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Physical Activity, Visceral Adipose Tissue, and Cardiovascular Disease in Older Adults - Associations and Effects

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Aula Biologica, Biologihuset, fredagen den 2 juni, kl. 09:00.

Avhandlingen kommer att försvaras på svenska.

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Title

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Abstract

BACKGROUND: Cardiovascular disease (CVD) is the leading cause of mortality in older adults. With the population aging rapidly, interventions aimed at improving modifiable risk factors for CVD, such as physical inactivity and visceral obesity, could play an important role in reducing its burden, provided they are proven effective.

AIMS: To investigate the associations of objectively measured physical activity of different intensities and visceral adipose tissue (VAT) with the risk of CVD and all-cause mortality, to investigate the effects of structured physical activity (exercise) on VAT, and to review the effects of exercise on CVD and all-cause mortality based on evidence from randomized controlled trials (RCTs).

METHODS: This thesis comprised two cohort studies, one RCT, and one narrative review of evidence from RCTs. The cohort studies included about 3,300 older adults with baseline data on physical activity and VAT mass, as obtained using accelerometry and dual-energy X-ray absorptiometry, respectively. Cases of stroke, myocardial infarction, and all-cause mortality during follow-up were collected from Swedish nationwide registers. The RCT included 77 men and women aged 70 years with visceral obesity who were randomly allocated to either 10 weeks of supervised vigorous-intensity exercise or to no exercise, with VAT mass measured before and after the intervention. In the review, evidence from RCTs and meta-analyses of RCTs on the effect of exercise on CVD ($N=19,162$) and all-cause mortality ($N=37,443$) in general older adults and in individuals with chronic conditions (such as obesity, type 2 diabetes, and preexisting CVD) were reviewed.

MAIN FINDINGS: Greater amounts of physical activity of any intensity, but especially that of at least moderate intensity, were associated with lower risk of stroke, myocardial infarction, and all-cause mortality. Conversely, greater VAT mass was associated with higher risk of stroke or myocardial infarction. In the RCT, short-term vigorous-intensity exercise seemed to decrease VAT mass slightly, but the effect was not statistically significant. Finally, the review showed that there is currently no convincing evidence from RCTs that exercise effectively reduces the risk of CVD or all-cause mortality, which is in sharp contrast to the strong associations typically reported in conventional observational studies. The reasons for the conflicting findings are likely complex and multifactorial. In the RCTs, a lack of statistical power could partly explain why no effects have been detected in the general population of older adults, but it is unlikely to explain the null findings in clinical populations, as some of these trials, including meta-analyses of such trials, have been large. Other potential explanations could be a ceiling effect due to the inclusion of participants who were healthier and more physically active than the general population, or that an effect of exercise was masked by the use of effective medications such as antihypertensives and lipid-lowering agents. On the other hand, observational studies have likely overestimated the benefits of physical activity, because these studies are vulnerable to selection bias, reverse causation, and unmeasured confounding, such as from heritable influences.

CONCLUSIONS AND IMPLICATIONS: Despite strong associations, the protective effect of physical activity as a single intervention against CVD and all-cause mortality in older adults is probably not as substantial as is commonly presumed. To uncover the true role of physical activity in preventing CVD, further high-quality trials would be valuable. However, because these trials are very difficult and resource demanding, they should be complemented by innovative observational studies that seek to strengthen causal inference through addressing sources of bias and confounding that are often incompletely accounted for in conventional observational studies. This could include a variety of methodologies, such as utilizing negative control outcomes, instrumental variables, sibling comparisons, and other genetically informed designs. As the aging population continues to grow, it becomes increasingly important to take these scientific steps in order to provide a more definitive answer to the question of the extent to which physical activity alone can reduce the risk of CVD.

Keywords

physical activity, exercise, obesity, stroke, myocardial infarction, death, aging, geriatrics, epidemiology, trial

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