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Research Article

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Physical activity and dementia: A meta-analysis of prospective studies

Shuqin Yin[1], Hongwei Nie[2#] and Yong Xu[3]*

[1]*Department of Preventive Medicine, Huzhou Teachers College, China*
[2]*Center for Reproductive Medicine, Shandong University, Jinan, China*
[3]*Department of Preventive Medicine, School of Public Health, Soochow University, Suzhou, China*

ABSTRACT

The association between higher levels of physical activity and the number of physical activities and dementia is of major interest. This study was to examine the effect of physical activity on risk of developing dementia. 10 prospective cohort studies that reported relative risks with 95% confidence intervals for the association of physical activity and dementia risk were chosen in this study. A random effects model was used to calculate the summary risk estimates. The summary relative risk of dementia for associated with physical activity was 0.48 (95% confidence interval: 0.33-0.64), with evidence of heterogeneity (P = 0.000, I^2 = 83.50%). Findings of the present meta-analysis indicate that physical activity was associated with a reduced risk of dementia and it is important for preventing it.

Keywords: Physical activity; Dementia Intervention; Cohort studies; Meta-analysis

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INTRODUCTION

Dementia is a loss of cognitive abilities in multiple domains that results in impairment in normal activities of daily living and loss of independence[1]. The dementing illnesses are increasing in prevalence and present a major public health problem for the upcoming decades (Peter et al., 2007)[2], which bring heavy burden to the families and society. However, few strategies are available for the prevention of dementia in elderly persons. Preventive strategies are of paramount importance to reduce the huge burden caused by dementia.

Elderly people with a poor aerobic capacity avoid physical activities and so lose their muscle mass and strength, with further reduction in aerobic capacity, causing a vicious cycle. Taking these concepts into account, the promotion of regular physical activity is one of the main non-pharmaceutical measures that should be promoted in older subjects, especially regarding a preventive approach for 'a successful ageing'. Several longitudinal cohort studies involving elderly people without cognitive impairment at enrolment have indicated that physical exercise is associated with reduced cognitive decline and reduced risk of dementia[3] (Lytle et al., 2004). However, other studies have failed to show a protective effect of physical exercise on cognitive decline and dementia[4] (Wilson et al., 2002). During the past decade, the number of subsequent original studies on this issue has increased constantly.

EXPERIMENTAL SECTION

Search strategy

We attempted to plan, conduct, and report this meta-analysis in accordance with the Meta-Analysis of Observational Studies in Epidemiology guidelines. We performed a Medline data-base search through July 2013 to identify relevant studies regarding the association between physical activity and risk of dementia. We used search terms "physical activity", "physical training" or "physical exercise" in combination with "dementia". In addition, we reviewed the reference lists of retrieved studies and recent reviews. No attempt was made to identify unpublished reports.

Study selection

Study selection was based on an initial screen of identified abstracts or titles and a second screen of full-text articles. Studies were considered eligible if they met the following criteria: (1) the study design was a prospective study, which provides stronger evidence than a retrospective design; (2) the main intervention of the study was physical activity; (3) the outcome of interest was dementia risk; and (4) relative risks (RRs) with corresponding 95% confidence intervals (CIs) for the use of station on dementia were reported.

Data extraction and quality assessment

We extracted all data using a standardized data-collection form. Information was recorded as follows: last name of the first author; publication year; country; mean follow-up (year); number of cases; risk estimate from multivariable model for physical activity on dementia with corresponding 95%CI. The data from all included studies were clearly tabulated and quality assessment was carried out independently by at least two reviewers. In the case of disagreement, data were reviewed by two other authors. The author (Y.S) independently performed the studies selection and data extraction. Any disagreements were resolved by discussion.

Statistical analysis

Our main analyses were focused on the associations between physical activity and risk of dementia. Body of evidence supports the role of physical activity as a tool to maintain cognitive performance. Absolute numbers of relevant outcomes were entered into database. The RR was used as the common measure of association across studies, and the hazard ratio and incidence rate ratio were directly considered as RR.

Homogeneity of RRs across studies was tested by Q statistic (significance level at $P<0.10$) and the I^2 statistic, which is a quantitative measure of inconsistency across studies. If substantial heterogeneity exists, the random-effects model is appropriate; otherwise, the fixed-effects model is preferred. Potential publication bias was assessed by both Begg rank correlation test and Egger linear regression test. All analyses were performed using STATA version 11.0 (Stata Corp, College Station, TX). $P<0.05$ was considered statistically significant, except where otherwise specified. All statistical tests were two-sided.

RESULTS AND DISCUSSION

Literature search

A flow chart showing the study selection is presented in Fig. 1. Briefly, we identified 12 potentially relevant studies for full-text review. Two studies were excluded, because they used a retrospective cohort design or nested case-control design. Finally, 10 studies were selected for analysis. Of 10 studies, two studies differ from the others: The study by Taaffe et al investigated which investigated only men and Rovio's et al study had an exceptionally long follow-up time of 21 years.

Study characteristics

The characteristics of the selected studies are presented in Table 1. The 10 prospective studies were published between 2001 and 2011[5-14]. Six studies were conducted in North America, three in Europe, and one in Australia. Of the included studies, the number of cases diagnosed in the original studies ranged from 86 to 590, with a sum of 2804. The number of participants ranged from 749 to 6434, with a sum of 28565. The median length of follow-up ranged from 3.2 to 21 years, with a median of 6.8 years.

Table 1 Characteristics of the included studies

First author and year	Country	Study design	Mean Follow-up (year)	Cases	RR and 95%CI
Laurin et al. (2001）	Canada	Cohort	5	285	0.63(0.40-0.98)
Podewils et al.(2005)	US	Cohort	5.4	480	0.51(0.33-0.79)
Rovio et al. (2005)	Sweden	Cohort	21	117	0.48(0.25-0.91)
Larson et al. (2006)	US	Cohort	6.2	158	0.62(0.44-0.86)
Pareja et al. (2006)	Spain	Cohort	3.2	131	0.32(0.19-0.53)
Barneset al. (2007)	US	Cohort	6	590	0.74(0.60-0.90)
Ravaglia et al. (2007)	Italy	Cohort	3.9	86	0.24(0.11-0.56)
Taaffe et al. (2008)	Australia	Cohort	6.1	173	0.50(0.28-0.89)
Scarmeas et al.(2009)	US	Cohort	5.4	282	0.67(0.47-0.95)
Scarmeas et al.(2011)	US	Cohort	5.2	502	0.20(0.13-0.31）

Main analysis

The summary RR for physical activity in relation to dementia risk was shown in Fig. 2. Results from 10 prospective cohort studies are included. The summary RR was 0.48 (95% CI: 0.33-0.64), with evidence of heterogeneity (P =

0.000, I^2 = 83.50%). It exhibits a significant association between physical activity and risk of dementia.

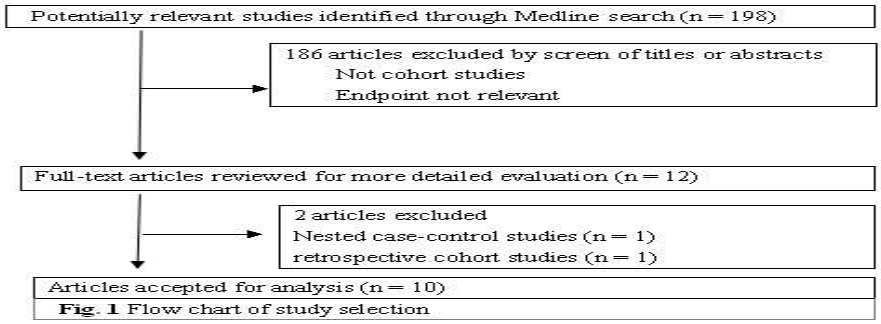

Fig. 1 Flow chart of study selection

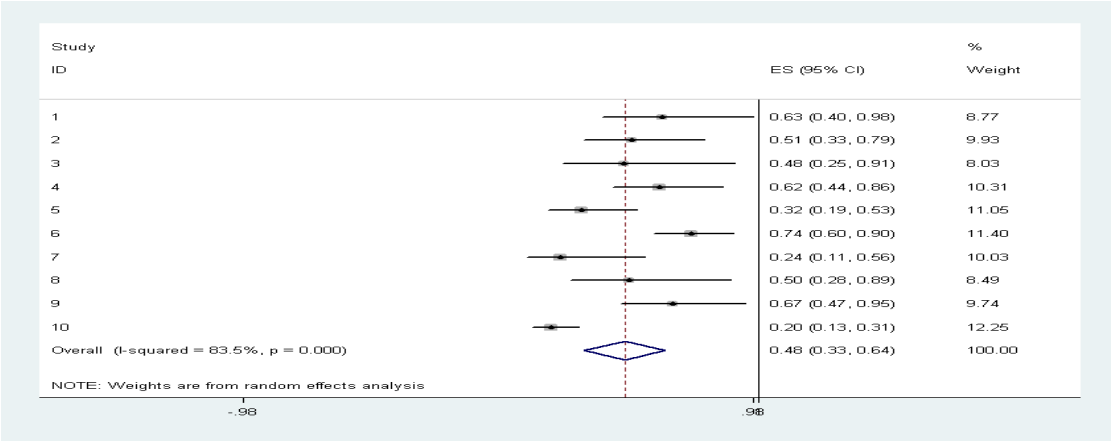

Fig. 2 Forest plot of studies examining the association between physical activity and risk of dementia

Subgroup analyses

Table 2 shows the results of subgroup analyses stratified by geographic region, duration of follow-up and number of cases. Physical activity was associated with a significant reduced risk of dementia in longer years of follow-up (summary RR = 0.53, 95% CI: 0.32-0.74, RR and 95%CI are shown in Fig.3) and in more number of cases (summary RR = 0.54, 95%CI: 0.27-0.81, RR and 95%CI are shown in Fig.4). Summary RRs were stratified by number of cases, length of follow-up, and analyses among studies with more cases, longer duration yielded significant results.

Table 2 Results of subgroup analyses of dementia

group	No. of Studies	Summary relative risk (95% CI)	P for heterogeneity	I^2,%
All	10	0.48(0.33-0.64)	0.000	83.50
follow-up (years)				
≦5	3	0.37(0.18-0.57)	0.099	56.70
＞5	7	0.53(0.32-0.74)	0.000	87.80
No. of cases				
≦280	5	0.42(0.27-0.57)	0.107	47.50
＞280	5	0.54(0.27-0.81)	0.000	91.50
Geographic area				
North America	6	0.55(0.32-0.79)	0.000	90.1
Europe	3	0.32(0.19-0.44)	0.500	0.0

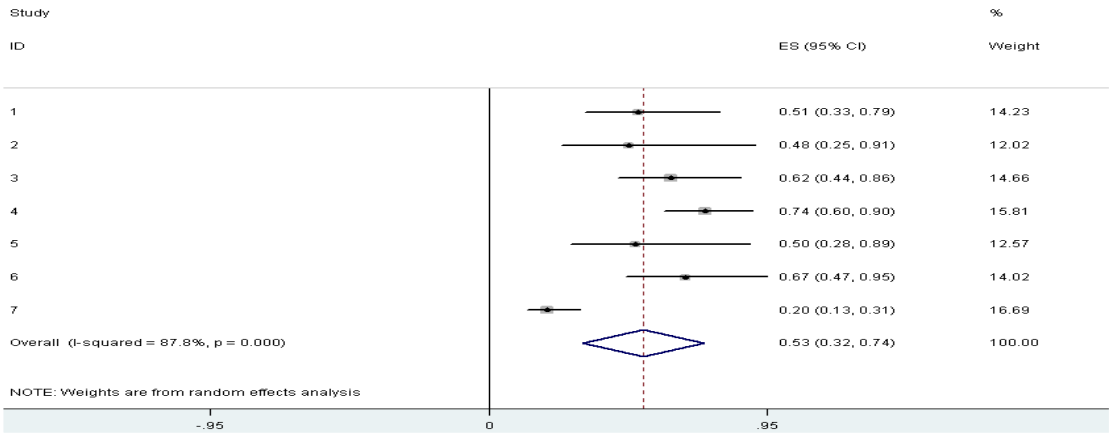

Fig. 3 Forest plot of studies examining the association between physical activity and risk of dementia in longer years of follow-up

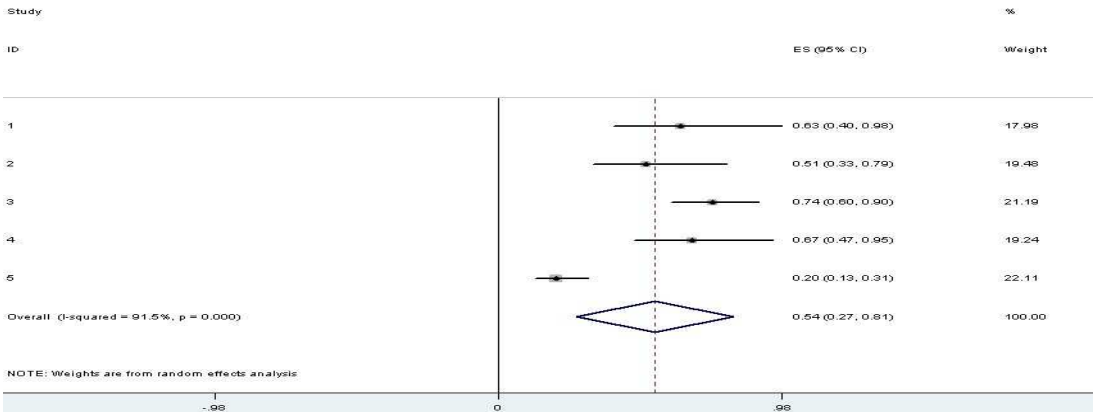

Fig. 4 Forest plot of studies examining the association between physical activity and risk of dementia in more number of cases

Publication bias

There was no evidence of publication bias with regard to physical activity in relation to dementia risk, as suggested by Begg rank correlation test and Egger linear regression test (all *P*>0.05, Fig. 5 and Fig. 6).

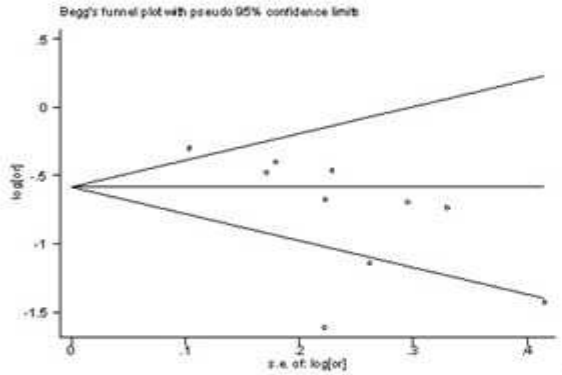

Fig. 5 Begg's funnel plot of physical activity and risk of dementia

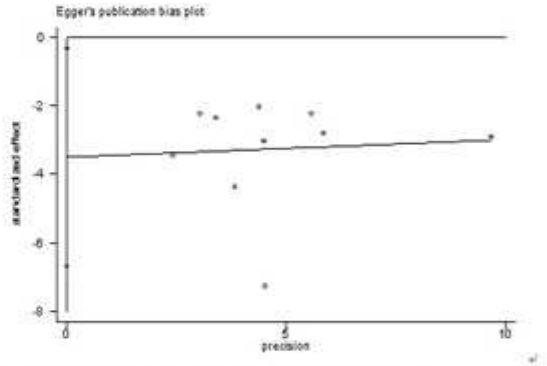

Fig. 6 Egger's funnel plot of physical activity and risk of dementia

In our meta-analysis we assessed the possible impact of physical activity on dementia. The results clearly show that increased physical activity when compared to low or no physical activity is associated with a modest reduction of incident dementia. Our findings support the notion that physical activity is not only good for the prevention of cardiovascular disease and colorectal cancer, but also for prevention of AD. The present results should be robust, since they are based on prospective cohort studies with predefined inclusion and exclusion criteria. In addition, the cohort studies included had adequate sample size and long observation periods to detect a sufficient quantity of incident dementia. A recent meta-analysis of 16 prospective studies with 163 797 participants without dementia at baseline and 3219 cases of dementia at follow-up found a decreased relative risk of dementia in the highest physical

activity category compared with the lowest (0.72; 95% CI, 0.60-0.86).

Meta-analyzing of these studies is a powerful tool to assess the long-term benefits of lifestyle factors like physical activity and overcome limitations (e.g., small sample size or low incidence) of individual smaller studies. A limitation of a meta-analysis is that absolute numbers of the outcomes of single studies are entered, whereas no effect sizes that are controlled for major confounding factors are entered.

Compared to the literature, our results are compatible with a recent meta-analysis done on Alzheimer's disease by Markus et al., who found a pooled relative risk for AD of 0.59 for physical activity in six studies. In addition, A review of the literature provides evidence that leisure activities, cognitive stimulation and physical activity should be promoted as part of a healthy lifestyle in elderly people and those with mild cognitive impairment.

Our study has strengths. With the meta-analysis using STATA software, we have enhanced statistical power to detect any associations between station use and risk of dementia, and to get expected results. In addition, all the original studies enrolled in the present meta-analysis used a prospective cohort design, which minimizes recall, interviewer, and selection biases that can always be concerns in retrospective studies.

It was found a significant association between physical activity and a reduced risk of dementia and our finding, therefore, provide some support to the hypothesis that physical activity may protect against the development of dementia. Yet, the research is not perfect and it needs further research in future.

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