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Reduction in incident stroke risk with vigorous physical activity. Evidence from 7.7-year follow-up of the National Runners' Health Study

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Abstract

Background and Purpose—To assess the dose-response relationship between vigorous physical activity (running distance, km/day) and the participant-reported physician-diagnosed stroke.

Methods—Age-adjusted survival analysis of 29,272 men and 12,123 women followed prospectively for 7.7 years.

Results—One-hundred men and 19 women reported incident strokes. Per km/day run, the age- and smoking-adjusted risk for stroke decreased 12% in men (P=0.0007), and 11% in men and women combined (P=0.001), which remained significant when further adjusted for baseline diabetes, hypercholesterolemia, hypertension, and BMI (8% and 7% reduction per km/day run, respectively, P=0.03). Men and women who exceed 2 km/day (i.e., exceed the recommended AHA/CDC and NIH guideline activity level) had significantly lower risk than those that ran less (P=0.05) and those that ran >4 km/day had significantly lower risk than those that ran 2–4 km/day (P=0.02). Men and women who ran >8 km/day were at 60% lower risk than those who ran <2 km/day (P=0.002).

Conclusions—The risk for incident stroke is substantially reduced in those who exceed the guideline physical activity level, which cannot be attributed to less hypertension, diabetes, hypercholesterolemia, or body weight.

Keywords

Physical activity; prevention; cerebrovascular disease

The American Heart Association (AHA) guidelines for the primary prevention of ischemic stroke recommend for 30 minutes of moderate-intensity physical activity on most, preferably all days of the week [1]. To assess whether exceeding guideline activity levels further reduces stroke risk, we compared running distance at baseline to incident participant-reported, physician-diagnosed stroke during 7.7-year follow-up in the National Runners' Health Study. The design and methods of this cohort are described in detail elsewhere [2]. Recruitment occurred between 1991 and 1994 by nationwide distribution of a two-page questionnaire to runners. Follow-up questionnaires, mailed between 1998 and 2001, asked participants whether they had been diagnosed for stroke by a physician and the year of diagnosis. Cox proportional hazard model (JMP software version 5.0, SAS Institute, Cary, NC) was used to assess risk ratio (specifically hazard ratios) with age (age and age^2), baseline smoking status, and other specified variables as covariates. The study protocol and informed consent were approved by the University of California Berkeley Committee for the Protection of Human Subjects.

Of the 36,547 men and 15,521 women with complete data on age, education, distance run, BMI and diet at baseline without a prior heart attack or stroke, follow-up questionnaires were obtained for 29,279 men (80%) and 12,123 women (78%). These included 100 men and 19 women who reported being diagnosed by a physician for stroke since their baseline survey. The small number of female cases precluded their separate analyses. Only seven of the 593 deaths identified through the National Death Index were coded as cerebrovascular deaths, which were also deemed to be too few for meaningful analyses. The baseline characteristics of the follow-up sample are displayed in Table 1.

Table 2 presents the risk ratios for reported distance run per day. The reduction in stroke risk was not significantly different between men and women (P=0.36 for sex by distance interaction, albeit there is limited power to detect an interaction) and therefore the sex-adjusted results for men and women combined are also displayed. The men's risk for stroke decreased 12% per km/day run, which could not be attributed to the lower baseline BMI or prevalence of diabetes or hypertension of the higher mileage runners. A significant 11% reduction in the risk per km/day run was also obtained when women were included in the analyses. The reduction in risk was attributed, in part, to the baseline leanness of the higher mileage runners. Reported aspirin use was unrelated to incident stroke (P=0.70) and adjustment for aspirin use did not affect the results of Table 2.

Table 3 presents the reduction in stroke risk in relation to the activity dose. Men who ran > 8 km/day had 71% fewer incident strokes than those who ran <2 km/day. Men who ran over 2 km/day were at significantly lower risk than those who ran less (P=0.03), and those that exceeded 4 km/day were at significantly lower risk than those that ran 2 to 4 km/day (P=0.02).

The men included in the referant category of Table 3 (<2 km/day) expended an average 605 MET*min per week [3], which corresponds to the minimum guideline activity level currently recommended [4]. Thus our analyses pertain specifically to the potential for additional reductions in stroke risk by exceeding guideline levels. The 71% lower risk for nonfatal stroke in men who ran >8 km/day versus AHA/ACSM guideline levels (60% lower risk for men and women combined) is substantially greater than the 25% risk reduction for high versus low activity levels reported from meta-analysis [5]. However, high activity in the 18 prospective cohort studies included in the meta-analysis was substantially less than our highest activity level (> 8 km/day), and less than 4 km/day, which was the point up to which our data show a significant dose-response relationship (Table 3).

The Physicians' Health Study 11-year follow-up of 21,823 men showed a significant trend (P=0.04) between lower stroke risk and greater frequency of vigorous exercise [6]. In contrast to our results, their trend was not significant when adjusted for baseline BMI, hypertension, diabetes, and high cholesterol (P=0.25). The risk reductions they reported for their highest versus lowest exercise category were 21% without adjustment, and 14% when adjusted for baseline BMI, hypertension, diabetes, and high cholesterol. These risk reductions were both less than one-third of the risk reductions we observed between the highest and lowest mileage male runners (69% unadjusted and 55% adjusted for BMI, hypertension, diabetes, and high cholesterol). Whereas they reported that there were no further reductions in stroke risk by exercising vigorously more than once per week, our Table 3 shows significant incremental reductions in stroke risk through at least 4 km/day. The Physicians' Health Study also concluded that physical activity does not have any significant effects on reducing stroke risk beyond those mediated by BMI, hypertension, hypercholesterolemia, and diabetes, while we observed that adjustment for these variables only moderately diminished the risk reduction (from 12% to 9% per km/day run in men). The greater risk reduction in our runners vis-à-vis the Physicians' Health Study men may be due to the health advantage of running over other vigorous activities, the statistical advantage of a single quantitatively well-defined activity (km/day run) vis-à-vis a composite measure based on intensity, duration and frequency or the smaller error for investigator-validated stroke from medical record review compared to the participant-reported strokes reported by us. However, imprecision associated with self-report should not lead to spurious associations with physical activity unless it varies systematically with activity levels. We also acknowledge that in our data there may be other factors related to both physical activity and stroke risk that contribute to the observed associated that have not been adjusted for.

These findings support a two-tiered formulation for public health physical activity guidelines: one for the 49.3% of men and 52.1% of women who fall short of the minimum recommendations (AHA guideline levels); a second for the 50.7% of men and 47.9% of women who already satisfy guideline levels (maximize the vigorous exercise dose) [5]. This two-tiered approach would satisfy the pragmatic need to promote achievable physical activity goals that provide important health benefits to mostly sedentary Americans, while not compromising the potential to maximize health in those already active.

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Table 1

Baseline characteristic of the follow-up sample who were with no prior history of heart attack or stroke at baseline.

	Males	**Females**
Sample size	29,279	12,123
Strokes (N)	100	19
Hypertension (%)	5.6	2.1
Hypercholesterolemia (%)	5.9	2.8
Diabetes (%)	0.6	0.3
Age (years) *	44.8±10.3	38.9±10.1
Education (years) *	16.5±2.4	15.9±2.4
Aspirin (tablets/wk) *	2.5±4.9	1.9±4.2
BMI (kg/m^2) *	23.9±2.6	21.3±2.4

* mean±SD

Table 2

Survival analyses (risk ratio) by participant-reported running distance (per km/day) from Cox-proportional hazard model.

	Males only	Males and females, sex adjusted
Unadjusted for baseline diabetes, hypertension, hypercholesterolemia or BMI	0.88 (0.81, 0.95) P=0.0007	0.89 (0.83, 0.96) P=0.001
Adjusted simultaneously for baseline hypertension, diabetes, hypercholesterolemia. and BMI	0.92 (0.85, 0.99) P=0.03	0.93 (0.86, 0.99) P=0.03

All results are adjusted for age (age and age^2) and baseline smoking. Ranges within parentheses are the 95% confidence intervals.

Table 3

Risk ratios for categories of daily running distance relative to current physical activity guideline levels (<2 km/day) from Cox-proportional hazard model.

	Males only	Males and females, sex adjusted
<2 km/day	1.00[†]	1.00[*]
2–3.9 km/day	0.76[‡] (0.44, 1.37) P=0.35	0.82[‡] (0.49, 1.42) P=0.47
4 to 6 km/day	0.48 (0.27, 0.90) P=0.02	0.55 (0.32, 0.99) P=0.04
6 to 8 km/day	0.59 (0.28, 1.21) P=0.15	0.54 (0.26, 1.10) P=0.09
>8 km/day	0.29 (0.13, 0.64) P=0.002	0.40 (0.19, 0.79) P=0.009

All results are adjusted for age (age and age^2) and baseline smoking. Ranges within parentheses are the 95% confidence intervals. Significance of difference from all greater running distances are coded:

[*] P=0.05

[†] P=0.03

[‡] P=0.02