

Cardiovascular Events in Diabetic Women Who Exercise

Hu FB, Stampfer MJ, Solomon C, et al. Physical activity and risk for cardiovascular events in diabetic women. *Ann Intern Med* 2001;134:96–105.

Study Overview

Objective. To determine if physical activity decreases risk for cardiovascular disease in diabetic women.

Design. Prospective cohort study.

Setting and participants. All patients were enrolled in the Nurses' Health Study (NHS), a cohort first established in 1976 with 121,700 female nurses between 30 and 55 years of age who resided in 11 large U.S. states. NHS participants completed a mailed questionnaire about their medical history and lifestyle, and biennial follow-up questionnaires updated information on potential risk factors and newly diagnosed illnesses, including cardiovascular disease. For the current study, 5125 women were selected who reported having physician-diagnosed diabetes mellitus on any questionnaire from 1976 to 1992 and who were aged 30 years or older at disease onset. Patients were excluded who reported a history of coronary heart disease (including myocardial infarction, angina, or coronary revascularization), stroke, or cancer on or before the 1980 questionnaire. Beginning in 1980, physical activity was assessed through questions about the average number of hours participants spent per week engaged in moderate or vigorous activities, such as jogging, brisk walking, bicycling, or heavy housework. Cases of diabetes among study patients were confirmed via a supplementary questionnaire that collected information on symptoms, diagnostic tests, and hypoglycemic therapy. Patients were followed from 1980 to 1994.

Main outcome measures. Primary endpoints were incidence of coronary heart disease (defined as nonfatal myocardial infarction or fatal coronary heart disease) and stroke that occurred after the 1980 questionnaire was returned and before 1 June 1994. Medical records were reviewed to confirm diagnoses of these diseases as well as causes of death listed on death certificates. Patient characteristics were also measured, including age, smoking status, insulin or other hypoglycemic therapy, aspirin use, vitamin supplement use, menopausal status (with or without hormone replacement therapy), baseline history of hypercholesterolemia and hypertension, and family history of premature myocardial infarction.

Main results. During the 14-year follow-up period (31,432 person-years), researchers recorded 323 new cases of cardiovascular disease, including 225 new cases of coronary heart disease and 98 new cases of stroke (71 of which were ischemic). Age-adjusted relative risks associated with 5 categories of moderate and vigorous activity per week (less than 1 hour, 1 to 1.9 hours, 2 to 3.9 hours, 4 to 6.9 hours, and 7 hours or more) were 1.0, 0.93, 0.82, 0.54, and 0.52, respectively ($P < 0.001$). These risks did not change after adjusting for smoking status, body mass index, and other cardiovascular risk factors. Multivariate relative risks for coronary heart disease across the 5 activity-level categories were 1.0, 1.07, 0.86, 0.61, and 0.49 ($P = 0.003$), while those for ischemic stroke were 1.0, 0.94, and 0.38 across 3 categories of moderate or vigorous activity (less than 1 hr/week, 1 to 3.9 hr/week, and 4 hr/week or more, respectively; $P = 0.01$).

Conclusion

Physical activity in diabetic women is associated with a significant reduction in risk for cardiovascular events.

Commentary

Numerous studies have shown that exercise decreases cardiovascular risk in the general population. Hu and colleagues' work is the first large study to examine risk reduction for cardiovascular events in diabetic women who exercise. The authors used a validated instrument [1] to measure physical activity, and it is unlikely that study subjects underestimated the amount of exercise performed. Also, the NHS has supported numerous publications and has itself been validated. One could argue that study results may be problematic because investigators did not use the most recent American Diabetic Association (ADA) diagnostic guidelines, which include milder diabetic cases. However, the authors acknowledge this limitation and further point out that new ADA guidelines were not published until 1997, after the study ended. Moreover, the use of older guidelines to diagnose diabetes seems to have strengthened results, since a positive treatment effect was seen even in more advanced cases.

One potential problem that may minimize the observed effects is that other lifestyle characteristics could by themselves

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have provided protection against cardiovascular disease for patients who exercised. Hu and colleagues tried to account for that possibility by analyzing confounding variables, such as use of folate and multivitamins. Although study results did not change when these variables were considered, there may have been other residual confounders that went unmeasured, such as the level of overall concern that a patient had about her health. In the data analysis, researchers found that aspirin use was associated with a trend toward a higher risk of cardiovascular events; however, the confidence interval for this finding crossed 1. One has to wonder if the small number of events during the study period affected these results. Another important measure not mentioned in the article was total mortality. Overall, though, this was a well-conducted observational study.

Applications for Clinical Practice

Exercise should be recommended for all diabetic women. This simple, nearly risk-free intervention could reduce coronary and cardiovascular events, particularly ischemic stroke. Other beneficial effects on lipid profile, increased insulin sensitivity, cardiovascular fitness, and improved glycemic control should be taken into account when advising patients. It seems logical to accept Hu et al's results without confirmation from further randomized controlled trials, which would be difficult to perform. To obtain benefit from exercise, a moderate to vigorous level of activity (eg, brisk walking) for at least 4 hours per week is required.

References

1. Wolf AM, Hunter DJ, Colditz GA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol* 1994;23:991-9.

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