Physical inactivity is a strong risk factor for stroke in the oldest old: findings from a multi-ethnic population (the Northern Manhattan Study)

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Abstract

Background—The fastest growing segment of the population is those age 80 who have the highest stroke incidence. Risk factor management is complicated by polypharmacy related adverse events.

Aims—to characterize the impact of physical inactivity for stroke by age in a multi-ethnic prospective cohort study (NOMAS, n = 3298).

Methods—Leisure-time physical activity was assessed by a validated questionnaire and our primary exposure was physical inactivity(PI). Participants were followed annually for incident stroke. We fit Cox-proportional hazard models to calculate hazard ratios and 95% confidence intervals (HR 95% CI) for the association of PI and other risk factors with risk of stroke including two-way interaction terms between the primary exposures and age (<80 vs. 80).

Results—The mean age was 69±10.3 years and 562(17%) were 80 at enrolment. PI was common in the cohort (40.8%). Over a median of 14 years we found 391 strokes. We found a significant interaction of age 80 on the risk of stroke with PI(p=0. 03). In stratified models, PI versus any activity(adjusted HR 1. 60, 95%CI 1.05–2.42) was associated with an increased risk of stroke among those 80.

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Conclusion—Physical inactivity is a treatable risk factor for stroke among those older than age 80. Improving activity may reduce the risk of stroke in this segment of the population.

Keywords

stroke; aging; physical inactivity; exercise; epidemiology; mortality

Introduction

In the United States the fastest growing segment of the population is those above the age of 80. The elderly live with a high burden of disability and the high incidence of stroke after age 80 compounds morbidity and disability[1].

Unfortunately little is known about the epidemiology and treatment of risk factors for stroke in the elderly. The decision on whether to aggressively treat risk factors for stroke in those over 80 is more complex than in younger counter-parts given the substantial risks of polypharmacy [2]. Leisure-time physical inactivity(PI) has several advantages as a modifiable condition, including no risk of polypharmacy, and health benefits across multiple domains.

Aims and hypothesis

To examine the association of PI with incident stroke stratified by age. We hypothesized that leisure-time physical inactivity would be associated with stroke differing by age<80 vs. >=80.

Methods

Recruitment of the Cohort

NOMAS is a population-based prospective cohort study designed to evaluate the effects of cardiovascular disease risk factors in a stroke-free multi-ethnic community cohort. Methods of participant recruitment, evaluation, and follow-up have been previously reported.[3] A total of 3298 stroke-free participants were recruited between the years 1993 to 2001 The study was approved by the Institutional Review Boards at CUMC and the University of Miami. All participants gave informed consent to participate in the study.

Cohort Evaluation

Assessment of leisure-time physical activity—LTPA was measured by an in-person questionnaire adapted from the National Health Interview Survey of the National Center for Health Statistics[4]. This questionnaire records the duration and frequency of various leisure time activities for the 2 weeks before the interview. The participants were then asked if they engaged in any LTPA in the preceding two weeks, and those who answered "no" were coded as physically inactive; if the duration of activity was less than 10 minutes it was coded as inactive. The questionnaire has been validated against proxies and correlated well with body-mass index (BMI), activities of daily living scores, and quality of well-being activity scores[5].

Study follow-up—All participants were followed annually via phone screening to detect any new neurological symptoms and events, as well as hospitalizations. Possible strokes were adjudicated by two neurologists independently after review of all data. The final diagnosis and stroke subtype were decided by consensus of the two neurologists; any disagreements were adjudicated by a third neurologist.

Statistical Analysis

Distributions of base line characteristics were calculated overall and by age < and 80 years, differences in characteristics were compared using the chi-squared test or Wilcoxon rank-sum test as appropriate. We fit Cox-proportional hazard models to calculate hazard ratios and 95% confidence intervals (HR 95% CI)for the association of cardiovascular disease risk factors with risk of stroke and confirmed the proportionality assumption. Multi-variable models were adjusted for socio-demographics (sex, race-ethnicity, education, insurance status) and medical comorbidities (alcohol use, HDL-C, LDL-C, tobacco use, diabetes, hypertension, atrial fibrillation, congestive heart failure, ischemic heart disease). To examine the differences in these associations between those age <80 and 80, multi-variable models included two-way interaction terms between age and risk factors. The models were stratified by age if the p for interaction was <0.05.

Results

Baseline demographics of the cohort (n = 3298) are presented in the supplemental table. The average age was 69±10 years and 562 (17%) were age 80 years. Leisure-time PI was common (40.8% overall) and did not differ by age.

Subjects were followed for a median of 14 years, and there were 391 total strokes(340 ischemic, 51 hemorrhagic). We found that there were significant interactions for age 80 on the risk of stroke with physical inactivity (p = 0.03), diabetes (p=0.04), hypertension (p=0.007), congestive heart failure (p = 0.04) and LDL-C (p=0.04). The statistical interaction for moderate alcohol use (p=0.06), ischemic heart disease (p=0.06), atrial fibrillation (p=0.11) and tobacco use (p=0.7)to be non-significant.

In models stratified by age (table) we found that PI versus any activity (adjusted HR 1.60, 95%CI 1.05–2.42)was associated with an increased risk of stroke among those age 80. Congestive heart failure, LDL-C, hypertension, and diabetes were not associated with risk of stroke in this age category.

Among those under the age of 80, there was no association between leisure time physical inactivity and stroke risk (table).

Discussion

We found that PI was associated with a greater risk of all stroke mainly among the oldest old (age 80), while diabetes and hypertension were not as strongly associated with stroke risk in this age group.

Leisure-time physical inactivity has been hypothesized to lead to stroke through an increased burden of other cardiovascular disease risk factors. The deleterious effect of PI in the elderly however, remained after adjusting for confounders. Physical inactivity has been postulated to have independent harms through modulation of endothelial function and vascular reactivity[6]. There has been considerable interest in improving PI in the elderly to prevent dementia[7], but fewer studies of PI on stroke risk. This is notable given that reducing leisure physical inactivity is feasible in older populations, is not associated with adverse events, and can reduce multiple other adverse health effects, including reduction in bone health and sarcopenia[8]. In this manner we cannot rule out reverse causality, namely that physical inactivity is a reflection of accumulated disability from medical comorbidities or frailty and that our findings reflect the association of general health with risk of stroke. This is unlikely to be the sole explanation for our findings given we adjusted for medical comorbidities and participants were followed for a mean of 12 years.

The strengths of our study include low loss to follow-up, systematic classification of all risk factors and outcome events, and a unique multi-ethnic population. This analysis has some important limitations. We did not assess occupational activity or walking for exercise which could offset the impact of leisure-time PI[9,10]. We used a self-reported physical activity questionnaire, which may be subject to information bias due to misclassification. In prior studies misclassification of moderate activity based on questionnaires in the elderly is common, especially among those who are frail[11], and we did not collect information on this important confounder. Our study also did not include more objective measures of fitness, which others have found to be protective, and which may be less influenced by known or unmeasured confounders[12,13]. Future studies using objective measures of inactivity are required to help address this difference. We also did not systematically collect data on important confounders, such as interval development of atrial fibrillation which could be significant predictors of stroke in the elderly[14]. Lastly the participants who were older than 80 and were well enough to participate in the initial assessment may not be representative of the broader population in that age group thereby limiting our generalizability.

Our study has important public health implications, and adds to the body of literature on the multiple health benefits of exercise even in older individuals[15,16]. Prevention of physical inactivity may be an important component of primary prevention in populations such as ours. These interventions may need to include novel approaches to account for the medical comorbidities in the oldest old, such as home-based exercise programs or mobile health solutions to minimize sedentary time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table

Association of physical inactivity and baseline medical comorbidities with risk of stroke overall and stratified by age less than 80 and greater than or equal to 80 in the Northern Manhattan Study.

	All participants (n = 3298) HR (95% CI)[*]	Participants with Age < 80 (n = 2736) HR (95% CI)[*]	Participants with Age 80 (n = 562) HR (95% CI)[*]
Leisure—time Physical inactivity (vs. Any physical activity) [¥]	0.89 (0.72–1.11)	1.03 (0.82–1.30)	1.60 (1.05–2.43)
Diabetes[¥]	2.02 (1.61–2.54)	2.23 (1.76–2.83)	1.09 (0.58–2.03)
Hypertension[¥]	1.61 (1.20–2.15)	1.75 (1.30–2.36)	1.02 (0.66–1.59)
Congestive heart failure [¥]	1.36 (0.92–2.02)	1.67 (1.12–2.51)	0.47 (0.15–1.49)

[*]
Multi-variable models adjusted for socio-demographics (sex, race-ethnicity, education, insurance status) and medical comorbidities (alcohol use, HDL-C, LDL-C, tobacco use, diabetes, hypertension, atrial fibrillation, ischemic heart disease, congestive heart failure, eGFR)

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p-value for interaction with age <0.05