

Cerebrovasc Dis 2008;25:457–507 DOI: 10.1159/000131083 Received: February 19, 2008 Accepted: March 27, 2008 Published online: May 6, 2008

Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008

The European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee

Key Words

Stroke prevention · Educational measures · Stroke Unit · Imaging · Acute treatment · Rehabilitation

Abstract

This article represents the update of the European Stroke Initiative Recommendations for Stroke Management. These guidelines cover both ischaemic stroke and transient ischaemic attacks, which are now considered to be a single entity. The article covers referral and emergency management, Stroke Unit service, diagnostics, primary and secondary prevention, general stroke treatment, specific treatment including acute management, management of complications, and rehabilitation.

Copyright © 2008 S. Karger AG, Basel / Translation is only granted with permission from the publisher and ESO, please contact p.roth@karger.ch

Foreword

This article represents the update of the European Stroke Initiative (EUSI) Recommendations for Stroke Management, which were first published in this journal in 2000 [1, 2], and subsequently translated into a number of languages including Spanish, Portuguese, Italian, German, Greek, Turkish, Lithuanian, Polish, Russian and Mandarin Chinese. The first update of the recommendations was published in 2003 [2]. In 2006, the EUSI decided that a larger group of authors should prepare the next update. In the meantime, a new European Stroke Society, the European Stroke Organisation (ESO), was established and took over the task of updating the guidelines. Accordingly, the new recommendations have been prepared by members of both the former EUSI Recommendations Writing Committee and the ESO (see appendix). The members of the Writing Group met in Heidelberg, Germany for 3 days in December 2007 to finalize the new

The ESO Writing Committee: Peter A. Ringleb, Heidelberg, Germany; Marie-Germaine Bousser, Paris, France; Gary Ford, Newcastle, UK; Philip Bath, Nottingham, UK; Michael Brainin, Krems, Austria; Valeria Caso, Perugia, Italy; Álvaro Cervera, Barcelona, Spain; Angel Chamorro, Barcelona, Spain; Charlotte Cordonnier, Lille, France; László Csiba, Debrecen, Hungary; Antoni Davalos, Barcelona, Spain; Hans-Christoph Diener, Essen, Germany; José Ferro, Lisbon, Portugal; Werner Hacke, Heidelberg, Germany; Michael Hennerici, Mannheim, Germany; Markku Kaste, Helsinki, Finland; Peter Langhorne, Glasgow, UK; Kennedy Lees, Glasgow, UK; Didier Leys, Lille, France; Jan Lodder, Maastricht, The Netherlands;

Hugh S. Markus, London, UK; Jean-Louis Mas, Paris, France; Heinrich P. Mattle, Bern, Switzerland; Keith Muir, Glasgow, UK; Bo Norrving, Lund, Sweden; Victor Obach, Barcelona, Spain; Stefano Paolucci, Rome, Italy; E. Bernd Ringelstein, Münster, Germany; Peter D. Schellinger, Erlangen, Germany; Juhani Sivenius, Kuopio, Finland; Veronika Skvortsova, Moscow, Russia; Katharina Stibrant Sunnerhagen, Göteborg, Sweden; Lars Thomassen, Bergen, Norway; Danilo Toni, Rome, Italy; Rüdiger von Kummer, Dresden, Germany; Nils Gunnar Wahlgren, Stockholm, Sweden; Marion F. Walker, Nottingham, UK; Joanna Wardlaw, Edinburgh, UK.

smoking doubles the risk of ischaemic stroke [230]. Subjects who stop smoking reduce this risk by 50% [225]. Making workplaces smoke-free would result in considerable health and economic benefits [231].

Alcohol Consumption

Heavy alcohol drinking (>60 g/day) increases the risk of ischaemic stroke (RR 1.69; 95% CI 1.34–2.15) and haemorrhagic stroke (RR 2.18; 95% CI 1.48–3.20). In contrast, light consumption (<12 g/day) is associated with a reduction in all stroke (RR 0.83; 95% CI 0.75–0.91) and ischaemic stroke (RR 0.80; 95% CI 0.67–0.96), and moderate consumption (12–24 g/day) with a reduction in ischaemic stroke (RR 0.72; 95% CI 0.57–0.91) [232]. Red wine consumption is associated with the lowest risk in comparison with other beverages [233]. BP elevation appears to be an important intermediary in the relation between alcohol consumption and stroke [234].

Physical Activity

In a meta-analysis of cohort and case-control studies, physically active individuals had a lower risk of stroke or death than those with low activity (RR 0.73; 95% CI 0.67–0.79). Similarly, moderately active individuals had a lower risk of stroke, compared with those who were inactive (RR 0.80; 95% CI 0.74–0.86) [235]. This association is mediated, in part, through beneficial effects on body weight, BP, serum cholesterol, and glucose tolerance. Leisure-based physical activity (2–5 h per week) has been independently associated with a reduced severity of ischaemic stroke at admission and better short-term outcome [236].

Diet

Fruit, Vegetable, and Fish Intake

In observational studies, high fruit and vegetable intake was associated with a decreased risk of stroke, compared with lower intake (RR 0.96 for each increment of 2 servings/day; 95% CI 0.93–1.00) [237]. The risk of ischaemic stroke was lower in people who consumed fish at least once per month (RR 0.69; 95% CI 0.48–0.99) [238]. Whole grain intake was associated with a reduction in CV disease (OR 0.79; 95% CI 0.73–0.85) but not stroke [239]. Dietary calcium intake from dairy products was associated with lower mortality from stroke in a Japanese population [240]. However, in a further study there was no interaction between the intake of total fat or cholesterol, and stroke risk in men [241].

In a randomized controlled trial in women, dietary interventions did not reduce the incidence of coronary events and stroke despite there being an 8.2% reduction of total fat intake and an increased consumption of vegetables, fruits and grains [242].

Body Weight

A high body mass index (≥25) is associated with an increased risk of stroke in men [243] and women [244], mainly mediated by concomitant arterial hypertension and diabetes. Abdominal adiposity is a risk factor for stroke in men but not women [245]. Although weight loss reduces BP [246], it does not lower stroke risk [247].

Vitamins

A low intake of vitamin D is associated with an increased risk of stroke [248], but supplements of calcium plus vitamin D do not reduce the risk of stroke [249]. Supplements of tocopherol and beta carotene do not reduce stroke [250]. A meta-analysis of trials with vitamin E supplementation found that it might increase mortality when used at high doses (≥400 IU/day) [251].

High homocysteine levels are associated with increased stroke risk (OR 1.19; 95% CI 1.05–1.31) [252]. Since folic acid fortification of enriched grain products was mandated by the US Food and Drug Administration, there has been a reduction in stroke mortality rates, in contrast to countries without fortification [253]. A meta-analysis concluded that folic acid supplementation can reduce the risk of stroke (RR 0.82; 95% CI 0.68–1.00) [254]; the benefit was greatest in trials with long treatment durations or larger homocysteine-lowering effects, and in countries where grain was not fortified.

Postmenopausal Oestrogen Replacement Therapy

Stroke rates rise rapidly in women after the menopause. However, in an analysis based on a 16-year follow-up of 59,337 postmenopausal women participating in the Nurses' Health Study, there was only a weak association between stroke and oestrogen replacement [255]. According to the HERS II trial, hormone replacement in healthy women is associated with an increased risk of ischaemic stroke [256]. A Cochrane systematic review [257] found hormone replacement therapy to be associated with an increased risk of stroke (RR 1.44; 95% CI 1.10–1.89). A secondary analysis of the Women's Health Initiative randomized controlled trial suggests that the risk of stroke is increased with hormone replacement therapy only in women with prolonged hormone use (>5 years; RR 1.32; 95% CI 1.12–1.56) [258, 259].

- ≥248 Marniemi J, Alanen E, Impivaara O, Sep- ≥259 Rossouw JE, Prentice RL, Manson JE, Wu panen R, Hakala P, Rajala T, Ronnemaa T: Dietary and serum vitamins and minerals as predictors of myocardial infarction and stroke in elderly subjects. Nutr Metab Cardiovasc Dis 2005;15:188-197.
- ≥249 Hsia J, Heiss G, Ren H, Allison M, Dolan N, ≥260 Greenland P, Heckbert S, Johnson K, Manson J, Sidney S, Trevisan M: Calcium/vitamin D supplementation and cardiovascular events. Circulation 2007;115:846-854.
- ≥250 Tornwall M, Virtamo J, Korhonen P, Virtanen M, Albanes D, Huttunen J: Postinter- >261 vention effect of alpha tocopherol and beta carotene on different strokes: a 6-year follow-up of the alpha tocopherol, beta carotene cancer prevention study. Stroke 2004; 35:1908-1913
- ≥251 * Miller E, Pastor-Barriuso R, Dalal D, Riemersma R, Appel L, Guallar E: Metaanalysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med 2005;142:37-46.
- ▶252 The Homocysteine Studies Collaboration: Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. JAMA 2002;288:2015-2022.
- ≥253 Yang Q, Botto LD, Erickson JD, Berry RJ, Sambell C, Johansen H, Friedman JM: Improvement in stroke mortality in Canada and the United States, 1990 to 2002. Circulation 2006;113:1335-1343.
- 254 Wang X, Qin X, Demirtas H, Li J, Mao G, Huo Y, Sun N, Liu L, Xu X: Efficacy of folic acid supplementation in stroke prevention: a meta-analysis. Lancet 2007;369:1876-1882.
- ≥255 Grodstein F, Manson JE, Stampfer MJ: Postmenopausal hormone use and secondary prevention of coronary events in the nurses' health study. A prospective, observational study. Ann Intern Med 2001;135: ▶266 1 - 8
- ≥256 Grady D, Herrington D, Bittner V, Blumenthal R, Davidson M, Hlatky M, Hsia J, Hulley S, Herd A, Khan S, Newby LK, Waters D, 267 Vittinghoff E, Wenger N: Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). JAMA 2002;288:49-57.
 - 257 * Gabriel S, Carmona L, Roque M, Sanchez ▶268 G, Bonfill X: Hormone replacement therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev 2005:CD002229.
- 258 Brunner R, Gass M, Aragaki A, Hays J, Granek I, Woods N, Mason E, Brzyski R, 269 Ockene J, Assaf A, LaCroix A, Matthews K, Wallace R: Effects of conjugated equine estrogen on health-related quality of life in postmenopausal women with hysterectomy: results from the women's health initiative randomized clinical trial. Arch Intern Med 2005;165:1976-1986.

- L, Barad D, Barnabei VM, Ko M, LaCroix AZ, Margolis KL, Stefanick ML: Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA 2007;297:1465-1477.
- Peto R, Gray R, Collins R, Wheatley K, Hennekens C, Jamrozik K, Warlow C, Hafner B, Thompson E, Norton S, et al: Randomised trial of prophylactic daily aspirin in British male doctors. BMJ (Clin Res Ed) 1988:296:313-316.
- Steering Committee of the Physicians' Health Study Research Group: Final report on the aspirin component of the ongoing Physicians' Health Study. N Engl J Med >273 1989;321:129-135.
- ▶262 ETDRS Investigators: Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study report 14. JAMA 1992; 268:1292-1300.
- ≥263 Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Menard J, Rahn KH, Wedel H, Westerling S: Effects of intensive blood-pressure lowering and lowdose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351:1755- 275 1762
- ≥264 de Gaetano G: Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001;357:89-95.
- 265 Iso H, Hennekens C, Stampfer M, Rexrode K, Colditz G, Speizer F, Willett W, Manson J: Prospective study of aspirin use and risk ▶276 Cannegieter SC, Rosendaal FR, Wintzen of stroke in women. Stroke 1999;30:1764-1771.
- Bartolucci A, Howard G: Meta-analysis of data from the six primary prevention trials of cardiovascular events using aspirin. Am J Cardiol 2006;98:746-750.
- *Berger J, Roncaglioni M, Avanzini F, Pangrazzi I, Tognoni G, Brown D: Aspirin for the primary prevention of cardiovascu- >278 lar events in women and men: A sex-specific meta-analysis of randomized controlled trials. JAMA 2006;295:306-313.
- Ridker PM, Cook NR, Lee IM, Gordon D, Gaziano JM, Manson JE, Hennekens CH, Buring JE: A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. N Engl J Med 2005;352:1293-1304.
 - * Bhatt D, Fox K, Hacke W, Berger P, Black H, Boden W, Cacoub P, Cohen E, Creager >280 M, Easton J, Flather M, Haffner S, Hamm C, Hankey G, Johnston S, Mak K, Mas J, Montalescot G, Pearson T, Steg P, Steinhubl S, Weber M, Brennan D, Fabry-Ribaudo L, Booth J, Topol E: Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med 2006;354:1706-1717.

- 270 Hobson R, 2nd, Krupski W, Weiss D: Influence of aspirin in the management of asymptomatic carotid artery stenosis. VA Cooperative Study Group on Asymptomatic Carotid Stenosis. J Vasc Surg 1993;17: 257-263.
- 271 Engelter S, Lyrer P: Antiplatelet therapy for preventing stroke and other vascular events after carotid endarterectomy. Cochrane Database Syst Rev 2003;CD001458.
- * Hart RG, Pearce LA, Aguilar MI: Metaanalysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007; 146:857-867.
- *Rash A, Downes T, Portner R, Yeo W, Morgan N, Channer K: A randomised controlled trial of warfarin versus aspirin for stroke prevention in octogenarians with atrial fibrillation (WASPO). Age Ageing 2007;36:151-156.
- Mant J, Hobbs FD, Fletcher K, Roalfe A, Fitzmaurice D, Lip GY, Murray E: Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. Lancet 2007;370:493-503.
- Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, Pfeffer M, Hohnloser S, Yusuf S: Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the atrial fibrillation clopidogrel trial with irbesartan for prevention of vascular events (ACTIVEW): a randomised controlled trial. Lancet 2006;367:1903-
- AR, van der Meer FJ, Vandenbroucke JP, Briet E: Optimal oral anticoagulant therapy in patients with mechanical heart valves. N Engl J Med 1995;333:11-17.
- * Chambers BR, Donnan GA: Carotid endarterectomy for asymptomatic carotid stenosis. Cochrane Database Syst Rev 2005: CD001923.
- Executive Committee for the Asymptomatic Carotid Atherosclerosis Study: Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-1428.
- * Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, Thomas D: Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms; randomised controlled trial. Lancet 2004;363:1491-1502.
- *North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-