Association of Physical Activity with Aortic Disease in Japanese Men and Women: The Japan Collaborative Cohort Study

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Aims: Evidence of the effects of physical activity on mortality from aortic diseases, especially in Asian populations, remains limited. This study aimed to examine these effects using data from a large long-term cohort study of Japanese men and women.

Methods: Between 1988 and 1990, 32,083 men and 43,454 women in Japan, aged 40–79 years with no history of coronary heart disease, stroke, aortic diseases, or cancer, filled in questionnaires on time spent walking and participating in sports and were followed up until 2009. Multivariable hazard ratios (HRs) with 95% confidence intervals (CIs) of aortic disease mortality and its types (aortic aneurysm and dissection) according to the time spent walking and participating in sports were calculated after adjusting for potential confounding factors using the Cox proportional hazards model.

Results: During a median follow-up of 19.1 years, a total of 173 deaths from aortic disease (91 cases of aortic dissection and 82 of aortic aneurysm) were documented. Sports participation time was inversely associated with the risk of death from aortic aneurysm: the multivariable HRs (95% CIs) were 0.68 (0.40–1.16) for ‘1 h/week, 0.50 (0.19–1.35) for 3–4 h/week, and 0.31 (0.10–0.93) for ≥ 5 h/week (p for trend=0.23) compared with 1–2 h/week. The time spent walking was not associated with death from aortic aneurysm, dissection, and total aortic diseases.

Conclusions: Greater time spent in sports participation was associated with a reduced risk of mortality from aortic aneurism in the Japanese population. Further studies are needed to investigate the relationship between physical activity and aortic dissection.

Key words: Sports, Physical activity, Aortic disease, Aneurysm, Risk factors

Introduction

Aortic diseases such as aortic dissection and aneurysm are highly fatal. More than 20% of patients with thoracic aortic diseases die before reaching the hospital, and the overall mortality rate from ruptured thoracic aortic aneurysms is >90%¹⁴. Trends in the prevalence and mortality are uncertain as there is mixed evidence partly because of diagnostic ascertainment difficulties due to the high prehospitalization case fatality¹⁴. Globally, men have a higher mortality rate related to aortic diseases than women, and mortality increases with age⁶. White Americans have a higher prevalence of aortic aneurysms than Asian, Hispanic, and African Americans in the United States⁶, ².⁸.

Other than reporting risk factors specific to the development of aortic dissection, including hereditary connective tissue disorders such as Marfan’s syndrome and direct blunt trauma such as car accidents, previous studies have also reported risk and preventative factors for the development of aortic diseases and the associated mortality. Smoking and hypertension are established risk factors for aortic diseases², 5, 9, ¹⁰. Body
mass index and height are associated with an increased risk of mortality from aortic aneurysm but not from aortic dissection. In contrast, moderate alcohol consumption and fish intake are associated with reduced risk and mortality from aortic diseases. Physical activity could reduce the risk of aortic diseases because it has a beneficial effect on cardiovascular risk factors such as hypertension and arterial stiffness as well as an anti-inflammatory effect. A previous meta-analysis of prospective studies suggested that higher levels of physical activity were associated with a reduced risk of aortic diseases; however, only five of nine studies showed no association, and three of five studies did not adjust for major confounders such as smoking, obesity, and hypertension.

**Assessment of Sports and Walking Time**

We asked the participants, “How long do you play sports or exercise on average in a week?” The list of possible answers was as follows: 1 h, 1 to 2 h, 3 to 4 h, and ≥ 5 h. We also asked, “How long, on average, do you walk indoors or outdoors per day?” Again, the possible answers were as follows: 0.5 h, 0.5 h, 0.6 to 0.9 h, and 1 h.

**Assessment of Confounding Variables**

Other demographic and lifestyle factors were derived from a self-administered questionnaire at baseline: age, sex, body mass index, medical history such as diabetes and hypertension, smoking, and alcohol consumption.

**Mortality Surveillance**

To determine the cause of death, a systematic review of death certificates was conducted for each community. Mortality data were sent centrally to the Ministry of Health and Welfare through a local public health center. The underlying cause of death was coded for the National Vital Statistics according to the International Classification of Diseases, 10th revision (ICD10). For all 45 areas, follow-up was concluded by the end of 1999 in four communities, by the end of 2003 in four other communities, by the end of 2008 in two communities, and by the end of 2009 in the remaining communities. The death endpoints in this study were aortic disease (I 710–I 719), aortic dissection (I 710), and aortic aneurysm (I 711–I 719). Movements of participants from their communities were verified using the population registration documents. When participants moved out, they were treated as censored cases.

**Statistical Analysis**

The person-years of follow-up were calculated as the time from the date of the baseline questionnaire to the date of death, emigration from the community, or end of the follow-up, whichever occurred first. Age-adjusted mean values and proportions of cardiovascular risk factors were calculated using generalized linear models. The age- and sex-adjusted and multivariable hazard ratios (HRs) with 95% confidence intervals (CIs) of mortality from aortic...
diseases (82 from aortic aneurysm and 91 from aortic dissection). In age- and sex-adjusted analyses, compared with 1–2 h/week of time spent participating in sports, participation of 3 h/week or more was inversely associated with mortality risk from aortic aneurysm and total aortic diseases but not from aortic dissection (Table 2). After additional adjustment for potential confounding factors, the association of time spent playing sports with aortic aneurysm remained statistically significant; the multivariable HRs (95% CIs) were 0.68 (0.40–1.16) for ʻ1 h/week, 0.50 (0.19–1.35) for 3–4 h/week, and 0.31 (0.11–0.93) for ≥ 5 h/week (p for trend 0.24) compared with 1–2 h/week. In contrast, after adjustment, the association of time spent participating in sports with aortic disease was of borderline statistical significance: the multivariable HRs (95% CIs) were 0.74 (0.51–1.09) for ʻ0.5 h/week, 0.52 (0.25–1.09) for 3–4 h/week, and 0.50 (0.25–1.02) for ≥ 5 h/week (p for trend=0.30), compared with 1–2 h/week. In addition, weaker and insignificant inverse associations were observed between time spent playing sports and aortic dissection, as well as between time spent walking and aortic aneurysm, dissection, and total aortic diseases. Analysis adjusted for height instead of body mass index did not change the findings (data not shown).

Results

Age-adjusted baseline characteristics of the participants are presented according to the time spent walking and participating in sports in Table 1. Individuals who spent greater time participating in sports (<1, 1–2 (reference group), 3–4, ≥ 5 h/week) and time spent walking (<0.5, 0.5 (reference group), 0.6–0.9, >1.0 h/week) were calculated using the Cox proportional hazards model after adjusting for potential confounding factors. The groups of the second lowest time spent walking and participating in sports were set as reference because the groups of the lowest time spent in physical activity may include participants who were unable to walk or play sports due to preclinical conditions. In multivariable analyses, we adjusted for age (continuous), sex, history of hypertension and diabetes (yes or no), smoking status (never, ex-smoker, current smoker), body mass index (sex-specific quintile), and alcohol consumption (never a drinker, ex-drinker, current drinker of 0.1–45.9 or ≥ 46.0 g ethanol per day). The linear trend test was conducted by assigning 0, 0.5, 0.75, and 1 for each walking category and 0, 1.5, 3.5, and 5.0 for each sports category as a continuous variable. SAS version 9.4 (SAS, Inc., Cary, NC, USA) was used for all statistical analyses.

Table 1. Age-adjusted baseline characteristics of the participants according to sports and walking time

<table>
<thead>
<tr>
<th></th>
<th>Sports Time (h/week)</th>
<th></th>
<th>Walking Time (h/day)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1</td>
<td>1-2</td>
<td>3-4</td>
<td>≥ 5</td>
</tr>
<tr>
<td>No. of participants</td>
<td>54667</td>
<td>11711</td>
<td>4634</td>
<td>4525</td>
</tr>
<tr>
<td>Age, y</td>
<td>56.4</td>
<td>56.2</td>
<td>58.9</td>
<td>61.9</td>
</tr>
<tr>
<td>Sex, % of men</td>
<td>39.9</td>
<td>47.2</td>
<td>49.6</td>
<td>54.0</td>
</tr>
<tr>
<td>History of hypertension,%</td>
<td>20.6</td>
<td>21.6</td>
<td>21.3</td>
<td>19.9</td>
</tr>
<tr>
<td>History of diabetes mellitus,%</td>
<td>4.7</td>
<td>5.7</td>
<td>5.8</td>
<td>5.7</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.8</td>
<td>22.8</td>
<td>22.7</td>
<td>22.6</td>
</tr>
<tr>
<td>Current smoker,%</td>
<td>26.0</td>
<td>27.0</td>
<td>28.4</td>
<td>31.0</td>
</tr>
<tr>
<td>Current drinker,%</td>
<td>39.0</td>
<td>47.6</td>
<td>48.0</td>
<td>52.4</td>
</tr>
</tbody>
</table>

Data are mean for continuous variables and percentages for categorical variables.

Discussion

In this analysis of a large and long-term Japanese cohort, ≥ 5 h/week of time spent participating in sports was associated with a lower risk of mortality from aortic aneurysm and total aortic diseases by approximately 70% and 50%, respectively, compared with that of 1–2 h/week. In contrast, the association between time spent playing sports and aortic dissection was not evident. Time spent walking was not associated with mortality from aortic aneurysm,
aortic dissection, and total aortic diseases. To the best of our knowledge, this study is the first to find an association between physical activity and lower mortality from aortic aneurysm and total aortic diseases in Japanese individuals.

Our findings support the results of a meta-analysis of prospective studies on the association between physical activity and incidence or mortality from abdominal aortic aneurysm. The summary relative risk for high versus low physical activity was 0.70 (95% CI: 0.56–0.87)\(^2\). However, in the abovementioned meta-analysis, no study on physical activity and mortality from aortic aneurysm showed a significant association between the two.

Physical activity is known to prevent established atherosclerotic risk factors such as elevated blood pressure, insulin resistance, elevated triglyceride concentrations, and obesity\(^2\). Aortic aneurysm has been associated with atherosclerosis and its risk factors\(^2, 5\). Among aortic dissection, the Stanford Type A aortic dissection (involving the ascending aorta), which shows lesser association with atherosclerosis than Stanford Type B aortic dissection (not including the ascending aorta), accounted for approximately two-thirds of aortic dissection cases according to the International Registry of Acute Aortic Dissections\(^6, 7\). Therefore, physical activity could have preventative effects on aortic diseases through its suppressive effects on atherosclerosis. In addition, physical activity has been reported to have an anti-inflammatory effect, which may play an important role in the infiltration of inflammatory cells, which is a major pathogenetic feature of aortic aneurysm and dissection\(^8, 9\). In contrast, another pathophysiological feature of aortic dissection that may not be affected by physical activity could partially explain the differential effects of physical activity on the type of aortic diseases, i.e., changes in the architecture of medial elastic fibers, which may lead to an aortic intimal tear and medical dissection\(^10\).

The strength of our research includes the fact that it is a long-term prospective cohort study with a large number of participants, yielding a sufficient number of aortic disease deaths for the present analysis. However, this study has several limitations. First, data on the intensity of physical activity beyond the time spent playing sports or walking were not collected in this study. This might have affected the accuracy of the grouping of individuals according to the time spent participating in sports and walking and

<table>
<thead>
<tr>
<th>Table 2. Hazard ratios (95% confidence intervals) of mortality from aortic diseases according to sports and walking time</th>
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</thead>
<tbody>
<tr>
<td>Sports Time (h/week)</td>
</tr>
<tr>
<td>&lt;1</td>
</tr>
<tr>
<td>Person-years</td>
</tr>
<tr>
<td>Aortic aneurysm No. of cases</td>
</tr>
<tr>
<td>Age- and sex-adjusted HR (95%CI)</td>
</tr>
<tr>
<td>Multivariable HR (95%CI)</td>
</tr>
<tr>
<td>Aortic dissection No. of cases</td>
</tr>
<tr>
<td>Age- and sex-adjusted HR (95%CI)</td>
</tr>
<tr>
<td>Multivariable HR (95%CI)</td>
</tr>
<tr>
<td>Total aortic disease No. of cases</td>
</tr>
<tr>
<td>Age- and sex-adjusted HR (95%CI)</td>
</tr>
<tr>
<td>Multivariable HR (95%CI)</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval.
Multivariable HR: adjusted for age, sex, history of hypertension, diabetes, body mass index, smoking status, alcohol consumption, and sports/walking time.
did not allow us to analyze the dose-response effect of physical activity on the risk of aortic diseases. Second, the data on physical activity and confounding variables were collected through self-reported questionnaires, and the validity of the questionnaire was not examined. We assume that there was nondifferential misclassification across the groups, which could lead to a weaker association between physical activity and mortality from aortic diseases. Third, deaths due to aortic diseases tend to be overlooked owing to difficulties in diagnosis; therefore, mortality may be underestimated. However, the diagnostic accuracy is likely to be higher in Japan than in other countries due to the high prevalence of imaging services used in Japanese hospitals (computerized tomography scan and magnetic resonance imaging), which are standard diagnostic tools for aortic diseases. We consider that our analysis of the association between physical activity and risk of aortic diseases is probably not affected by underestimation arising from challenges in diagnosis.

**Conclusion**

Longer time spent participating in sports was associated with a reduced risk of mortality from aortic aneurysm in the Japanese population. However, further studies are needed to investigate the association between physical activity and aortic dissection.

**Conflict of Interest**

Tadayuki Tanimura is an employee of Roche Diagnostics, but this study is neither supported by it nor is it relevant to its business. The authors declare no conflicts of interest associated with the contents of this article.

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