Physical Activity Does Not Reduce Aortic Valve Stenosis Incidence

Philip Sarajlic, MD; Alicja Wolk; Magnus Bäck, MD, PhD; Susanna C. Larsson, PhD

Background: Physical activity is associated with lower risk of coronary and cerebrovascular disease but its potential role in prevention of aortic valve stenosis (AVS) is unclear.

Methods and Results: We investigated whether physical activity influences AVS risk in a cohort of 69,288 adults. During a mean follow-up of 15.3 years, 1,238 AVS cases were diagnosed. No associations were observed between AVS and walking/bicycling (≥1 h/day vs. almost never: hazard ratio 0.92, 95% CI 0.74–1.15) or exercise (≥4 h/week vs. <1 h/week: hazard ratio 1.18, 95% CI 0.97–1.43).

Conclusions: Physical activity did not reduce the incidence of AVS.

Key Words: Aortic valve stenosis; Physical activity; Prospective studies

In the Western world, aortic valve stenosis (AVS) is the most prevalent form of valvular heart disease, and is associated with high morbidity and death from cardiovascular disease. As no medical treatments for AVS have proved to be efficacious in slowing down progression, it is of great importance to identify lifestyle factors that can prevent the development of the condition. Physical activity has been associated with reduced risk of coronary and cerebrovascular disease and improved vascular and ventricular function. However, studies of the potential role of physical activity for the prevention of AVS are scarce. The aim of this study was therefore to establish whether physical activity reduces the risk of AVS.

Methods

Study Population
We used data from the Swedish Infrastructure for Medical Population-based Life-course Environmental Research (SIMPLER), which includes 2 population-based cohorts: the Cohort of Swedish Men and the Swedish Mammography Cohort. In the fall of 1997, participants of these cohorts completed a questionnaire about physical activity, weight, height, smoking, alcohol consumption, education, and medical history. The present study included 69,288 participants aged 45–83 years (Figure S1).

Physical Activity Assessment
A validated questionnaire was used to assess physical activity. Participants were asked to specify the amount of time walking or bicycling (almost never or <20, 20–40, 40–60, 60–90, and >90 min/day) and amount of time spent on leisure-time exercise (<1, 1, 2–3, 4–5, and >5 h/week) in the past year. Few participants reported high levels of physical activity. The 2 highest categories for each physical activity measure were therefore combined, resulting in, respectively, 5 and 4 exposure categories for walking/bicycling and exercise.

Diagnosis Ascertainment and Case Follow-up
Medical diagnoses of participants were acquired by linkage to the Swedish National Patient and Causes of Death Registers. Incident AVS cases were identified using the International Classification of Diseases 10th revision codes 135.0 and 135.2. From the National Patient Register we also acquired information on aortic valve replacement, defined according to surgical and interventional cardiology procedures.

Statistical Analysis
Hazard ratios of AVS by physical activity categories were estimated using Cox proportional hazards regression models with age as the time scale and stratified by sex. All multivariable models were adjusted for education, smoking, alcohol consumption, and atrial fibrillation. A second multivariable model was further adjusted for potential mediators, including body mass index (BMI) and history of hypertension, hypercholesterolemia, and diabetes.
Walking/bicycling and exercise were mutually adjusted by inclusion of both variables in the same multivariable model. We had 80% and 100% power to detect hazard ratios of 0.8 and 0.7, respectively, for the highest vs. lowest categories.

Results

Participants reporting more dedication towards physical activity were more likely to have a postsecondary education, had lower BMI and drank less alcohol, and were less likely to smoke and to have a history of comorbidities compared with inactive individuals (Table S1).

During a mean follow-up of 15.3 years (1,059,122 person-years), 1,238 AVS cases were diagnosed. No significant associations were observed across categories of walking/bicycling and exercise and AVS incidence (Table). In the most fully adjusted model, the hazard ratios (95% confidence interval) comparing the highest and lowest categories of physical activity were 0.92 (0.74–1.15) for walking/bicycling and 1.18 (0.97–1.43) for exercise. There was a small, but significant increase in AVS risk in the group exercising 1 h/week. Results were similar for AVS requiring aortic valve replacement (Table) and in both cohorts.

Discussion

In this study, we found that physical activity defined as either walking/bicycling or leisure-time exercise did not decrease the risk of AVS overall or of AVS requiring aortic valve replacement. Our finding was consistent with results from a cohort study of 3,273 Norwegian adults followed up by echocardiography showing no significant association between physical activity (assessed by questionnaire) and AVS risk. We observed a barely significant increase in AVS risk among participants who exercised ≥1 h/day, which should be interpreted as a statistical anomaly as there were no significant differences in AVS incidence in the other categories.

The protective effects of physical activity on other cardiovascular outcomes may relate to modest reductions in inflammation and blood pressure and enhanced endothelial function, all of which have been implicated in AVS. Improvements in those factors would thus be expected to be beneficial also in AVS. Although exercise has also been associated with a positive effect on blood lipids, potential differences in lipid-attributable risk between, for example, atherosclerosis and AVS have been suggested. In addition, there are no intervention studies showing that exercise influences inflammatory markers, blood pressure or endothelial function in AVS patients. Finally, because obesity and diabetes are risk factors for AVS, additional benefit would be expected if physical activity leads to weight loss and reduced risk of diabetes. Nevertheless, we observed no association between physical activity and risk of AVS in the model that was not adjusted for potential intermediates, including BMI and history of diabetes, hypertension, and hypercholesterolemia.

A strength of this study is the large number of AVS events, ensuring sufficient statistical power to draw meaningful conclusions. Moreover, we could assess associations of both less strenuous and more strenuous physical activity

Table.

<table>
<thead>
<tr>
<th>Walking/bicycling</th>
<th>Analysis including all diagnosed AVS cases with/without AVR</th>
<th>Analysis including AVS cases with AVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>Person-years of follow-up</td>
<td>Age- and sex-adjusted model</td>
</tr>
<tr>
<td>Almost never</td>
<td>153</td>
<td>117,750</td>
</tr>
<tr>
<td>&lt;20 min/day</td>
<td>257</td>
<td>237,516</td>
</tr>
<tr>
<td>20–40 min/day</td>
<td>382</td>
<td>343,835</td>
</tr>
<tr>
<td>40–60 min/day</td>
<td>204</td>
<td>179,466</td>
</tr>
<tr>
<td>≥1 h/day</td>
<td>242</td>
<td>180,555</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.08</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Exercise

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>Multivariable model 1*</th>
<th>Multivariable model 2†</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 h/week</td>
<td>205</td>
<td>217,881</td>
</tr>
<tr>
<td>1 h/week</td>
<td>254</td>
<td>232,063</td>
</tr>
<tr>
<td>2–3 h/week</td>
<td>411</td>
<td>347,352</td>
</tr>
<tr>
<td>≥4 h/week</td>
<td>368</td>
<td>261,826</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.66</td>
<td>0.48</td>
</tr>
</tbody>
</table>

*Adjusted for age (time scale), sex, educational level (less than high school, high school, or university), smoking (never, past <20 pack-years, past ≥20 pack-years, current <20 pack-years, current ≥20 pack-years), alcohol consumption (never drinkers, past drinkers, and current drinkers of <1, 1–6, 7–14, 15–21 or >21 drinks/week), and atrial fibrillation (yes/no). Walking/bicycling and exercise are adjusted for each other through inclusion of both variables in the same multivariable model. †Further adjusted for potential intermediates, including body mass index (<22.5, 22.5–24.9, 25.0–29.9, or ≥30 kg/m²) and history of hypertension (yes/no), hypercholesterolemia (yes/no), and diabetes (yes/no). AVR, aortic valve replacement; AVS, aortic valve stenosis.
with AVS incidence and adjust for other potential risk factors. Physical activity was assessed before the diagnosis of AVS, thereby reducing reverse causation bias. The questionnaire has been validated and showed adequate validity. The inverse association between moderate physical activity and risk of other cardiovascular diseases in this population indicates that the questionnaire can capture potential causal associations between physical activity and disease.

A limitation is the possibility of recall bias because participants were asked to report their level of physical activity by themselves. Another shortcoming is that we might have missed asymptomatic cases not diagnosed with AVS. It can therefore not be excluded that physically active individuals were more prone to experience symptoms from AVS and therefore seek medical care detecting AVS.

In conclusion, findings from this large cohort study provided no support that physical activity may reduce AVS incidence.

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Declaration of Conflict of Interest
The authors have no conflicts of interest to declare.

References

Supplementary Files
Supplementary File 1
Figure S1. Flow chart of study participants.
Table S1. Baseline characteristics of participants by categories of walking/bicycling and exercise
Please find supplementary file(s); http://dx.doi.org/10.1253/cirj.CJ-18-0598