Physical Activity and Stroke Mortality in Women : Ten-Year Follow-Up of the Nord-Trondelag Health Survey, 1984-1986

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Physical Activity and Stroke Mortality in Women
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Background and Purpose—Few studies have reported a protective effect of physical activity on stroke in women, particularly among elderly women. This study was conducted to examine the association between different levels of leisure-time physical activity and stroke mortality in a large prospective study of middle-aged and elderly women.

Methods—We conducted a 10-year mortality follow-up of women aged ≥50 years, free from stroke at baseline (n=14 101), who participated in the Nord-Trøndelag Health Survey in Norway during 1984–1986. Main outcome measures were relative risk of stroke mortality according to increasing levels of physical activity, with the least active group used as reference.

Results—In groups aged 50 to 69, 70 to 79, and 80 to 101 years, the relative risk of dying decreased with increasing physical activity, after adjustment for potentially confounding factors. In groups aged 50 to 69 and 70 to 79 years, the most active women had an adjusted relative risk of 0.42 (95% CI, 0.24 to 0.75) and 0.56 (95% CI, 0.36 to 0.88), respectively. In the group aged 80 to 101 years, there was a consistent negative association with physical activity; the adjusted relative risk for the most active was 0.57 (95% CI, 0.30 to 1.09).

Conclusions—Physical activity was associated with reduced risk of death from stroke in middle-aged and elderly women. This association persisted after we excluded individuals with prevalent cardiovascular and cerebrovascular disease at baseline and women who died during the first 2 years of follow-up. These observations strengthen the evidence that physical activity should be part of a primary prevention strategy against stroke in women. **(*Stroke*. 2000;31:14-18.)**

Key Words: epidemiology ■ exercise ■ risk factors ■ stroke prevention

Stroke is the third leading cause of death and a major cause of mental and physical disability in the elderly. Specific treatment is not available for most types of stroke, and the identification of modifiable risk factors is necessary for primary prevention. Studies that have shown a negative association between physical activity and atherosclerotic disease have focused on coronary heart disease in middle-aged men. There is increasing evidence that physical activity may also be negatively associated with the risk of stroke,[1–11] but only a few studies have examined physical activity and stroke in women, particularly among elderly women.[1–4,8,9,12–15]

Results of prospective studies among women have been divergent, showing no association,[1,14,16] increased risk only in the low-activity group,[2–4,12] and a negative dose-risk association between levels of physical activity and stroke morbidity and mortality.[8,9,15]

Physical activity may have beneficial effects on biochemical (glucose intolerance, HDL cholesterol, fibrinolytic activity) and physiological (body mass index [BMI], blood pressure, pulse rate, vital capacity, O_2 uptake) factors. A recent study[6] suggested that physical activity may mediate its effect by lowering body weight, blood pressure, and serum cholesterol, whereas others claim that physical activity may exert effects independent of these factors.[1,5,9]

The extent of physical activity is likely to vary between populations. Few studies have been conducted in Scandinavia, where leisure-time activities may differ from those in urban populations studied in the United States. The aim of this study was to examine the association between levels of leisure-time physical activity and stroke mortality in a large prospective study of middle-aged and elderly women.

Subjects and Methods

Subjects

During 1984–1986, a general health survey was conducted among men and women aged ≥20 years in Nord-Trøndelag county in Norway. Among 85 100 eligible persons, 77 310 (90.8%) returned the questionnaire that was mailed with the invitation (questionnaire 1), and 74 977 (88.1%) participated in the health examination. At the examination, a second questionnaire (questionnaire 2) was distributed, which the participants were asked to complete and return by mail. In all, 18 627 women aged ≥50 years attended and received the second questionnaire, which included questions on physical activity.

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TABLE 1. Self-Reported Diseases and Health Measurements According to Level of Physical Activity in Women Aged ≥50 Years Free From Stroke at Baseline, 1984–1986 (n=14 101)

	Physical Activity		
	Low (n=5 115)	Medium (n=4 725)	High (n=4 261)
Age 1984–1986 (SD)	67.7 (10.6)	64.8 (9.1)	62.9 (8.4)
Myocardial infarction, %	3.0	2.3	2.1
Angina pectoris, %	9.4	6.7	5.2
Diabetes, %	6.9	4.4	3.7
Antihypertensive medication, %	31.9	27.1	22.8
Current smoking, %	20.1	19.1	19.1
Mean BMI, kg/m^2 (SD)	27.4 (5.0)	26.8 (4.3)	26.0 (4.0)
Mean systolic blood pressure, mm Hg (SD)	157.6 (27.2)	153.9 (26.1)	150.8 (26.0)
Mean pulse rate, bpm (SD)	77.7 (13.1)	76.3 (12.8)	75.5 (12.4)
Years of education, %			
<10	88.9	86.0	78.4
10–12	9.3	11.7	17.2
>12	1.8	2.3	4.4
Long-term illness that impairs function in daily life, %	52.7	40.9	35.9

Among those, 14 101 women (75.7%) who were free from stroke at baseline completed questions about leisure-time physical activity and were eligible for the follow-up. A detailed description of participants, questionnaires, and screening procedures in the Nord-Trøndelag Health Survey is given elsewhere.[17]

Assessment of Physical Activity and Other Characteristics

Information on physical activity and risk factors for stroke was provided by the 2 self-administered questionnaires (questionnaires 1 and 2) and clinical measurements included in the screening program. From questionnaire 2, detailed information about leisure-time physical activity was obtained and used to classify activity into 3 separate levels: low, medium, and high (Appendix). Activity among women who exercised less than once per week was classified as low. For those who engaged in physical activity once or several times per week, we also queried about intensity and duration, and we constructed a summary measure (index) that was dichotomized at the median value and labeled medium and high activity.

Information on prevalent and current diseases (questionnaire 1) was provided, including diabetes, stroke, coronary heart disease, and long-term illness, in addition to use of antihypertensive medication. Information on current smoking and years of education was also available (questionnaire 2). Measurements of height, weight, systolic blood pressure (mm Hg), and pulse rate (bpm) were made at the health examination.

Follow-Up and End Points

The unique 11-digit identification number of every Norwegian citizen enabled individual linkage between the collected information and the register of deaths at Statistics Norway to determine vital status (alive, emigrated, dead) and cause-specific deaths. Each participant contributed person-years from the date of study entry until the date of death from stroke (n=457), death from other causes (n=3314), emigration (n=18), or the end of follow-up of December 31, 1994 (n=10 312). Median follow-up time was 9.8 years (mean, 9.0 years). Stroke-specific deaths were identified by death certificates using underlying cause of death from stroke according to the *International Classification of Diseases* (ICD) codes of cerebrovascular disease: ICD-8 codes 430 to 438 until December 31, 1985, and ICD-9 codes 430 to 438 from 1986.

Ethics

The Stroke in Nord-Trøndelag Study was approved by the Regional Committee for Ethics in Medical Research and the Norwegian Data Inspectorate. The Ministry of Health and Social Affairs accepted linkage to mortality statistics.

Statistical Analyses

We used Cox regression analysis[18] to calculate age- and multivariate-adjusted risk ratios (with 95% CIs) for death of stroke associated with different levels of physical activity, using the least active group as reference. We evaluated potentially confounding factors in a multivariate analysis including history of diabetes (yes/no), history of myocardial infarction or angina pectoris (yes/no), use of antihypertensive medication (yes/no), diabetes (yes/no), years of education (3 categories: primary and lower secondary school [<10 years], upper secondary school [10 to 12 years], and college or university [>12 years]), long-term illness that impairs function in daily life (yes/no), current smoking (yes/no), BMI (kg/m^2), systolic blood pressure (mm Hg), and age (years). Tests of significance of trend in relative risks (RRs) across categories of physical activity were conducted by treating the levels of physical activity as a single ordinal variable in the proportional hazards model. Trend was considered statistically significant at $P<0.05$. To reduce any further confounding with underlying disease, we performed secondary analyses by (1) excluding subjects with prevalent coronary heart disease (angina pectoris and myocardial infarction), subjects with diabetes, and users of antihypertensive medication at baseline, and (2) excluding individuals who died during the first 2 years of follow-up.

We used the SPSS statistical package, version 8.0, for the analyses.

Results

During 127 253 person-years of follow-up, 457 fatal strokes were recorded.

The health characteristics at baseline are shown in Table 1. Women with a high level of physical activity tended to be

TABLE 2. Relative Risk of Death From Stroke According to Level of Physical Activity in Women Aged ≥50 Years Free From Stroke (n=14 101)

Physical Activity	Subjects	Person-Years	Stroke Deaths	Age-Adjusted RR*	Multivariate RR†‡	95% CI
Age 50–69 y						
Low	2 892	27 440	49	1.00	1.00	Referent
Medium	3 279	31 544	29	0.51	0.57	0.34–0.95
High	3 289	31 867	21	0.39	0.42	0.24–0.75
				P=0.0001§	*P*=0.0021§	
Age 70–79 y						
Low	1 452	11 628	109	1.00	1.00	Referent
Medium	1 132	9 713	64	0.78	0.79	0.55–1.12
High	833	7 365	30	0.48	0.56	0.36–0.88
				P=0.0003§	*P*=0.0093§	
Age 80–101 y						
Low	771	4 538	99	1.00	1.00	Referent
Medium	314	2 121	45	0.98	0.91	0.60–1.39
High	139	1 038	11	0.50	0.57	0.30–1.09
				P=0.0648§	*P*=0.1089§	
All						
Low	5 115	43 606	257	1.00	1.00	Referent
Medium	4 725	43 377	138	0.77	0.77	0.61–0.98
High	4 261	40 270	62	0.47	0.52	0.38–0.72
				P<0.0001§	*P*<0.0001§	

*Age adjusted by 1 year.

†Multivariate relative risks adjusted for age (1 year), smoking status, diabetes, BMI, antihypertensive medication, systolic blood pressure, angina pectoris, myocardial infarction, illness that impairs function in daily life, and years of education.

‡Subjects may vary because of missing data.

§*P* for trend.

younger, leaner, and had lower systolic blood pressure than less active women. There was a decline in resting pulse across categories of physical activity, and the prevalence of coronary heart disease, diabetes, and use of antihypertensive medication decreased with increasing physical activity. Smoking tended to be more prevalent among the least physically active, and there was an increasing level of education with increasing physical activity.

In Table 2, we show age-adjusted and multivariate-adjusted analyses for women aged 50 to 69 years, 70 to 79 years, and 80 to 101 years. In all age groups, the age-adjusted RRs decreased with increasing physical activity. The negative association was slightly weaker in the multivariate analyses, but tests for trend were significant in groups aged 50 to 69 and 70 to 79 years ($P=0.0021$ and $P=0.0093$ for trend, respectively). In groups aged 50 to 69 and 70 to 79 years, the most active women had a multivariate adjusted RR of 0.39 (95% CI, 0.24 to 0.75) and 0.48 (95% CI, 0.36 to 0.88), respectively. In the group aged 80 to 101 years, there was a consistent negative association of similar magnitude in both age-adjusted and multivariate analyses, but the estimates of effect were not statistically significant.

Women in the least active category were more likely to report ill health and prevalent diseases. In separate analyses, we therefore restricted the participants to women who were free from cerebrovascular and cardiovascular diseases, and we excluded individuals who died during the first 2 years of follow-up (Tables 3 and 4). Among the former, the overall multivariate-adjusted RR in the high-physical-activity group was 0.47 (95% CI, 0.29 to 0.75) and in the latter, the adjusted RR was 0.54 (95% CI, 0.39 to 0.75). In both groups, the test for trend across levels of physical activity was statistically significant.

Discussion

This study demonstrates a consistent, negative association between levels of physical activity and stroke mortality in women. When we compared inactive women with women categorized by a physical activity index combining frequency, intensity, and duration, the most active had approximately 50% lower risk of death from stroke. The association was present in all age groups, including the oldest group, and the exclusion of individuals with cardiovascular and cerebrovascular morbidity at baseline and women who died within the first 2 years of follow-up did not materially change these results.

Our findings are consistent with those of previous studies,[3,4,8,9,12,13,15] but only 3 studies[8,9,15] have shown a graded

TABLE 3. Relative Risk of Death From Stroke According to Level of Physical Activity in Women Aged ≥50 Years Free From Stroke, Angina Pectoris, Myocardial Infarction, Antihypertensive Medication, and Diabetes at Baseline: Follow-Up of the Nord-Trøndelag Health Survey 1984–1986 (n=9 386)

Physical Activity	Subjects	Deaths	Age-Adjusted RR*	Multivariate RR†‡	95% CI
Low	3 018	102	1.00	1.00	Referent
Medium	3 108	67	0.89	0.87	0.62–1.26
High	3 064	27	0.45	0.47	0.29–0.75
			$P=0.0005$§	$P=0.0027$§	

*Age adjusted by 1 year.

†Multivariate RR adjusted for age (1 year), smoking status, BMI, systolic blood pressure, illness that impairs function in daily life, and years of education.

‡Subjects may vary because of missing data.

§*P* for trend.

negative effect. In 2 of these studies,[13,15] the combined effects on fatal myocardial infarction and stroke were assessed.

Comparison of results between studies is complicated by differences in design, assessment of physical activity, and different outcomes. For example, discrepancies in results may be due to inadequate assessment of physical activity in women, as suggested by Blair et al.[19] Most physical activity questionnaires have been developed for and validated in male populations, and activities traditionally related to women, such as child care and housework, are usually not recorded.[20,21] Therefore, Weller and Corey[13] have argued that failing to take into account nonleisure physical activity among women would lead to misclassification that may result in an underestimate of the RR. In this study, the validity of the reported physical activity could be indirectly validated by surrogate measures of physical fitness, as reflected by decreasing resting pulse and BMI with increasing physical activity (Table 1).[21–23] The potential bias of misclassification due to inaccuracy of diagnosis coded on death certificates is unlikely to be related to different levels of physical activity and to explain the negative association observed.

The prospective design of the study makes it unlikely that the results may be biased because of selection of participants or misclassification of information. After the exclusion of women with a previous stroke, 75.7% of all women who received the physical activity questionnaire (questionnaire 2) were included in the analyses. Reasons for not completing the physical activity questions are not known. However, individuals not performing regular exercise because of illness are more likely to omit these questions. Among women who did not answer the questions, it is therefore conceivable that mortality, including stroke mortality, may be highest among the least active. As a consequence, our results would be an underestimate of the true negative association between physical activity and stroke mortality.

The possible biological mechanisms of a negative association between physical activity and stroke mortality may be mediated by decelerating the atherosclerotic process, modifying the structure of the arteries, reducing vasospasm, enhancing myocardial electric stability, or increasing fibrinolysis.[24] Physical activity is also associated with improved diabetes control,[25] increased HDL levels,[26] and lower body weight.[27] Nonsmokers and people of higher education are more likely to participate in physical activities.[28] BMI, blood pressure, history of hypertension, history of high cholesterol, and diabetes mellitus may be considered intermediate factors, and one may argue not to adjust for such baseline factors in the analysis. However, adjustment had only a minor influence on the estimates of RR, suggesting no material confounding with physical activity. Whether other, unmeasured factors could explain the strong negative association between phys-

TABLE 4. Relative Risk of Death From Stroke According to Level of Physical Activity in Women Aged ≥50 Years Free From Stroke Who Survived the First 2 Years of Follow-Up: The Nord-Trøndelag Health Survey 1984–1986 (n=13 669)

Physical Activity	Subjects	Deaths	Age-Adjusted RR*	Multivariate RR†‡	95% CI
Low	4 862	221	1.00	1.00	Referent
Medium	4 608	120	0.75	0.75	0.58–0.97
High	4 199	57	0.47	0.54	0.39–0.75
			$P<0.0001$§	$P=0.0001$§	

*Age adjusted by 1 unit.

†Multivariate relative risks adjusted for age, smoking status, BMI, systolic blood pressure, angina pectoris, myocardial infarction, antihypertensive medication, diabetes, illness that impairs function in daily life, and years of education.

‡Subjects may vary because of missing data.

§*P* for trend.

ical activity and stroke mortality, however, cannot be excluded.

Appendix

Questions From Questionnaire 2

By exercise we mean walking, skiing, swimming, or working out with sports.

How often do you exercise?

Never
Less than once a week
Once a week
2 to 3 times a week
Nearly every day

If you exercise as often as once or several times a week:

How hard do you exercise?

I take it easy without losing my breath or breaking into sweat
I push until I lose my breath and break into sweat
I practically exhaust myself

How long do you exercise each time?

Less than 15 minutes
16 to 30 minutes
30 minutes to 1 hour
More than 1 hour

Acknowledgment

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