Physical Activity and Cardiovascular Disease: Directions for Future Research

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Abstract: Regular physical activity is widely accepted as playing a crucial role in cardiovascular disease (CVD) prevention. However, despite extensive research in this field there are crucial gaps in our knowledge. This paper discusses future research directions including population subgroup-specific exercise doses, research in under represented populations, the role of cardiorespiratory fitness in predicting CVD risk, and novel biological mechanisms that might mediate the inverse association between physical activity and CVD risk.

Regular physical activity is widely accepted as playing a crucial role in cardiovascular disease (CVD) prevention [1-6]. Current physical activity recommendations for the general population advocate the accumulation of at least 30 minutes of moderate intensity physical activity on five or more days a week or vigorous activity at least three times per week [7]. However, despite extensive research in this field there are crucial gaps in our knowledge. Several important areas have emerged that include examining population subgroup-specific exercise doses that are required for primary and secondary CVD prevention; the association between physical activity and CVD in under-represented populations such as women, children, ethnic minorities, and clinical patient groups; the role of physical activity and cardiorespiratory fitness (CRF) in predicting future risk for CVD, and novel biological and physiological mechanisms that might mediate the inverse association between physical activity and CVD risk.

There is surprisingly little epidemiological evidence on the cardio-protective effects of physical activity in relation to current recommendations. In a large prospective study of over 200,000 participants, those meeting the physical activity recommendations had the lowest risk of CVD, although those that met the recommendations through vigorous activity benefited to a greater degree (32% risk reduction) than those meeting recommendations through moderate activity (27% risk reduction) [8]. One of the key messages of these recommendations is that activities performed during daily living, (e.g. walking or cycling, stair-climbing, gardening, home improvement work, intense housework) may be sufficient for the prevention of CVD and premature death. Although the evidence on the health benefits of walking, cycling, or stair-climbing is compelling, the degree of protection conferred from intense domestic physical activity is less clear and future research must address this issue. Several large scale prospective cohort studies in men suggest that vigorous activity is more beneficial for protection against CVD [3,4]. For example, in the Health Professional's follow up study, men who ran for an hour or more per week had a 42% CVD risk reduction compared with 18% lowered risk in men that only walked briskly for half an hour per day [4]. These associations, however, have not been substantiated in women. In the Nurse's Health Study, for example, both moderate and vigorous intensity exercise provided similar levels of protection against CVD [2]. It is possible that the disparate results reflect differences in training adaptations between men and women or given that levels of vigorous exercise in women was relatively low compared with men, the findings may reflect a lack of range of vigorous exercise in women to detect significant effects. Interestingly, exercise intensity has not been associated with any of the favourable training effects on key risk factors such as HDL cholesterol and blood pressure [9,10], thus it is possible that a threshold effect may exist for some risk factors or that there is an intensity versus volume trade-off.

The role of regular exercise and the dose of activity required to achieve benefit in specific populations is not well established. In participants with existing CVD, for example, light or moderate activity was more beneficial than vigorous sporting activities for protection against CVD mortality [11]. Nevertheless, recent training studies in cardiac patients suggest that high intensity or high volume exercise training is more beneficial in reversing left ventricular remodeling, diminishing expression of atherogenic adhesion molecules, and improving aerobic capacity, endothelial function, and quality of life in comparison with a moderate exercise intensity/volume interventions [12,13]. Emerging evidence is beginning to uncover an association between physical activity and CVD risk factors in children [14], which may have significance in adulthood [15]. Therefore, future research in under represented populations is critical.

The precise mechanisms through which physical activity lowers CVD risk are incompletely understood. Even after adjustments for traditional CVD risk factors, such as blood pressure, lipids, and adiposity, the inverse association between physical activity and CVD persists. Recent research has examined the effects of physical activity on novel risk factors, such as inflammatory and hemostatic markers and glucose metabolism. There is presently little information, however, about the relative contribution of various risk factors to activity related reduction in CVD risk. In the only study to date that has examined this issue, known risk factors explained a large proportion (59%) of the inverse association

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between physical activity and incident CVD events in women, with inflammatory and haemostatic risk factors and blood pressure making the largest contribution [16]. Thus, future studies of this nature will be required to confirm and extend these findings.

Low CRF and low physical activity levels are independently associated with an increased risk for CVD and CHD. Although the exact mechanisms through which physical activity and fitness interact and jointly relate to CVD risk are not clear [17], there are studies showing that CRF [18-21] and physical activity [22] predict CVD risk equally well or better than conventional CVD risk factors such as blood pressure, high density and total cholesterol, smoking, and body mass index. Unlike these conventional risk factors, however, CRF and physical activity are not routinely assessed in primary care settings to identify individuals at high risk for CVD. This is mainly due to practical considerations (e.g. lack of resources to perform exercise testing in primary care), the widespread belief held by the medical establishment that physical activity modification is not possible [23], and the lack of randomised controlled trial evidence showing that improvement in physical activity or CRF will lead to proportional decreases in CVD risk. Given that existing methods for estimating future CVD risk and taking preventive action often perform poorly [24] these are promising areas of research that need to be expanded. For example, an international group of experts have proposed a method to assess CRF in healthcare settings using non-exercise testing variables that are relatively easy and inexpensive to obtain, which include gender, age, body mass index, resting pulse rate and self-reported physical activity [25].

In summary, future research is required in critical areas to further extend our knowledge about the cardio-protective effects of physical activity. Future advances in the measurement of physical activity will also provide researchers with more accurate estimates of exposure on a population level that may help to resolve unanswered issues.

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