

Scanning the Literature

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Fruit for Thought

Kurl S, Tuomainen TO, Laukkanen JA, et al. Plasma vitamin C modifies the association between hypertension and risk of stroke. *Stroke* 2002; 33: 1568-1573.

Background and Purpose: There are no prospective studies to determine whether plasma vitamin C modifies the risk of stroke among hypertensive and overweight individuals. We sought to examine whether plasma vitamin C modifies the association between overweight and hypertension and the risk of stroke in middle-aged men from eastern Finland. **Methods:** We conducted a 10.4-year prospective population-based cohort study of 2419 randomly selected middle-aged men (42 to 60 years) with no history of stroke at baseline examination. A total of 120 men developed a stroke, of which 96 were ischemic and 24 hemorrhagic strokes. **Results:** Men with the lowest levels of plasma vitamin C ($<28.4 \mu\text{mol/L}$, lowest quarter) had a 2.4-fold (95% CI, 1.4 to 4.3; $P=0.002$) risk of any stroke compared with men with highest levels of plasma vitamin C ($>64.96 \mu\text{mol/L}$, highest quarter) after adjustment for age and examination months. An additional adjustment for body mass index, systolic blood pressure, smoking, alcohol consumption, serum total cholesterol, diabetes, and exercise-induced myocardial ischemia attenuated the association marginally (relative risk, 2.1; 95% CI, 1.2 to 3.8; $P=0.01$). Adjustment for prevalent coronary heart disease and atrial fibrillation did not attenuate the association any further. Furthermore, hypertensive men with the lowest vitamin C levels ($<28.4 \mu\text{mol/L}$) had a 2.6-fold risk (95% CI, 1.52 to 4.48; $P<0.001$), and overweight men (25 kg/m²) with low plasma vitamin C had a 2.7-fold risk (95% CI, 1.48 to 4.90; $P=0.001$) for any stroke after adjustment for age, examination months, and other risk factors. **Conclusions:** Low plasma vitamin C was associated with increased risk of stroke, especially among hypertensive and overweight men.

Comments: The use of Vitamin C as an antioxidant to reduce the risk of atherosclerotic cardiovascular disease has gained wide acceptance over the last decade. Studies have shown low plasma vitamin C concentration has been related to increased progression

of carotid disease and increased risk of acute myocardial infarction. This Finnish study looked at the association of plasma vitamin C with the risk of stroke in middle-aged men with no history of stroke and if vitamin C modified the association between blood pressure and body weight and the risk of stroke. While this study seems to support ascorbate as an effective antioxidant, further investigation would be worthwhile to define dose-related differences and the most effective form of administration. Surely this is something we can feel comfortable recommending to our patients in this era of "natural medicine."

Chill Out?

Kammersgaard LP, Jørgensen HS, Rungby JA, et al. admission body temperature predicts long-term mortality after acute stroke: The Copenhagen Stroke Study. *Stroke* 2002; 33:1759-1762.

Background and Purpose: Body temperature is considered crucial in the management of acute stroke patients. Recently hypothermia applied as a therapy for stroke has been demonstrated to be feasible and safe in acute stroke patients. In the present study, we investigated the predictive role of admission body temperature to the long-term mortality in stroke patients. **Methods:** We studied 390 patients with acute stroke admitted within 6 hours from stroke onset. Admission clinical characteristics (age, sex, admission stroke severity, admission blood glucose, cardiovascular risk factor profile, and stroke subtype) were recorded for patients with hypothermia (body temperature 37°C) versus patients with hyperthermia (body temperature $\geq 37^{\circ}\text{C}$). Univariately the mortality rates for all patients were studied by Kaplan-Meier statistics. To find independent predictors of long-term mortality for all patients, Cox proportional-hazards models were built. We included all clinical characteristics and body temperature as a continuous variable. **Results:** Patients with hyperthermia had more severe strokes and more frequently diabetes, whereas no difference was found for the other clinical characteristics. For all patients mortality rate at 60 months after stroke was higher for patients with hyperthermia (73 per 100 cases versus 59 per 100 cases,

P=0.001). When body temperature was studied in a multivariate Cox proportional-hazards model, a 1°C increase of admission body temperature independently predicted a 30% relative increase (95% CI, 4% to 57%) in long-term mortality risk. For 3-month survivors we found no association between body temperature and long-term survival when studied in a multivariate Cox proportional hazard model (hazards ratio, 1.11 per 1°C; 95% CI, 0.82 to 1.52). **Conclusion:** Low body temperature on admission is considered to be an independent predictor of good short-term outcome. The present study suggests that admission body temperature seems to be a major determinant even for long-term mortality after stroke. Hypothermic therapy in the early stage in which body temperature is kept low for a longer period after ictus could be a long-lasting neuroprotective measure.

Comments: For years we have heard about drowning victims who have suffered little or no neurological damage after prolonged submersion in cold water. This study from Denmark suggests that hypothermia applied deliberately in the early stages of a stroke could also be neuroprotective. Consistent with the trend toward more aggressive management of acute stroke, it is not unreasonable to pursue further investigation into this potentially simple method to reduce neuronal damage.

Where Things Stand

Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention. Scientific review. JAMA 2002; 288:1388-1395.

Context: Stroke is a major cause of morbidity and mortality, and the application of evidence for stroke prevention varies considerably. **Objective:** To review the most recent, high-quality evidence for primary and secondary stroke prevention. **Data Sources and Study Selection:** Searches of MEDLINE, The Cochrane Library, and the ACP Journal Club were performed to identify English-language articles published from 1998 to 2001 that focused on primary and secondary stroke prevention. The references of each retrieved article were scanned, and experts in the field were contacted to identify additional relevant articles. **Data Extraction:** Each of the articles was appraised, and its quality was graded with levels of evidence based on specific scientific methods that affect a

study's validity. **Data Synthesis:** For primary prevention of stroke, adequate blood pressure reduction, and treatment of hyperlipidemia, use of antithrombotic therapy in patients with atrial fibrillation and of antiplatelet therapy in patients with myocardial infarction are effective and supported by evidence from several randomized trials. Effective strategies for the secondary prevention of stroke include treatment of hypertension and hyperlipidemia, antithrombotic therapy for patients with atrial fibrillation, antiplatelet therapy, and carotid endarterectomy in patients with severe carotid artery stenosis. **Conclusions:** Stroke is a major public health concern, and a significant body of evidence supports many primary and secondary prevention strategies.

Comments: This excellent review of the recent literature gives a good perspective on the current evidence for stroke prevention. It touches on the major primary and secondary prevention strategies and supports the conclusions with a collection of relevant articles from 1998-2001. Each study referenced was graded, with Level 1 high-quality randomized trial being the best level of evidence and a Level 2 high-quality observational study being next best, Level 3 evidence was provided by case reports or case series, and Level 4 evidence implied expert opinion. As the various points are addressed the "level of evidence" is noted after a specific conclusion. This critical approach is a refreshing way to bring the myriad of offerings on this complicated topic into better focus. The authors also take the exercise one step further in a companion article that describes how to apply evidence to individual patients. Physicians and other medical providers should enjoy this chance to hone their critical thinking skills.



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