Leisure-Time Physical Activity in Midlife Is Related to Old Age Frailty

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Background. There are scarce studies of the long-term associations between leisure-time physical activity (LTPA) in midlife and phenotypic frailty in old age.

Methods. We studied healthy Caucasian men of high socioeconomic status (N = 514), who had participated in health checkups during the 1960s (the Helsinki Businessmen Study, Finland). In 1974, they were examined with questionnaires and clinical examinations, and LTPA was collapsed into three categories: low (n = 87), moderate (n = 256), and high (n = 171). In 2000, at mean age of 74, survivors were assessed for physical activity and frailty phenotype using the modified Fried criteria validated in our cohort. Four criteria were used: (a) weight loss > 5% from midlife or current body mass index < 21 kg/m2, (b) physical inactivity, (c) low vitality, and (d) physical weakness. Responders with 3–4, 1–2, and zero criteria were classified as frail, prefrail, and nonfrail, respectively.

Results. The prevalence of frailty was 16.1%, 10.2%, and 4.7% in the low, moderate, and high LTPA groups, respectively. Higher midlife LTPA was significantly related to lower prevalence of both frailty and prefrailty in old age. After adjusting for baseline age, smoking, body mass index, blood pressure, and alcohol, the risk of frailty was 80% lower in the high LTPA group compared with the low LTPA group (odds ratio = 0.20; 95% confidence interval 0.07–0.55). This finding was supported by the relationships between the change of physical activity and frailty in old age.

Conclusions. In this socioeconomically homogenous male cohort, higher physical activity since midlife was strongly associated with less frailty in old age.

Key Words: Physical activity—Frailty—Preventative health care—Successful aging.

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Frailty is a common geriatric syndrome affecting 5%–10% of community-living older individuals, whereas prefrailty can be discerned even in 30%–40% (1–4). No universal consensus on the definition of old age frailty exists so far, but physical phenotype of frailty was initially defined according to a combination of weight loss, subjective exhaustion, physical inactivity, slowness, and physical weakness (1). Frail people are vulnerable to various stressors, and the development of sarcopenia and impaired muscle strength are common characteristics (3). Although frailty is a separate entity, it predisposes, and is often associated, with comorbidities and disability (2,3). Frailty slows recovery from acute illnesses and increases the need for health and social care.

Consequently, prevention of frailty is one of the major public health challenges in rapidly aging societies. Lifestyle factors are considered to have a role in the development of frailty (5), and increasing physical activity with its various health benefits (6–8) has been proposed as a promising preventive strategy (9).

Although several cross-sectional or short-term studies have evaluated physical activity and frailty, long-term studies of their mutual relationships among initially healthy people are lacking. Therefore, we tested the hypothesis that regular leisure-time physical activity (LTPA) in healthy midlife would be associated with reduced risk of frailty in older men.
METHODS

Study Design and Participants

The cohort and examinations of the Helsinki Businessmen Study have been described earlier (10–14), and the study procedures have been approved by the Ethics Committee of the Department of Medicine, University of Helsinki, Finland. In brief, initially healthy Caucasian men of high socioeconomic status, mostly business executives born in 1919–1934, had participated in structured health check-ups during the 1960s and early 1970s at the Institute of Occupational Health in Helsinki. They were evaluated with questionnaires, clinical and laboratory examinations in 1974, whereupon 1,815 men were found to be actively working and healthy without diabetes, clinical cardiovascular disease, or regular medications. A structured questionnaire about details of their physical activity during the past year was available for 782 men. The majority (90.7%, n = 709) of these men were assessed to be at high cardiovascular risk according to their risk factor profile (11). Their age distribution 47.8 (SD = 4.1) versus 47.5 (4.1) (p = .12) and long-term mortality up to 2000 (22.3% vs. 24.1%, p = .35) were not statistically different from the rest of the cohort. Although part of the men participated in a controlled multifactorial prevention trial during the 1970s (10), preliminary analyses showed that this did not affect the prevalence of frailty 26 years later (10.0% and 12.2% in the participants and nonparticipants, respectively, p = .61). Therefore, all men are included in the present analyses to improve statistical power, and the final analyses are based on the 514 men (83% of the 617 survivors) in whom the frailty status could be defined in the year 2000.

Assessment of Physical Activity and Its Changes During Follow-up

LTPA was assessed in 1974 by asking the common activities during the past year (11) with the following four categories: (a) activity mainly reading, watching television, going to the cinema, or other sedentary activity; (b) walking, cycling, low-intensity cross-country skiing, gardening, bowling, fishing, or other light exercise weekly; (c) jogging, running, cross-country skiing, swimming, tennis, badminton, heavy gardening, or similar exercise weekly on a regular basis; and (d) vigorous/competitive exercise several times a week on a regular basis. Only few men reported competitive activity, and therefore, groups 3 and 4 were combined in the analyses. Men answering “Yes” to question 1 were categorized as low; 2 as moderate; and 3 or 4 as high LTPA group.

In old age in 2000, physical activity was assessed in questionnaires with three questions (no time period was specified): “Do you exercise regularly weekly?”, “if yes, how many hours per week?” and “how many times a week do you have exercise leading to sweating and breathlessness?” We used the question about hours per week to categorize the men into activity groups in 2000, which were similar in distribution to those in 1974: low, <2 hours/week (21.9%), moderate, 2–6 hours/week (50.5%), and high, >6 hours/week (27.6%). Thereafter, we identified five groups according to the change in activity between 1974 and 2000 (constantly low, constantly moderate, constantly high, increase in category, decrease in category), and these were related to stages of frailty in 2000.

Assessment of Frailty

In midlife, frailty was not assessed with formal criteria, but in 1974, the men were asked questions on how they rated their present health and physical fitness on a five-step scale (“Very good,” “Fairly good,” “Average,” “Fairly poor,” “Very poor”).

After a 26-year follow-up in 2000, disease prevalence and frailty status were appraised using a mailed questionnaire as described earlier (12). The translated version of the RAND-36-Item Health Survey 1.0 (which is practically the same as SF-36 and has been validated in the Finnish population) was embedded into the questionnaire (12,14).

Frailty was defined according to a modification of the criteria described by Fried and coworkers (1). As walking speed was not measured, we used the following four criteria: (a) Shrinking was defined as weight loss of >5% from baseline in 1974 or having current body mass index below 21 kg/m²; (b) evaluation of physical weakness was based on self-reported difficulty (not at all = 0) in carrying or lifting a grocery bag (one question of the physical function scale of RAND-36); (c) assessment of exhaustion was based on reported low energy most or all of the time during the preceding 4 weeks (one question of the vitality scale of RAND-36); and (d) evaluation of physical activity was based on the question: “Do you exercise regularly weekly?” The answer “No” was taken to denote low physical activity or sedentary living. The participant was classified to be frail or prefrail if three to four or one to two of the above-mentioned criteria were met, respectively, and nonfrail if zero criteria was present. Those men not providing answers to all questions were excluded. The present definition of frailty has been shown to predict important endpoints, such as total mortality and the development of mobility disability during a 7-year follow-up in our cohort (12).

A summary comorbidity measure was calculated from the reported diseases in 2000 according to the Charlson comorbidity index (15). This index was used to adjust for the relationship between midlife LTPA and disease burden in old age.

Mortality Follow-up

Total mortality of the study cohort up to December 31, 2000 was retrieved from the Population Information System, which keeps registry of all Finnish citizens.
Analyses
NCSS statistical software (2007 version, www.ncss.com) was used for the analyses. Descriptive statistics include means with SD or SE. Comparisons across physical activity groups (baseline 1974 and change between 1974–2000) were performed with chi-square and trend tests for categorical variables. t-Tests, nonparametric tests, and analyses of covariance (ANCOVA) were used where appropriate to compare continuous variables across LTPA groups. Odd ratios with their 95% confidence intervals for frailty or prefrailty associated with LTPA at baseline were calculated using multinomial logistic regression models with nonfrail men as referent. Other risk factors (age, smoking, body mass index, cholesterol, blood pressure, and alcohol consumption) in 1974 and Charlson comorbidity index in 2000 were adjusted for in respective models. In statistical analyses, two-tailed tests were used, and p values < .05 were taken as significant.

Results
The baseline characteristics including LTPA in 1974 were comparable between the 514 men with and 103 men without frailty assessment in 2000 (Table 1). In 1974, only one man rated his health as “Very poor,” and the proportions of men with subjectively “Fairly poor” health were 2.8%, 4.3%, and 4.7% in the low, moderate, and high LTPA groups, respectively. Only two men (0.3%) rated their subjective fitness as “Very poor.” Because all men were also clinically healthy and actively working, it is unlikely that anyone would have filled the frailty criteria at that time.

In 2000, the median of reported weekly exercise was 4 hours (interquartile range 2–7 hours), and 99 men (19%) reported no weekly exercise. Of all participants in 2000, 9.3% (n = 48) were defined as frail, and their proportion was inversely and significantly (p < .001) related to the LTPA level in midlife (Figure 1). Also the age-adjusted means of the comorbidity index in old age showed an inverse relationship with midlife LTPA being 1.7 (SE = 0.1), 1.4 (0.1), and 1.2 (0.1) in low, moderate, and high LTPA groups, respectively (p = .02). The age-adjusted means of the comorbidity index increased, in turn, with the frailty status being 1.1 (SE = 0.09), 1.5 (0.08), and 2.1 (0.2) among nonfrail, prefrail, and frail participants, respectively (p < .001).

In adjusted analyses, the level of LTPA in midlife significantly predicted frailty and prefrailty in 2000 (Table 2). In the high LTPA group, the risk was 80% lower for frailty and 47% lower for prefrailty compared with the low LTPA group independently of age, smoking, body mass index, cholesterol, blood pressure, and alcohol consumption in 1974. Although the point estimate for moderate LTPA suggested a 32% lowered risk for frailty (adjusted for age, smoking, body mass index, cholesterol, blood pressure, and alcohol consumption in 1974), the association was not statistically significant. We also tested the effect of baseline one-hour postload glucose as a covariate, but the relationship between LTPA and old age frailty was virtually unaltered (data not shown).

To examine the role of chronic conditions as a possible explanation for the association between LTPA and frailty, the models were adjusted for the comorbidity index in 2000 (Table 2, Model C). This adjustment did not substantially change the results: the risk of frailty was still 77% lower in the high LTPA group compared with the low LTPA group, reaching statistical significance. However, the 43% lowered risk for prefrailty was no more statistically significant.

Because physical activity and muscle strength are dimensions of the frailty phenotype, it can be argued that midlife exercise, like midlife strength, simply predicts physical activity and strength in old age. Therefore, we made sensitivity analyses by adjusting the analyses for reported exercise in old age. Even in these analyses, the power of midlife LTPA to predict frailty prevailed (fully adjusted odd ratios 0.31, 95% confidence intervals 0.10–0.97). This suggests that frailty phenotype gives extra value for risk prediction.

Finally, we compared the relationship between the change in physical activity between 1974 and 2000 and stage of frailty in old age (Table 3). A decrease in activity was associated with higher and an increase in activity with lower prevalence of frailty. Of the men with constantly low and high physical activity, 40.7% and 0%, respectively, were frail in 2000 (p < .001).

Discussion
Our 26-year follow-up of a homogenous male cohort shows that LTPA in healthy midlife is a strong and graded predictor of frailty in old age. The men with high LTPA in midlife had up to 80% lower risk of frailty compared with the men with sedentary lifestyle. The association was
independent of several midlife variables including age, smoking, body mass index, cholesterol, blood pressure, and alcohol consumption. Neither did the results change substantially when the index of comorbid conditions in old age were taken into account, suggesting a unique role for physical activity in preventing phenotypic frailty. The result was also insensitive to the adjustment for physical activity in old age. In addition, decline in physical activity during the 26 years of follow-up was associated with a higher prevalence of frailty in old age. The results emphasize the importance of regular physical activity early in the life course to avoid frailty in old age. It is notable that especially regular vigorous or high-intensity exercise habit seems to remain over decades (11).

To the best of our knowledge, there is only one previous study examining the significance of physical activity (or the lack of it) in the prediction of frailty (16). Sedentary older adults were reported to have increased odds of developing frailty (defined as having a gait speed of less than 0.6 m/s or being unable to rise from a chair once with arms folded) compared with those participating in regular exercise activities during a 5-year follow-up. The baseline number of diagnoses was the strongest predictor of frailty. However, that study population was 70–79 years of age (mean 74 years) and had various comorbidities at baseline. It, therefore, clearly differed from our population with a mean age of 48 years and clinically normal health status at baseline.

Our results are in line with previous studies, which have shown that physical activity reduces the risk of various common characteristics of frailty, such as sarcopenia (17), allostatic load (18), cognitive decline, and diseases (6–8). In recent studies, better midlife fitness was associated with

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**Table 2. Odds Ratios of Frailty in 2000 According to the Leisure-Time Physical Activity (LTPA) Level in Midlife**

<table>
<thead>
<tr>
<th>Stage of Frailty (Nonfrail Men as Referent)</th>
<th>Low LTPA in 1974, n = 87 (16.9%)</th>
<th>Moderate LTPA in 1974, n = 256 (49.7%)</th>
<th>High LTPA in 1974, n = 171 (33.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prefrailty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model A</td>
<td>1.0 (Referent)</td>
<td>0.92 (0.53–1.60)</td>
<td>0.50 (0.28–0.89)</td>
</tr>
<tr>
<td>Model B</td>
<td>1.0</td>
<td>0.98 (0.55–1.72)</td>
<td>0.53 (0.29–0.95)</td>
</tr>
<tr>
<td>Model C</td>
<td>1.0</td>
<td>1.00 (0.57–1.78)</td>
<td>0.57 (0.31–1.03)</td>
</tr>
<tr>
<td>Frailty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model A</td>
<td>1.0</td>
<td>0.60 (0.27–1.33)</td>
<td>0.18 (0.07–0.48)</td>
</tr>
<tr>
<td>Model B</td>
<td>1.0</td>
<td>0.68 (0.30–1.54)</td>
<td>0.20 (0.07–0.55)</td>
</tr>
<tr>
<td>Model C</td>
<td>1.0</td>
<td>0.75 (0.32–1.74)</td>
<td>0.23 (0.08–0.65)</td>
</tr>
</tbody>
</table>

*Note. Model A: adjusted for age; Model B: adjusted for age, body mass index, smoking, blood pressure, and alcohol consumption in 1974; Model C: adjusted as in Model B and for the comorbidity index in 2000.*

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**Table 3. Stage of Frailty in 2000 According to Change in Physical Activity Between 1974 and 2000**

<table>
<thead>
<tr>
<th>Change of Physical Activity Between a Mean of 48 and 74 Years of Age</th>
<th>Stage of Frailty in 2000</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constantly: Low, n = 27</td>
<td>Nonfrail</td>
<td>Prefrailty</td>
</tr>
<tr>
<td>Low: n = 139</td>
<td>1 (3.7)</td>
<td>15 (55.6)</td>
</tr>
<tr>
<td>Moderate: n = 55</td>
<td>66 (47.5)</td>
<td>70 (50.4)</td>
</tr>
<tr>
<td>High: n = 55</td>
<td>32 (58.2)</td>
<td>23 (41.8)</td>
</tr>
<tr>
<td>Increase: n = 118</td>
<td>45 (38.1)</td>
<td>68 (57.6)</td>
</tr>
<tr>
<td>Decrease: n = 175</td>
<td>57 (32.6)</td>
<td>89 (50.9)</td>
</tr>
</tbody>
</table>

*Note. Percentages are shown in parentheses.

*Global value between groups.
lower risk of developing chronic conditions in old age (19), and higher levels of cardiorespiratory or muscular fitness predicted a better cardiovascular prognosis and survival (20,21). These associations may point to the pathways through which physical activity can prevent frailty. Midlife physical activity has also been shown to have a strong protective effect on later life mobility disability (22–24), falls (25), and mortality (8,11,26–28).

It is of note that in our study, the association between higher midlife LTPA and lower risk of frailty in old age remained despite the adjustment for chronic diseases and for several other possible explanatory factors. However, a very challenging point relates to the definition of phenotypic frailty, which includes physical activity as one of its moderately important domains (29). Is the association between midlife LTPA and old age frailty a “self-fulfilling prophecy” in our study? This is unlikely because of the long follow-up and especially because the relationship prevailed after physical activity in old age was adjusted for. Nevertheless, the primary aim of our study was to establish an association between a modifiable midlife predictor (LTPA) of phenotypic frailty—as it is de facto defined—in old age.

Strengths and Limitations

The main strengths of our study are the initially healthy participants and the long follow-up, which reduces the possibility of reverse causation. Physical activity at work and leisure time, lifestyle, and other stress factors differ in various socioeconomic groups (30), and social factors have been shown to affect the frailty syndrome (31–35). Our cohort was socioeconomically homogenous.

But there are some limitations in our study that are important to consider. The participants were evaluated clinically only at baseline in 1974, and although it is unlikely that any man was frail at that time, the exact onset of frailty during the 26-year follow-up is unknown. The definition of frailty was based on questionnaire data in 2000, and because walking speed was not measured, only four criteria modified from the Fried criteria were used to estimate frailty. Moreover, the assessment of physical activity was quite crude, and weight loss was based on long-term change. Despite these limitations, however, this definition of frailty has been shown to predict reduced walking speed and other important endpoints such as total mortality and the development of mobility disability during a 7-year follow-up (12). Therefore, our criteria could be considered to be a valid method to determine physical frailty in line with another study using SF-36 data (36). It is also important to note that the concept of frailty as a whole has still variable definitions in the literature, and there is no global consensus definition or standardized assessment tool to be used in clinical practice and research (2).

Physical activity was determined by self-report, which may overestimate the actual amount of physical activity and thus underestimate the benefits of physical activity among older adults (37). Overlap may also occur within the three LTPA categories. On the other hand, we have demonstrated earlier that midlife physical activity patterns tend to tract until advanced age (11), and also the change in physical activity was significantly related to frailty.

Because of the long follow-up, mortality is a potential source of selection bias. Both frailty (12) and lower LTPA (11) have been shown to associate with higher mortality in our cohort, and therefore mortality before frailty assessments probably dilutes the association between frailty and LTPA.

An interesting issue—yet a limitation in this study—is the social and community aspects of LTPA. The development of frailty is not a purely physical phenomenon (31–35). Low level of LTPA may be correlated to passivity in general—for instance, private home-bound pursuits—which may also have an impact on the development on frailty. Closer analyses of these aspects are, however, beyond the scope of this article.

Finally, although the socioeconomically homogenous Caucasian male cohort is one of the strengths of this study, it also limits its comparability and generalizability to women, other social classes, and ethnic groups.

In conclusion, despite limitations, our results strongly suggest that continuous physical activity since midlife has a strong and independent effect on the frailty phenotype in old age and emphasize the importance of starting regular physical activity early in life to prevent the development of this important geriatric condition.

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Professor Tatu A Miettinen contributed to the design and initial preparation of the present report. He passed away in November 2011.

Conflict of Interest

None relevant to this article.

References