



Guidelines for Management of Ischaemic Stroke 2008

The European Stroke Organization
- ESO -

Executive Committee and
Writing Committee



- Prevention
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Definitions of Levels of Evidence

Level A	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective or harmful for a therapeutic intervention; requires at least one convincing Class I study or at least two consistent, convincing Class II studies.
Level B	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective or harmful for a therapeutic intervention; requires at least one convincing Class II study or overwhelming Class III evidence.
Level C	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective or harmful for a therapeutic intervention; requires at least two Class III studies.
Good Clinical Practice (GCP)	Recommended best practice based on the experience of the guideline development group. Usually based on Class IV evidence indicating large clinical uncertainty, such GCP points can be useful for health workers.

Classification of Evidence

	Evidence classification scheme for a <u>therapeutic</u> intervention
Class I	An adequately powered, prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations.
Class II	Prospective matched-group cohort study in a representative population with masked outcome assessment or a randomized, controlled trial in a representative population that lacks one criterion for class I evidence.
Class III	All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment.
Class IV	Evidence from uncontrolled studies, case series, case reports, or expert opinion.

Classification of Evidence

	Evidence classification scheme for a <u>diagnostic</u> measure
Class I	A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.
Class II	A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.
Class III	Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.
Class IV	Evidence from uncontrolled studies, case series, case reports, or expert opinion.

Vascular Risk Factors

- Conditions and lifestyle characteristics identified as a risk factors for stroke

High blood pressure

Atrial fibrillation

Diabetes mellitus

Carotid artery disease

Myocardial infarction

High Cholesterol

Hyper-homocysteinaemia

Smoking

Heavy alcohol use

Physical inactivity

Obesity

High blood pressure (BP)

- Background
 - High blood pressure (>120/80mmHg) is the most important and prevalent modifiable risk factor for stroke
 - Significant reduction of stroke incidence with a decrease in BP¹
 - No class of antihypertensive is clearly superior
 - LIFE: losartan is superior to atenolol²
 - ALLHAT: chlorthalidone is more effective than amlodipine and lisinopril³

1: Neal B et al. Lancet (2000) 356:1955-64

2: Dahlof B et al. Lancet (2002) 359:995-1003.

3: Mancia G et al. Eur Heart J (2007) 28:1462-536

Diabetes mellitus

- Background
 - Independent risk factor for ischaemic stroke
 - Improving glucose control may not reduce stroke¹
 - BP in patients with diabetes should be <130/80mmHg²
 - Statin treatment reduces the risk of major vascular events, including stroke³
 - Elevated blood glucose in the early phase of stroke is associated with death and poor recovery

1: Turner RC et al. JAMA (1999) 281:2005-12

2: Mancia GJ: Hypertens Suppl (2007) 25:S7-12

3: Sever PS et al. Diabetes Care (2005) 28:1151-7

High Cholesterol

- Background
 - Statin treatment reduces the incidence of stroke from 3.4% to 2.7%¹
 - No significant effect for prevention of fatal stroke¹
 - Heart Protection Study found an excess of myopathy of one per 10,000 patients per annum²
 - No data support statin treatment in patients with LDL-cholesterol <150 mg/dl (3.9 mmol/l)

1: Amarenco P et al.: Stroke (2004) 35:2902-2909
2: HPS Group: Lancet (2002) 360:7-22.

Cigarette Smoking

- Background
 - Independent risk factor for ischaemic stroke in men and women
 - 2-3 fold increased risk compared to non-smokers¹
 - Spousal cigarette smoking may be associated with an increased stroke risk²
 - 50% risk reduction by 2 years after stopping smoking³

1: Shinton R et al.: BMJ (1989) 298:789-94.

2: Qureshi A et al.: Stroke (2005) 36:74-76

3: Colditz GA et al.: N Engl J Med (1988) 318:937-41.

Alcohol Consumption

- Background
 - Increased risk for both ischaemic (RR 1.69) and haemorrhagic stroke (RR 2.18) with heavy alcohol consumption (>60g/day)¹
 - BP elevation might be a reasonable explanation³
 - Light alcohol consumption (<12g/day) associated with reduced ischaemic (RR 0.80) and haemorrhagic stroke¹
 - Red wine consumption carries the lowest risk²

1: Reynolds K et al.: JAMA (2003) 289:579-88

2: Mukamal K et al.: Ann Intern Med (2005) 142:11-19

3: Bazzano LA et al.: Ann Neurol (2007)

Physical Activity

- Background
 - Regular exercise (at least 3x30min/week) is associated with a decreased risk of stroke
 - Physically active individuals have a lower risk of stroke or death than those with low activity (RR 0.73)¹
 - This is mediated, in part, through beneficial effects on body weight, blood pressure, serum cholesterol, and glucose tolerance²

1: Lee C et al.: Stroke (2003) 34:2475-2481

2: Deplanque D et al.: Neurology (2006) 67:1403-1410)

Body Weight, Diet, Nutrition

- Background
 - High body mass index (BMI ≥ 25) increases risk of stroke in men and women¹
 - Abdominal adiposity is a risk factor for stroke in men but not women²
 - A randomized trial in women found no effect of dietary interventions to reduce the incidence of stroke³
 - Tocopherol and beta carotene supplementation do not reduce the risk of stroke. Vitamin E might increase mortality when used at high-dose (≥ 400 IU/d)

1: Kurth T et al.: Circulation (2005) 111:1992-1998

2: Hu G et al.: Arch Intern Med (2007) 167:1420-1427

3: Howard B et al.: JAMA (2006) 295:655-666

Hormone Replacement Therapy

- Background
 - Stroke rates rise rapidly in women after the menopause
 - Hormone replacement therapy in postmenopausal women is associated with an 44% increased risk of stroke¹

Recommendations (1/4)

- Blood pressure should be checked regularly. High blood pressure should be managed with lifestyle modification and individualized pharmacological therapy (**Class I, Level A**) aiming at normal levels of 120/80 mmHg (**Class IV, GCP**)

Risk Factor Management

Recommendations (2/4)

- Blood glucose should be checked regularly. Diabetes should be managed with lifestyle modification and individualized pharmacological therapy **(Class IV, Level C)**.
- In diabetic patients, high blood pressure should be managed intensively **(Class I, Level A)** aiming for levels below 130/80 mmHg **(Class IV, Level C)**. Where possible, treatment should include an angiotensin converting enzyme inhibitor or angiotensin receptor antagonist **(Class I, Level A)**

Risk Factor Management

Recommendations (3/4)

- Blood cholesterol should be checked regularly. High blood cholesterol (e.g. LDL>150mg/dl [3,9mMol/l]) should be managed with lifestyle modification (**Class IV, Level C**) and a statin (**Class I, Level A**)
- Cigarette smoking should be discouraged (**Class III, Level B**)
- Heavy use of alcohol should be discouraged (**Class III, Level B**)
- Regular physical activity is recommended (**Class III, Level B**)

Risk Factor Management

Recommendations (4/4)

- A diet low in salt and saturated fat, high in fruit and vegetables and rich in fibre is recommended **(Class III, Level B)**
- Subjects with an elevated body mass index are recommended to take a weight-reducing diet **(Class III, Level B)**
- Antioxidant vitamin supplements are not recommended **(Class I, Level A)**
- Hormone replacement therapy is not recommended for the primary prevention of stroke **(Class I, Level A)**

Antithrombotic Therapy

- Background
 - In low risk persons low dose aspirin reduced coronary events, but not stroke¹
 - In women over 45 years aspirin reduces the risk of ischaemic stroke (OR 0.76; 95%CI 0.63-0.93)²
 - Aspirin reduces MI in patients with asymptomatic carotid artery disease³

1: Bartolucci A et al.: Am J Cardiol (2006) 98:746-750

2: Berger J et al.: JAMA (2006) 295:306-313

3: Hobson R, 2nd et al.: J Vasc Surg (1993) 17:257-263

Atrial fibrillation (AF)

- Background
 - Average stroke rate of 5% per year
 - Aspirin reduces stroke (RR 0.78) in patients with non-valvular AF¹
 - Warfarin (INR 2.0-3.0) is more effective than aspirin at reducing stroke (RR 0.36; 95%CI 0.26-0.51)¹
 - Combination of aspirin and clopidogrel is less effective than warfarin and has a similar bleeding rate²

1: Hart RG et al.: Ann Intern Med (2007) 146:857-867

2: Connolly S et al.: Lancet (2006) 367:1903-1912

Atrial fibrillation (AF)

- Background
 - Anticoagulation with an INR below 2.0 is not effective
 - Increased risk for bleeding complications with an INR > 3.5
 - Patients <65 years of age with “lone AF” (without other risk factors) are at low risk, whereas patients older than 65 years are at a higher risk for embolic stroke
 - Anticoagulation can be safe and effective in older individuals^{1, 2}

1: Rash A et al.: Age Ageing (2007) 36:151-156

2: Mant J et al.: Lancet (2007) 370:493-503

Recommendations (1/4)

- Low-dose aspirin is recommended in women aged 45 years or more who are not at increased risk for intracerebral haemorrhage and who have good gastrointestinal tolerance; however, its effect is very small **(Class I, Level A)**
- Low-dose aspirin may be considered in men for the primary prevention of myocardial infarction; however, it does not reduce the risk of ischaemic stroke **(Class I, Level A)**

Recommendations (2/4)

- Antiplatelet agents other than aspirin are not recommended for primary stroke prevention (**Class IV, GCP**)
- Aspirin may be recommended for patients with non-valvular AF who are younger than 65 years and free of vascular risk factors (**Class I, Level A**)
- Unless contraindicated, either aspirin or an oral anticoagulant (international normalized ratio [INR] 2.0-3.0) is recommended for patients with non-valvular AF who are aged 65-75 years and free of vascular risk factors (**Class I, Level A**)

Recommendations (3/4)

- Unless contraindicated, an oral anticoagulant (INR 2.0–3.0) is recommended for patients with non-valvular AF who are aged >75, or who are younger but have risk factors such as high blood pressure, left ventricular dysfunction, or diabetes mellitus (**Class I, Level A**)

Antithrombotic Therapy

Recommendations (4/4)

- Patients with AF who are unable to receive oral anticoagulants should be offered aspirin (**Class I, Level A**)
- Patients with AF who have mechanical prosthetic heart valves should receive long-term anticoagulation with a target INR based on the prosthesis type, but not less than INR 2–3 (**Class II, Level B**)
- Low dose aspirin is recommended for patients with asymptomatic internal carotid artery (ICA) stenosis >50% to reduce their risk of vascular events (**Class II, Level B**)

Asymptomatic carotid artery (ICA) stenosis

- Background^{1,2}
 - Carotid endarterectomy (CEA) is still a matter of controversy in asymptomatic individuals
 - RRR for stenosis >60%^{NASCET} is 38-53%
 - ARR is 5.9-12.6%
 - NNT to avoid one stroke/year is 63-166
 - The combined surgical risk must not exceed 3%

1: ACAS: JAMA (1995) 273:1421-8.
2: ACST: Lancet (2004) 363:1491-1502

Asymptomatic carotid artery (ICA) stenosis

- Specific issues
 - No prospective trials tested the benefit of antiplatelet drugs in patients with asymptomatic carotid stenosis¹
 - The ipsilateral stroke risk increases with the degree of the stenosis²
 - Patients with an occlusion of the contralateral ICA do not benefit from endarterectomy³
 - Women have lower benefit from CEA than men³
 - Aspirin reduces stroke risk during and after CEA⁴

1: Chambers BR et al.: Cochrane Review (2005)

2: ECST Group: Lancet (1995) 345:209-12

3: Baker WH et al.: Stroke (2000) 31:2330-4

4: Engelter S et al.: Cochrane Reviews (2003)

Recommendations

- Carotid surgery is not recommended for asymptomatic individuals with significant carotid stenosis (NASCET 60-99%), except in those at high risk of stroke (**Class I, Level C**)
- Carotid angioplasty, with or without stenting, is not recommended for patients with asymptomatic carotid stenosis (**Class IV, GCP**)
- Patients should take aspirin before and after CEA (**Class I, Level A**)

Secondary Prevention

- Content
 - Management of vascular risk factors
 - Antithrombotic therapy
 - Surgery and angioplasty

Blood pressure control

- Background
 - Antihypertensive drugs reduce stroke recurrence risk after stroke or TIA (RR 0.76; 95%CI 0.63-0.92)¹
 - Target BP level and reduction should be individualized
 - The reduction in stroke occurs regardless of baseline BP and type of stroke²

1: Rashid P et al.: Stroke (2003) 34:2741-8

2: PROGRESS group: Lancet (2001) 358:1033-41

Diabetes mellitus

- Background
 - In people with type 2 diabetes with previous stroke pioglitazone reduces fatal or nonfatal stroke (HR 0.53; 95%CI 0.34-0.85; P=0.0085)¹
 - In addition there is a trend to reduce the combined end point of death and major vascular events (HR 0.78; 95%CI 0.60-1.02; P=0.067)¹

High Cholesterol

- Background
 - Atorvastatin (80mg) reduces stroke recurrence by 16%¹
 - Simvastatin (40mg) reduces risk of vascular events in patients with prior stroke, and of stroke in patients with other vascular disease (RR 0.76)²
 - ARR for statin treatment is low (NNT 112-143 for 1 year)¹
 - Statin withdrawal at the acute stage of stroke may be harmful³

1: Amarenco P et al.: N Engl J Med (2006) 355:549-559

2: Heart Protection Study: Lancet (2002) 360:7-22

3: Blanco M et al.: Neurology (2007) 69:904-10

Vitamins

- Background
 - Beta carotene increased the risk (RR 1.10) of cardiovascular death¹
 - Antioxidant supplements may increase mortality²
 - Folate, B12, B6 vitamins given to lower homocysteine levels may not reduce stroke recurrence and may increase vascular events³

1: Vivekananthan D et al.: Lancet (2003) 361:2017-2023

2: Bjelakovic G et al.: JAMA (2007) 297:842-857

3: Bonna K et al.: N Engl J Med (2006) 354:1578-1588

Hormone Replacement Therapy

- Background
 - Oestrogen therapy is not effective in secondary prevention after TIA or stroke and may increase stroke severity¹

Sleep-disordered Breathing

- Background
 - Sleep-disordered breathing (SDB) is both a risk factor and a consequence of stroke
 - More than 50% of stroke patients have SDB, mostly in the form of obstructive sleep apnoea (OSA).
 - SDB is linked with poorer long-term outcome and increased long-term stroke mortality¹
 - Continuous positive airway pressure is the treatment of choice for OSA.

Risk Factor Management

Recommendations (1/3)

- Blood pressure should be checked regularly. Blood pressure lowering is recommended after the acute phase, including in patients with normal blood pressure (**Class I, Level A**)
- Blood glucose should be checked regularly. Diabetes should be managed with lifestyle modification and individualized pharmacological therapy (**Class IV, GCP**)
- In patients with type 2 diabetes who do not need insulin, treatment with pioglitazone is recommended after stroke (**Class III, Level B**)

Risk Factor Management

Recommendations (2/3)

- Statin therapy is recommended **(Class I, Level A)**
- Cigarette smoking should be stopped **(Class III, Level C)**
- Heavy use of alcohol should be discouraged **(Class IV, GCP)**
- Regular physical activity is recommended **(Class IV, GCP)**
- A diet low in salt and saturated fat, high in fruit and vegetables, and rich in fibre is recommended **(Class IV, GCP)**

Risk Factor Management

Recommendations (3/3)

- Subjects with an elevated body mass index are recommended to take a weight-reducing diet (**Class IV, Level C**)
- Antioxidant vitamins supplements are not recommended (**Class I, Level A**)
- Hormone replacement therapy is not recommended for the secondary prevention of stroke (**Class I, Level A**)
- Sleep-disordered breathing such as obstructive sleep apnoea is recommended to be treated with continuous positive airway pressure breathing (**Class III, Level GCP**)

Antithrombotic Therapy

- Background: Aspirin
 - 13% relative risk reduction for stroke after TIA or stroke¹
 - Most widely studied dosages of aspirin are 50-150mg
 - The incidence of GI-disturbances with aspirin is dose dependent
 - No difference in effectiveness amongst low (< 160mg), medium (160 – 325mg) or high (500 - 1500mg) dose aspirin

Antithrombotic Therapy

- Background: Dipyridamole plus aspirin
 - Relative risk reduction of vascular death, stroke or myocardial infarction with the combination is significantly greater (RR 0.82; 95%CI 0.71-0.91) than with aspirin alone^{1,2}
 - ARR 1.0% per year (NNT 100)²
 - Incidence of dipyridamole induced headache may be reduced by increasing the dose gradually³

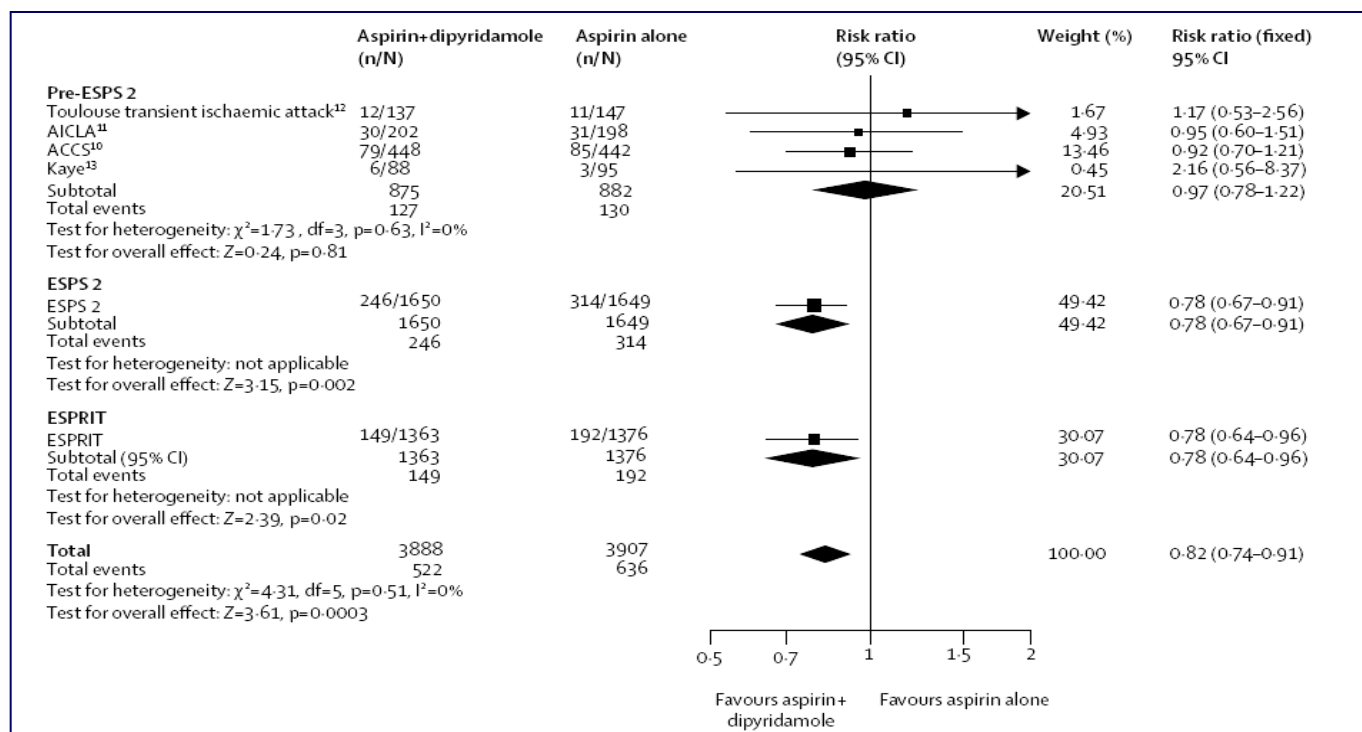
1: Diener HC et al.: J Neurol Sci (1996) 143:1-13

2: Halkes P et al.: Lancet (2006) 367:1665-1673

3: Chang YJ et al.: Cerebrovasc Dis (2006) 22:258-62

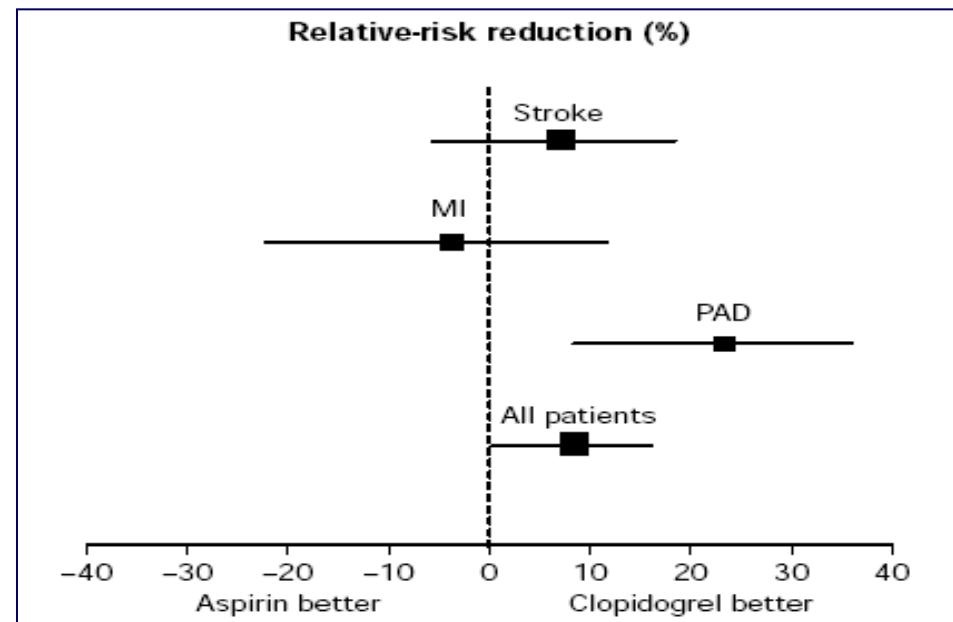
Antithrombotic Therapy

- Dipyridamole plus aspirin versus aspirin: Meta-analysis¹
 - Reduced vascular endpoint (vascular death, stroke, myocardial infarction) with dipyridamole plus aspirin



Antithrombotic Therapy

- Background: Clopidogrel:
 - Clopidogrel is slightly but significantly more effective than medium-dose aspirin (RRR 8.7%, ARR 0,5%) in preventing vascular events in patients with previous stroke, MI or PAD¹



Antithrombotic Therapy

- Background: Clopidogrel plus aspirin
 - Compared with clopidogrel the combination of aspirin and clopidogrel does not reduce the risk of ischaemic stroke, myocardial infarction, vascular death, or re-hospitalisation¹
 - Compared with aspirin alone the combination does not reduce the risk of myocardial infarction, stroke, or cardiovascular death²
 - Risk of life-threatening or major bleeding is increased^{1,2}

1: Diener H et al.: Lancet (2004) 364:331-337

2: Bhatt D et al.: N Engl J Med (2006) 354:1706-1717

Antithrombotic Therapy

Recommendations (1/4)

- Patients should receive antithrombotic therapy **(Class I, Level A)**
- Patients not requiring anticoagulation should receive antiplatelet therapy **(Class I, Level A)**. Where possible, combined aspirin and dipyridamole, or clopidogrel alone, should be given. Alternatively, aspirin alone, or triflusal alone, may be used **(Class I, Level A)**

Recommendations (2/4)

- The combination of aspirin and clopidogrel is not recommended in patients with recent ischaemic stroke, except in patients with specific indications (e.g. unstable angina or non-Q-wave MI during the last 12 months, or recent stenting); treatment should be given for up to 9 months after the event **(Class I, Level A)**
- Patients who have a stroke on antiplatelet therapy should be re-evaluated for pathophysiology and risk factors **(Class IV, GCP)**

Anticoagulation

- Background
 - Oral anticoagulation (target INR 2.0 – 3.0) reduces the risk of recurrent stroke in patients with AF¹
 - Oral anticoagulation is well established for other causes of embolism such as mechanical prosthetic valve replacement, rheumatic valvular heart disease, ventricular aneurysm and cardiomyopathy
 - There is no indication for oral anticoagulation in patients with non-cardiac cause of ischaemic stroke²

1: EAFT Study Group: Lancet (1993) 342:1255-1262
2: Mohr JP et al.: N Engl J Med (2001) 345:1444-1451

Anticoagulation

- Specific issues
 - In patients with AF and stable coronary disease, aspirin should not be added to oral anticoagulation¹
 - Some retrospective studies suggest that anticoagulation may be beneficial in aortic atheroma², fusiform basilar artery aneurysms³, or arterial dissection⁴
 - It is unclear if patients with patent foramen ovale (PFO) benefit from oral anticoagulation⁵

1: Flaker GC et al.: Am Heart J (2006) 152:967-73

2: Dressler FA et al.: J Am Coll Cardiol (1998) 31:134-8

3: Echiverri HC et al.: Stroke (1989) 20:1741-7

4: Engelter ST et al.: Stroke (2007) 38:2605-11

5: Mas JL et al.: N Engl J Med (2001) 345:1740-6

Recommendations (3/4)

- Anticoagulation should not be used after non-cardio-embolic ischaemic stroke, except in some specific situations, such as aortic atheromas, fusiform aneurysms of the basilar artery, cervical artery dissection, or patent foramen ovale in the presence of proven deep vein thrombosis (DVT) or atrial septal aneurysm (**Class IV, GCP**)
- If oral anticoagulation is contraindicated, combined low dose aspirin and dipyridamole should be given (**Class IV, GCP**)

Antithrombotic Therapy

Recommendations (4/4)

- Oral anticoagulation (INR 2.0–3.0) is recommended after ischaemic stroke associated with AF (**Class I, Level A**). Oral anticoagulation is not recommended in patients with co-morbid conditions such as falls, poor compliance, uncontrolled epilepsy, or gastrointestinal bleeding (**Class III, Level C**). Increasing age alone is not a contraindication to oral anticoagulation (**Class I, Level A**)
- Patients with cardioembolic stroke unrelated to AF should receive anticoagulants (INR 2.0-3.0) if the risk of recurrence is high (**Class III, Level C**)

Carotid Endarterectomy (CEA)

- Background^{1,2}
 - CEA reduces the risk by 48% of recurrent disabling stroke or death in patients with 70-99%^{NASCET} ipsilateral carotid artery stenosis
 - If perioperative complications exceed 6%, the benefit of CEA will diminish; if it approaches 10%, the benefit will vanish entirely
 - There is also some risk reduction in male patients with 50 - 69% stenosis of the ipsilateral carotid artery, provided that the complication rate is below 3%

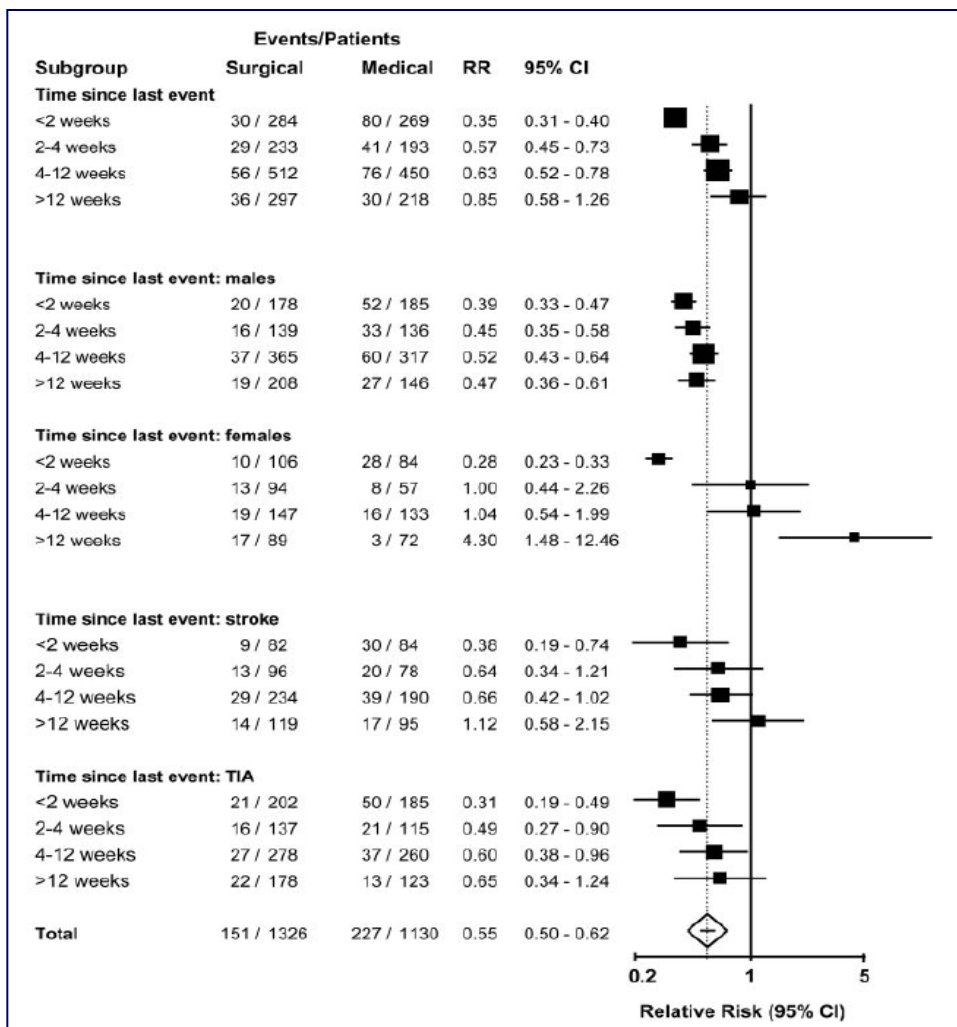
1: NASCET Collaborators: NEJM (1991) 325:445-453

2: Warlow C: Lancet (1991) 337:1235-1243

Carotid Endarterectomy

- Specific issues
 - CEA should be performed as soon as possible (ideally within 2 weeks) after the last cerebrovascular event^{1,2}
 - Elderly patients (>75 years) without organ failure or serious cardiac dysfunction benefit from CEA¹
 - Women with symptomatic stenosis >70% should undergo CEA. Women with moderate stenosis should be treated medically²

Carotid Endarterectomy



Effect of time from last symptomatic event to randomisation on the 5-year relative risk (RR) of ipsilateral ischaemic stroke and any operative stroke or death with CEA (pooled data from ECST and NASCET¹)

Carotid Endarterectomy

- Specific issues
 - The benefit from CEA is lower with lacunar stroke
 - Patients with leuko-araiosis should be made aware of the increased operative risk
 - Occlusion of the contralateral ICA carries a higher perioperative risk
 - Continuation of aspirin is required until surgery, but heparin may be used in very severe stenosis
 - All grading of stenoses should be according to NASCET-criteria

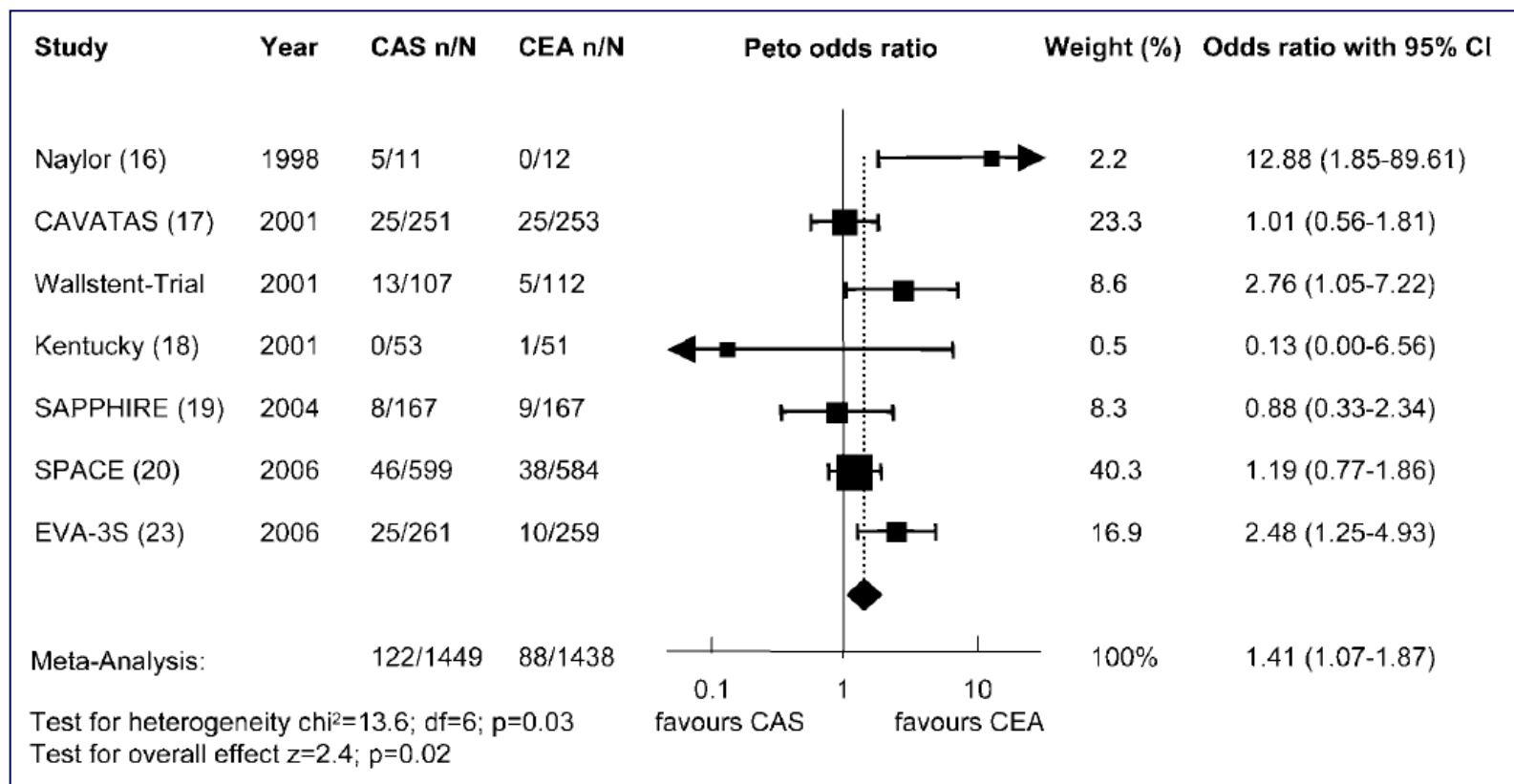
Carotid Artery Stenting (CAS)

- Background
 - No randomized trial has demonstrated equivalent periprocedural risk for CAS compared to CEA in treatment of symptomatic carotid artery stenosis
 - A European study only marginally failed to prove the non-inferiority of CAS compared to CEA
 - A French study was stopped prematurely because of a 2.5 fold higher risk of any stroke or death after CAS²

Carotid Artery Stenting

Metaanalysis CAS vs. CEA Endpoint: any periprocedural stroke or death

Secondary Prevention



Intracranial Occlusive Disease

- Background
 - Extracranial-Intracranial bypass is not beneficial in preventing stroke in patients with MCA or ICA stenosis or occlusion¹
 - No randomized controlled trials have evaluated angioplasty, stenting, or both for intracranial stenosis
 - Several non-randomized trials have shown feasibility and acceptable safety of intracranial stenting, but the risk of re-stenosis remains high^{2,3}

1: The EC/IC Bypass Grp: N Engl J Med (1985) 313:1191-200

2: Bose A et al.: Stroke (2007) 38:1531-7

3: SSYLVA Study investigators: Stroke (2004) 35:1388-92

Surgery and Angioplasty

Recommendations (1/4)

- CEA is recommended for patients with 70–99% stenosis (NASCET criteria) **(Class I, Level A)**. CEA should only be performed in centres with a perioperative complication rate (all strokes and death) of less than 6% **(Class I, Level A)**
- CEA should be performed as soon as possible after the last ischaemic event, ideally within 2 weeks **(Class II, Level B)**

Surgery and Angioplasty

Recommendations (2/4)

- CEA may be indicated for certain patients with stenosis of 50–69% (NASCET criteria); males with very recent hemispheric symptoms are most likely to benefit (**Class III, Level C**). CEA for stenosis of 50–69% (NASCET criteria) should only be performed in centres with a perioperative complication rate (all stroke and death) of less than 3% (**Class I, Level A**)
- CEA is not recommended for patients with stenosis of less than 50% (NASCET criteria) (**Class I, Level A**)

Surgery and Angioplasty

Recommendations (3/4)

- Patients should remain on antiplatelet therapy both before and after surgery **(Class I, Level A)**
- Carotid percutaneous transluminal angioplasty and/or stenting (CAS) is only recommended in selected patients **(Class I, Level A)**. It should be restricted to the following subgroups of patients with severe symptomatic carotid artery stenosis: those with contra-indications to CEA, stenosis at a surgically inaccessible site, re-stenosis after earlier CEA, and post-radiation stenosis **(Class IV, GCP)**

Surgery and Angioplasty

Recommendations (4/4)

- Patients should receive a combination of clopidogrel and aspirin immediately before and for at least 1 months after stenting (**Class IV, GCP**)
- Endovascular treatment may be considered in patients with symptomatic intracranial stenosis (**Class IV, GPC**)