explored in any large prospective study. PA has also a secondary preventive role for CVD regarding T2D, because strong evidence indicates that PA decreases the risk of CVD in subjects with T2D or impaired glucose tolerance. Furthermore, several studies have found a steeper response of CVD risk to PA in diabetic subjects than in those with normal glucose tolerance.

Metabolic syndrome. Regular PA is associated with a substantially decreased risk of metabolic syndrome, and several cross-sectional and one prospective study strongly suggest dose-response between the amount of PA and metabolic syndrome in men and women (PAGACR, 2008).

Overweight and obesity. There is a favourable and consistent effect of aerobic PA on achieving weight maintenance (less than 3% change in body weight). There is large inter-individual variability with weight stability and PA, and many individuals need more than 150 minutes per week of moderate PA to maintain a stable weight. The currently recommended amount of PA needed to prevent weight gain is between 150 and 250 minutes per week of moderate-intensity aerobic activity (PAGACR, 2008; Donnelly, et al., 2009). A recent analysis of weight gain of ca. 34,000 healthy US women consuming a usual diet revealed that initially normal weight women (BMI of less than 25) needed to perform about a one hour moderate-intensity activity daily in order to maintain their weight or to prevent weight gain more than 2.3 kg during 13 years (Lee, Djousse, Sesso, Wang, & Buring, 2010). This amount of activity corresponds to one current US recommendation for the prevention of unhealthy weight gain (Institute of Medicine, 2002). Among heavier women no relationship was found between PA and weight gain suggesting that PA alone, at least in the amounts the study subjects performed, was not sufficient to maintain energy balance.

Greater amounts of aerobic PA than 150 to 250 minutes per week is needed to achieve clinically significant weight loss (at least 5% of body weight), but moderate-intensity PA will improve weight loss in connection with moderate dietary restriction (PAGACR, 2008; Donnelly, et al., 2009; Brown, et al., 2009; Söderlund, Fischer, & Johansson, 2009; Wu, Gao, Chen, & van Dam, 2009). The evidence from cross-sectional and prospective studies indicates that after weight loss, weight maintenance is improved with moderate-intensity aerobic PA more than 250 minutes per week, but there is a lack of well-designed randomized controlled trials. There is a dose effect of PA, with greater weight loss and enhanced prevention of weight regain with doses of PA that approximate 250 to 300 minutes per week. The evidence on the effects of resistance training in prevention of weight gain or in weight reduction is less consistent (PAGACR, 2008; Donnelly, et al., 2009).

Aerobic PA decreases also total abdominal adiposity and intra-abdominal adiposity. Moderate-intensity aerobic activity approximately 150 to 300 minutes per week leads to a reduction of abdominal obesity that is consistent with improved metabolic function. Limited evidence suggests that resistance training has a small and less consistent effect on abdominal obesity (Braith & Stewart, 2006; PAGACR, 2008; Donnelly, et al., 2009).

Regarding the risk of CVD, it is important to note that prevention of weight gain is an effective way to prevent the development of undesirable changes in the metabolic CVD risk factors, and even small (less than 3%) or no decrease of body weight by PA leads to significant beneficial changes in those risk factors (ACSM, 2009). Furthermore, PA also counterbalances the risk caused by overweight (BMI 25.0 to 29.9) on CVD mortality or events (Fogelholm, 2009).

Other mechanisms. Several studies have reported that the reduced risk of CVD in the active subjects is not fully explained by the traditional risk factors such as hypertension, high cholesterol, high BMI and diabetes (Sesso, Paffenbarger, & Lee, 2000; Hu, Tuomilehto, Silventoinen, Barengo, & Jousilahti, 2004; Weinstein, et al., 2008). A recent study in a large cohort of women (Mora, Cook, Buring, Ridker, & Lee, 2007) found that 59% of the PA-induced reduction in CVD events was explained by differences in a large number of traditional and novel cardiometabolic risk factors, particularly by inflammatory/haemostatic factors and blood pressure. However, the remaining 4% of the risk reduction due to PA was independent of these effects. In another study the 52% lower risk of CVD in physically inactive as compared with physically active (at least 150 min/wk) men and women was not mediated by the measured cardiometabolic risk factors (blood pressure, triglycerides, low-density lipoprotein cholesterol, high density lipoprotein cholesterol, glucose, and waist circumference) (McGuire, et al., 2009). The findings of these studies strongly suggest that even in the absence of positive changes in cardiometabolic risk factors, increasing PA level would decrease the risk of CVD.

The reduced risk of CVD related to PA beyond the traditional and even novel risk factors may be explained by several mechanisms. PA has been shown to decrease chronic low-grade inflammation that is an important factor in the pathogenesis of atherosclerosis, as well as insulin resistance (Wilund, 2007; Mathur & Pedersen, 2008). PA also exerts several direct effects on the vascular wall. Habitual PA favourably modulates several expressions of arterial aging and preserves vascular function. Thus, adults who regularly perform aerobic PA demonstrate smaller or no age-associated increases in large elastic artery stiffness, reductions in vascular wall endothelial function, and increases in carotid artery intimal medial thickness. Moderate-intensity aerobic exercise training improves carotid artery compliance and can improve vascular endothelial function in previously sedentary middle-aged and older individuals by several mechanisms (Leung, et al., 2008; PAGACR, 2008; Seals, DeSouza, Donato, & Tanaka, 2008; Di Francescomarino, Sciartilli, Di Valerio, Baldassarre, & Gallina, 2009; Yung, et al., 2009). The effects of exercise on the vascular wall may be induced via the impact of repetitive increases in the shear stress on the endothelium, which transduce structural and functional adaptations that decrease the arteriosclerotic risk. The beneficial effects of PA on the vascular wall may be enhanced by a decreased sympathetic and an increased parasympathetic outflow caused by PA (Green, O´Driscoll, Joyner, & Cable, 2008; Joyner & Green, 2009).

Health-enhancing potential of PA

In addition to the substantial benefits to CV health, physical activity is associated with a lower risk of several of the most common chronic diseases and manifestations of ill health as follows (PAGACR, 2008):

- type 2 diabetes and metabolic syndrome: 30% to 40% lower risk (strong evidence),
- hip fracture: 36% to 68% lower risk (moderate evidence),
- osteoarthritis: 22% to 83% lower risk (weak evidence),
- functional or role limitations: about 30% lower risk (moderate to strong evidence),
- falls: 30% lower risk (strong evidence),
- colon cancer: 30% lower risk (strong evidence),
- breast cancer: 20% to 40% lower risk (strong evidence),
- depression: 20% to 30% lower risk (strong evidence),
- dementia: 20% to 30% lower risk (strong evidence)

The risk reduction of various diseases is reflected in the reduced risk of all-cause mortality of 30% (strong evidence).

If a reversed expression is used, burden to health of physical inactivity (PIA), the estimated number of deaths in Europe in 2004 caused by PIA is 992,000 annually, 10.4% of all deaths. About half of these deaths are caused by CVD. The loss of disability adjusted life years (DALYs) in Europe caused by PIA is estimated as 5.5% of all DALYs. Among the factors influencing the burden to health, PIA ranks fourth as a risk factor for all-cause mortality and sixth among the risk factors for loss of DALYs (WHO, 2009).

It is also worth mentioning that PA not only decreases risk of diseases but also improves cardiovascular and muscular fitness (strong evidence), cognitive function in the elderly (strong evidence), functional health in the elderly (moderate evidence) and sleep quality (moderate evidence) (PAGACR, 2008).

All data presented above indicates that PA is one of the major factors that has a very large potential to maintain and improve health and decrease the burden of ill health in Europe. A substantial part of all of the risk reducing and health-enhancing effects of PA is attained by a moderate amount and intensity of aerobic PA, e.g., by brisk walking (4 to 6 km/h depending on the fitness of the subject) 150 minutes per week. This dose and type of physical activity strongly supports the view that it is a feasible population-level means to enhance health.

However, for most of the major health benefits of PA, including the reduction of the risk of the most common cardiovascular diseases, there is a dose-response relationship between the risk and PA, especially the amount of PA (PAGACR, 2008). Thus, by increasing the amount of daily or weekly PA above the current recommendation, the risk of most of the most common non-communicable chronic diseases would further decrease, although with diminishing gain. One target level for a large number of the European people employed in sedentary occupations could be about a one hour moderate-intensity PA daily, based on the evidence and recommendation to prevent weight gain (see above). Adoption of this level of PA would lead to a massive avoidance of overweight and obesity and the associated health losses.

All data on the associations of PA and risk of chronic non-communicable diseases, and a major part of the data as the basis for the current PA recommendations, are derived from studies assessing PA by self report using various questionnaires. This leads to an underestimation of the preventive potential of PA due to misclassifications and over-reporting of the activity, may increase the relative weight of LTPA on the cost of the other domains of PA in attempts to assess the total activity, and hinders a reliable quantitative assessment of PA in research and surveillance. In the light of the great potential of PA for health, and consequently the need to promote it using valid quantitative recommendations, as well as to monitor and to survey it reliably at individual, group and population level, objective methods to assess PA should be taken into much wider use. Appropriate technologies are available (Welk, 2002). Funds should be allocated for their use on a sufficiently large scale at national and international level in order, e.g., to begin to collect data for a new generation of epidemiological studies that would increase the reliability and accuracy of the use of PA for health. Objective data are needed also to survey PA levels and trends in populations in order to evaluate the effectiveness and cost-effectiveness of the attempts to increase PA.

An example of the value of objective, accurate methods in assessing PA are the recent studies revealing the health risks of sedentariness, especially sitting, e.g., in driving a car and viewing TV. A large amount of especially uninterrupted sitting has been shown convincingly to be a risk factor of, e.g., overweight and obesity (Must, et al., 2007; Cleland, Schmidt, Dwyer, & Venn, 2008; Eisenmann, Bartee, Smith, Welk, & Fu, 2008), as well as of metabolic diseases (Healy, et al., 2008; Helmerhorst, Wijndaele, Brage, Wareham, & Ekelund, 2009; Sisson, et al., 2009) and all-cause and CVD mortality (Dunstan, et al., 2010) even independently of PA. Increased emphasis on sedentariness is important not only for human but also for environmental health. A substantial increase of PA and a decrease of sitting in large numbers of people, and increasing and improving the environmental conditions to enhance this development, would support substantially in striving for important societal goals such as saving energy, decreasing environmental hazards due to, e.g., motorized transport, and deterring climate warming.

Conclusions

The quantity and quality of scientific data on the cardiovascular and other health-related effects of physical activity has increased greatly during the past decade. The evidence now shows convincingly that insufficient physical activity is one of the key causal risk factors of CVD, particularly of the most prevalent of them, CHD and stroke. Because of the high prevalence of insufficient physical activity, the CVD burden caused by it is great. The effects of insufficient physical activity are mediated partly through the traditional major risk factors, and partly they are independent. This rather recently shown fact emphasizes the essential, irreplaceable role of PA for cardiovascular health.

Strong epidemiological evidence indicates that a major part of the preventive effect of PA can be attained by activity that is applicable on a large scale in all European populations: moderate-intensity endurance or aerobic activity such as brisk walking on several days during the week, in total approximately 150 minutes per week. Higher, still attainable amounts of moderate-intensity PA would further increase the CV and other health benefits, particularly because PA in all domains, during leisure time, in domestic chores, in transport, and in occupational work has been shown to be effective.

Prevention of CVD through increased PA brings also several other health benefits by decreasing substantially the risk of several of the most common chronic diseases and by improving and maintaining physical, mental, and cognitive functions. PA also decreases, even totally counterbalances in overweight persons the risk of CVD, as well as several other health hazards of being overweight and obesity, probably because a large part of overweight and obese individuals are insufficiently physically active. It is clear that sufficient physical activity is an essential factor in attaining and maintaining health and functional capacity at all ages, and without sufficient physical activity all attempts to improve the health of the Europeans remain deficient.

Rapidly increased scientific evidence indicates that complete sedentariness, especially sitting, increases the risk of overweight and obesity, and of metabolic and cardiovascular diseases even independently of PA. Thus, sedentariness is a domain of its own that has to be tackled by efficient policies and actions.

Prevention of CVD through PA by increasing opportunities and motivation to participate in it and by decreasing sitting during leisure time, in transport, and in occupational life gives strong support also to other important societal goals such as fighting against obesity, traffic congestion and accidents, air pollution, excess use of energy, and climate warming.

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TJELESNA AKTIVNOST I PREVENCIJA KARDIOVASKULARNIH BOLESTI U EUROPI: NOVA SAZNANJA

Članak sažima dokaze o odnosu između tjelesne aktivnosti i kardiovaskularnih bolesti objavljene pretežno tijekom posljednjih 10 godina. Žarište je stavljeno na aspekte povezane s primarnom prevencijom kliničkih pojava koronarne bolesti srca i moždanog udara. Materijal je prikupljen pretraživanjem elektroničkih baza podataka Medline, Embase i Cochrane s ciljem pronalaženja sustavnih preglednih članaka i meta-analiza objavljenih na ovu temu u razdoblju od 2002. godine. Ključne riječi za pretraživanje bile su: tjelesna aktivnost (*physical activity*) ili tjelovježba (*exercise*), odnosno, za bolesti: kardiovaskularna bolest (*cardiovascular disease*), koronarna bolest srca (*coronary heart disease*), koronarna arterijska bolest (*coronary artery disease*), koronarna bolest (*coronary disease*), infarkt miokarda (*myocardial infarction*), moždani udar (*stroke*), periferna vaskularna bolest (*peripheral vascular disease*) ili periferna arterijska bolest (*peripheral arterial disease*). Nadalje, odborska izvješća na ovu temu pribavljena su preko znanstvenih skupova i osobnom komunikacijom. Velika većina istraživanja obuhvaćenih preglednim člancima bila su prospektivna kohortna istraživanja populacija pod rizikom.

Kvantiteta i kvaliteta znanstvenih podataka o kardiovaskularnim i ostalim zdravstvenim učincima tjelesne aktivnosti značajno su porasle tijekom prošlog desetljeća. Dokazi danas uvjerljivo pokazuju da je nedovoljna tjelesna aktivnost jedan od ključnih uzročnih rizičnih čimbenika kardiovaskularnih bolesti, a posebice najučestalijih među njima – koronarne bolesti srca i moždanog udara. Učinci nedovoljne tjelesne aktivnosti dijelom su posredovani tradicionalnim velikim rizičnim čimbenicima (poput visokog arterijskog krvnog tlaka ili koncentracije masnoća u krvi), a dijelom su i neovisni. Ova relativno recentno utvrđena činjenica naglašava esencijalnu, nezamjenjivu ulogu tjelesne aktivnosti u očuvanju kardiovaskularnog zdravlja.

Čvrsti epidemiološki dokazi ukazuju na to da se veći dio preventivnog učinka tjelesne aktivnosti može postići aktivnošću koja je u velikoj mjeri primjenjiva kod svih europskih populacija – to je aerobna aktivnost ili aktivnost izdržljivosti umjerenog intenziteta, poput žustrog hodanja tijekom nekoliko dana u tjednu, u ukupnom trajanju od približno 150 minuta tjedno. Veće, ali još uvijek ostvarive količine tjelesne aktivnosti umjerenog intenziteta još bi više povećale pozitivan kardiovaskularni, a i općeniti zdravstveni učinak, posebno stoga što se tjelesna aktivnost u svim domenama (u slobodnom vremenu, u kućanstvu, u svrhu prijevoza te na radnom mjestu) pokazala učinkovitom.

Prevencija kardiovaskularnih bolesti pojačanom tjelesnom aktivnošću pruža i dodatne zdravstvene blagodati značajnim smanjenjem rizika od nekoliko najčešćih kroničnih bolesti, kao i unaprjeđenjem i održavanjem tjelesnih, mentalnih i kognitivnih funkcija. Tjelesna aktivnost također smanjuje, pa čak i u potpunosti predstavlja protutežu riziku od kardiovaskularnih bolesti kod osoba s prekomjernom tjelesnom masom, a jednako djeluje i na više ostalih zdravstvenih rizika prekomjerne tjelesne mase i pretilosti. Jasno je da je zadovoljavajuća razina tjelesne aktivnosti esencijalni čimbenik postizanja i održavanja zdravlja i funkcionalnog kapaciteta u svakoj dobi, te da će bez zadovoljavajuće razine tjelesne aktivnosti svi pokušaji unaprjeđenja zdravlja Europljana ostati neuspješni.

Ključne riječi: *koronarna bolest srca, moždani udar, vježba*

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