Exercise for stroke prevention

The neglected prescription

Seemant Chaturvedi, MD
Fadi Nahab, MD

Correspondence to
Dr. Chaturvedi:
SChaturvedi@med.miami.edu

Neurology® 2017;88:342–343

For over a decade, clinicians have used multimodal pharmacologic therapy for optimal stroke prevention based in part on promising results from clinical trials demonstrating the value of blood pressure and cholesterol lowering for secondary stroke prevention. Patients are typically treated with a cocktail of medications, including antithrombotic agents, antihypertensives, and statins.[1]

A key fourth component of the armamentarium, lifestyle modification, incorporates dietary change, smoking cessation, and reducing physical inactivity.[1] The Mediterranean diet has been associated with an approximately 40% reduction in stroke in the primary prevention setting.[2] Although randomized trials would not be ethical, smoking cessation is certainly recommended for stroke survivors to curtail the progression of vascular disease. What about exercise? How strongly should clinicians be recommending this intervention?

In this issue of *Neurology*®, Turan et al.[3] report the effects of physical activity levels and other risk factors on subsequent major vascular events in patients with intracranial atherosclerotic disease. The authors utilized the database from the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial. In this study, patients with stroke or TIA in the preceding 30 days, secondary to 70%–99% stenosis of a major intracranial vessel, were randomly assigned to intracranial stenting plus aggressive medical management or medical management alone.[4] The study was halted early due to the superiority of aggressive medical management alone.

In SAMMPRIS, aggressive medical management included the following 4 components: (1) dual antiplatelet therapy for 90 days followed by monotherapy, (2) targeted blood pressure reduction, (3) use of high-potency statins, and (4) lifestyle modification. There has been interest as to which of the 4 components of medical therapy was the most important with regard to preventing stroke and other events such as myocardial infarction (MI) or vascular death. In the current analysis, patients were defined as in target or out of target for various risk factors, according to the predefined study goals. For example, achieving a low-density lipoprotein (LDL) value of <70 mg/dL was defined as a target. For physical activity, the Physician-based Assessment and Counseling for Exercise (PACE) score was used, with a score of ≥ 4 being considered in target, which equates to any amount of regular weekly exercise. This low bar for exercise frequency was achieved in only 32% of SAMMPRIS participants at baseline who were randomized to aggressive medical management alone.

In univariate analyses that looked at risk factor control and subsequent major vascular events (stroke, MI, vascular death), patients who were in target for systolic blood pressure and physical activity had a lower risk of major vascular events at 3 years. As a continuous variable, lower levels of LDL and non–high-density lipoprotein (HDL) were also associated with a reduction in major vascular events. Physically inactive patients had up to 5 times the risk of a major vascular event compared to those who were physically active. In multivariable analysis, when the PACE score was analyzed as a continuous variable, greater physical activity was the only factor associated with a reduced rate of stroke, MI, or vascular death (odds ratio [OR] 0.6, confidence interval 0.4–0.8); the OR of physical activity was similar for patients regardless of whether they were in target or out of target at baseline.

A previous systematic review did not find direct evidence that participation in exercise reduces the rate of recurrent stroke.[5] However, a network meta-analysis suggested that exercise could be as important as antithrombotic medications in preventing mortality.[6] Mechanistically, exercise has been associated with a wide variety of benefits, including lowering of blood pressure, decreased arterial stiffness, more robust collateral circulation, weight reduction, reduction in LDL level, increase in HDL level, reduction in insulin resistance, and potentially improved cognition.[7–9] The current results are also consistent with data from the INTERSTROKE study. In this international study, hypertension (48%), lack of exercise (36%), and

See page 379

From the Department of Neurology and Stroke Program (S.C.), University of Miami Miller School of Medicine, FL; and Department of Neurology and Pediatrics (F.N.), Emory University, Atlanta, GA.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the editorial.

elevated blood lipids (27%) had the highest attributable risks for stroke.[10]

Limitations of the study include a relatively small number of patients (227) with a limited number of outcome events (49). In addition, physical activity was self-reported by study participants, whereas other measures were more objectively assessed. Finally, SAMMPRIS used a comprehensive lifestyle management program and it is not clear if physical activity levels can be improved substantially in other settings. Given the established benefits and generalizability of a comprehensive lifestyle management program incorporating physical exercise (e.g., cardiac rehabilitation) on reducing mortality following MI, a similar approach for stroke patients offers hope.

Turan et al. have provided stroke survivors with an important incentive to increase their physical activity level. Regular weekly exercise can lead to a reduction in serious events such as recurrent stroke, MI, and vascular death. So for both patients and clinicians, what are you waiting for? Reaching for your exercise shoes may be as important as reaching for your medications.

AUTHOR CONTRIBUTIONS

Dr. Chaturvedi: wrote first draft, data analysis, critical revision. Dr. Nahab: critical revision.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

Dr. Chaturvedi is Assistant editor of *Stroke* and is on the editorial board of *Neurology®*, *Journal of Stroke & Cerebrovascular Disease*, and *Journal Watch Neurology*. He is on the executive committee of the ACT-1 and CREST-2 studies. Dr. Nahab has received honoraria from Medtronic and has provided expert testimony and consultation for legal proceedings. Go to Neurology.org for full disclosures.

REFERENCES

1. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45:2160–2236.
2. Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013;368:1279–1290.
3. Turan TN, Nizam A, Lynn MJ, et al. Relationship between risk factor control and vascular events in the SAMMPRIS trial. Neurology 2017;88:379–385.
4. Chimowitz MI, Lynn MJ, Derdeyn CP, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. N Engl J Med 2011;365:993–1003.
5. Saunders DH, Greig CA, Mead GE. Physical activity and exercise after stroke. Stroke 2014;45:3742–3747.
6. Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: meta-epidemiological study. BMJ 2013;347:f5577.
7. Cox KL, Burke V, Morton AR, Gillam HF, Beilin LJ, Puddey IB. Long-term effects of exercise on blood pressure and lipids in healthy women aged 40-65 years: The Sedentary Women Exercise Adherence Trial (SWEAT). J Hypertens 2001;19:1733–1743.
8. Willey JZ, Gardener H, Caunca MR, et al. Leisure-time physical activity associates with cognitive decline: The Northern Manhattan Study. Neurology 2016;86:1897–1903.
9. Myers J. Exercise and cardiovascular health. Circulation 2003;107:e2–e5.
10. O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet 2016;388:761–775.