ACCIDENTE VASCULARE CEREBRALE STROKE MANAGEMENT

Elena Copaciu
Baza Clinică ATI
Spitalul Universitar ELIAS Bucureşti

European Stroke Initiative
Recommendations 2003
EUSI
Ischaemic Stroke
Prophylaxis and Treatment
Information for doctors in hospitals and practice

Written by:
the EUSI Executive Committee:
Werner Hacke, Heidelberg, GER;
Markku Kaste, Helsinki, FIN;
Julien Bogousslavsky, Lausanne SUI;
Michael Brainin, Maria Gugging, AUS;
Angel Chamorro, Barcelona, SPA;
Kennedy Lees, Glasgow, UK;
Didier Leys, Lille, FRA;
Hubert Kwiecinski, Warsaw, POL;
Danilo Toni, Rome, ITA
and
the EUSI Writing Committee:
Tom Skyhøj Olsen, Copenhagen, DEN;
Peter Langhorne, Glasgow, UK;
Hans Christoph Diener, Essen, GER;
Michael Hennerici, Mannheim, GER;
Jose Ferro, Lisbon, POR;
Johani Sivenius, Kuopiu, FIN;
Nils Gunnar Wahlgren, Stockholm, SWE;
Philip Bath, Nottingham, UK;

Editorial assistance:
Sonja Kulkens, Peter Ringleb, Heidelberg, GER

EUSI

EUSI (The European Stroke Initiative)

Is the common body of the
- ESC (European Stroke Council)
- ENS (European Neurological Society
- EFNS (European Federation of Neurological Societies)

EUSI is supported by:
- Sanofi-Synthelabo
- Boehringer Ingelheim
- Servier

The writing and printing of the recommendations and this leaflet was entirely independent of industry support.
In additons, authors who may have had conflicts of interest regarding certain topics did not participate in the writing of such chapters.

Verantwortlich für den Inhalt im Sinne des Pressegesetzes:
Professor Dr. Werner Hacke
Department of Neurology
University of Heidelberg
Im Neuenheimer Feld 400
69120 Heidelberg, Germany
Tel.: +49 6221 568210
Fax: +49 6221 565348
e-mail:werner_hacke@med.uni-heidelberg.de

ETIOLOGIE

- LEZIUNI ATEROSCLEROTICE ŞI ATEROTROMBOTICE la nivelul arterelor cerebrale bazale cu lumen larg sau vaselor cervicale exrtracraniene cu hipoperfuzie critică distal de stenozele strânse
- Emboli arterio arteriali din leziuni aterotrombotice cu ocluzia vaselor intracraniene
- Embolii sistemice: surse cardiace: valve protezate, fibrilaţie atrială, trombi cardiaci, cardiomiopatie dilatativă, infarct miocardic recent, şunt intracardiac
- Lipohialinoză a vasselor mici cu leziuni lacunare microangiopatice
- Rar: disecţia arterei cervicale, vasculite, tromboze în cadrul unor arteriopatii

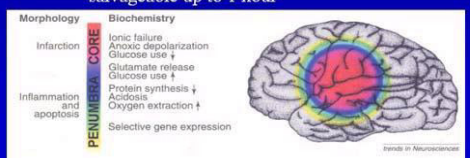
DEFINIŢIE

- **DEFICIT NEUROLOGIC BRUSC INSTALAT DE NATURĂ ISCHEMICĂ SAU HEMORAGICĂ**

8/25

Cerebral ischemia: focal *vs.* global

	Focal	*Global*
Model	MCA occlusion	Forebrain ischemia
Mimics	Stroke	Cardiac arrest
Blood flow	↓	↓↓↓
Time Course	Sustained (4-8 hours)	Transient (60 minutes)
Pathology	Densely ischemic central core with penumbral zone; salvageable up to 1 hour	Selective neuronal necrosis



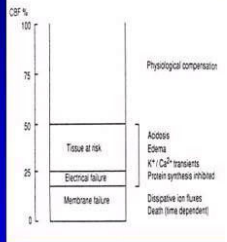
EPIDEMIOLOGIE

- A treia cauză de deces în tările industrializate
- Europa : 63,5- 273 decese/ 100000 locuitori
- Cea mai importantă cauză de morbiditate şi dizabilitate pe termen lung în Europa
- Impact economic deosebit asupra societăţii, familiei şi bolnavului
- Incidenţă: 100-200 AVC noi/ 100000 locuitori/an-Europa

6/25

Critical cerebral blood flow thresholds

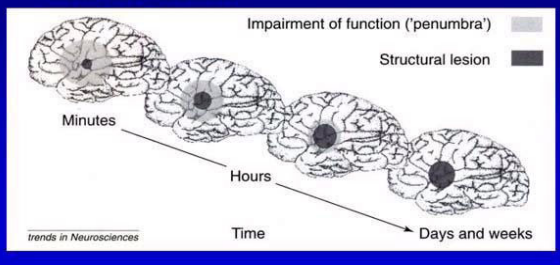
	Blood flow (ml/100g/min)
Normal	20-25
Electrical activity (spontaneous and evoked)	16-18
Acidosis, edema, ↓ protein synthesis	>10-12
Ion homeostasis	10-12
Energy homeostasis	10-12
Infarction	
Transient ischemia (1-3 hours)	10-12
Irreversible ischemia	17-18



9/25

Penumbra

- Zone of reversible impairment; window of opportunity
- Residual electrical activity and receptor activation amenable to blockade



MANAGEMENTUL AVC ACUT

- CONFIRMAREA DIAGNOSTICULUI PENTRU DECIZII TERAPEUTICE OPTIME ŞI RAPIDE
- Tratamentul condiţiilor generale care influenţează prognosticul funcţional pe termen lung: TA, glicemie, temperatură
- Terapii specifice care se adresează aspectelor particulare de patogeneză: recanalizarea unui vas ocluzionat, prevenţia mecanismelor care conduc la moartea neuronală(neuroprotecţie)
- Profilaxia şi tratamentul complicaţiilor medicale sau neurologice
- Profilaxia recurenţelor precoce
- Debut rapid al recuperării neuromotorii

10/25

Mechanisms of ischemic brain damage

Ischemia

↓

Energy failure

↓

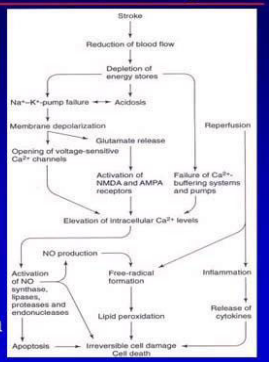
Acidosis

Ca^{2+} overload

Free radicals

↓

Cell damage/inflammation/death



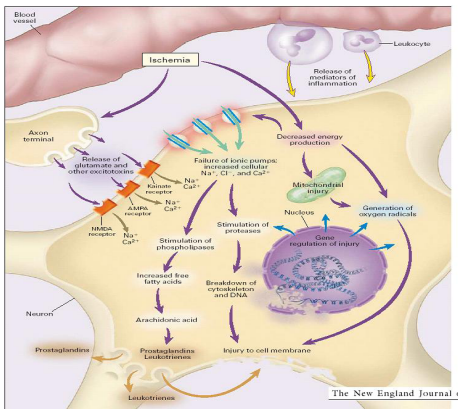
Recommendations

1 Stroke patients should be treated in stroke units (level I). Therefore, suspected stroke victims should be transported without delay to the nearest medical centre with an available stroke unit, or to a hospital providing organised acute stroke care if a stroke unit is not available.

2 Once stroke symptoms are suspected, patients or their proxies should call the EMS or a similar system (level III).

3 Patients with subarachnoid haemorrhage should be referred urgently to a centre with facilities for neurosurgical treatment, neuroradiological interventions and neurointensive care (level I).

Cerebrovasc Dis 2003;16:311–337



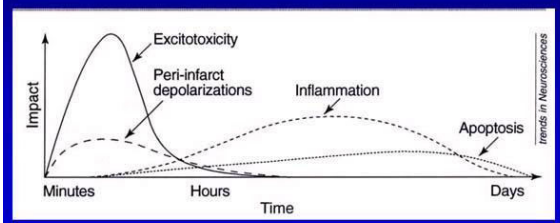
UNITĂŢILE STROKE

- Au scăzut rata mortalităţii la bolnavii cu AVC cu cca. 18%
- Au scăzut rata recuperării cu sechele neurologice invalidante şi a gradului de dependenţă
- Au redus spitalizarea pe termen lung a bolnavilor dependenţi

12/25

Progression of ischemic insults

- Excitotoxicity - glutamate-mediated neuronal damage
- Inflammation
- Apoptosis - programmed cell death



STROKE UNITS

- Compartiment spitalicesc
- Tratează aproape în exclusivitate bolnavii cu AVC
- Asigură abordare multidisciplinară coordonată:
  - Tratamant medical, nursing, fizioterapie, terapie ocupaţională, logopedie, ergoterapie, terapie socială, etc
  - Întruniri periodice pentru evaluarea bolnavilor şi stabilirea planului terapeutic
  - Protocoale de evaluare medicală şi diagnostic(inclusiv imagistică cerebrală)
  - Debut rapid a terapiei specifice

STROKE UNITS

- Unităţi de terapie acută- staţionare bolnavi max. 1 săptămână
- Unităţi de abordare completă (comprehensive stroke units)- terapie acută + terapie continuă, inclusiv 1-2 săptămâni de recuperare
- Rehabilitation stroke units- bolnavi preluaţi la 1-2 săpt de la debut, recuperare până la câteva luni
- Echipe mobile – bolnavi cu AVC evaluaţi şi trataţi în saloanele în care sunt internaţi

Stroke Units Trialists Colaboration. 2002

Funcţia pulmonară şi protecţia căilor aeriene

- IOT de protecţie +/- VM la bolnavi cu:
  - Hipoxemie/ hipercapnie severe
  - GCS< 8
  - Risc crescut de aspiraţie
  - ➢ prognosticul bolnavului cu AVC şi IOT nu este obligatoriu nefavorabil [Berrouschot et al., 2000]
  - ➢ 1/3 din bolnavii IOT au supravieţuit la un an de zile de la accidentul acut [Steiner et al., 1997]

Cerebrovasc Dis 2003;16:311–337. Of course, before intubation is performed, the general prognosis, co-existing life-threatening medical conditions and the presumed will of the patient and his/her family have to be taken into account.

European Stroke Initiative Recommendations for Stroke Management

Dotări minime necesare în centrele STROKE

- Examinare CT disponibilă 24 ore/24
- Protocoale de diagfnostic şi tratamnet a bolnavilor cu AVC validate de specialişti
- Cooperare strânsă neurologi, internişti, recuperare neuro-motorie
- Personal de nursing cu pregătire adecvată
- Recuperare neuromotorie precoce instituită, inclusiv logopedie, terapie ocupaţională şi fizicală
- Asigurarea continuării programului de recuperare pe durate lungi d etimp
- Investigaţii neurochirurgicale în 24 de ore(vase extracraniene, Doppler, etc.)
- Ex. laborator
- Monitorizare TA, ECG, SaO2, glicemie, temperatură

Complicaţii cardiovasculare la bolnavul cu AVC acut

- Aritmii cardiace(frecvent- fibrilaţia atrială)
- Decompensare cardiacă [Bamford et al., 1990; Broderick et al., 1992]
- Infarct miocardic acut, moarte subită
- Modificări traseu Ecg:
  - Segm ST, unda T, prelungire QT- similare ischemiei miocardice [Furlan, 1987]
  - Creşterea enzimelor de citoliză miocardică [Norris, 1983]
  - Corelaţie infarct insular- complicaţii cardiace [Oppenheimer et al., 1996]

Teste diagnostice de urgenţă în AVC acut

- CT
- ECG şi radiografie pulmonară
- Biochimie sanguină
  - HLG, NT, tp de protrombină, INR, PTT
  - Electroliţi sanguini, glicemie
  - PCR, VSH
  - Gaze sanguine arteriale
  - Teste de funcţie hepatică şi renală
  - SaO2
  - EchoDoppler vase extracraniene
  - EEG, RMN, Ct cu substanţă de contrast
  - RMN de difuzie/perfuzie
  - ECG, ECHOcardio transtoracic, transesofagian

Complicaţii cardiovasculare la bolnavul cu AVC acut- tratament

- Optimizarea debitului cardiac:
- Permite restabilrea perfuziei cerebrale în zone de ischemie cu alterarea auttoreglării fluxului sanguin cerebral
  - Suport inotrop- Dobutamină/ Dopamină-
  - PVC: 8- 10 cm H2O- NORMOVOLEMIE PT A MENŢINE PPC
  - De evitat hiper/ hipovolemie- efect negativ asupra PPC
  - PA medie de menţinut la limita superioară a normalului(high normal)
  - AV la valori normale(antiaritmice, cardioversie, pacing temporar sau definitiv)

Funcţia pulmonară şi protecţia căilor aeriene

- Menţinerea PaO2 esenţială pentru funcţia metabolică a neuronilor din zona de penumbră ischemică
- Bolnavii cu risc crescut de hipoxie:
  - Suferinţă evolutivă de trunchi cerebral
  - Infarcte de emisfer cerebral
  - Convulsii subintrante
  - Complicaţii:
    - Pneumonie, sindrom de inhalare
    - Embolie pulmonară
    - Edem pulmonar acut, decompensare cardiacă
    - Depresie respiratorie în somn profund!

PRESIUNEA ARTERIALĂ LA BOLNAVUL CU AVC ACUT

- Autoreglarea fluxului sanguin cerebral poate fi alterată în zonele de infarct cerebral
- Fluxul sanguin în zonele de penunbra ischemică poate fi dependent pasiv de PAM
- Variaţiile PAM pot fi foarte importante pt perfuzia zonei ischemice
- HIPOTENSIUNEA ARTERIALĂ CATASTROFALĂ PT PROGNOSTICUL NERUROLOGIC
- Valori ţintă TA:
  - 180 mmHg- TA sistolică, 100-105 mmHg TA diastolică
  - Inacceptabile valori > 220 mmHg TA sistolică, > 120 mmHg TA diastolică

PRESIUNEA ARTERIALĂ LA BOLNAVUL CU AVC ACUT

- Indicaţii de tratament hipotensor de urgenţă:
  - Ischemie miocardică acută
  - Insuficienţă cardiacă
  - Insuficienţa renală acută
  - Disecţia de arc aortic
  - La bolnavii anticoagulaţi sau sub tromboliză TA
  - Dg. CT cerebral- leziuni nonischemice

NU NIFEDIPINĂ SUBLINGUAL:

» Scădere bruscă TA
» HTA rebound
» Posibil furt ischemic!

Characteristic	Median	Interquartile range
Initial hemodynamic profile		
Admission heart rate, /min	80	68, 90
Admission systolic blood pressure, mm Hg	160	140, 183
Admission diastolic blood pressure, mm Hg	80	68, 92
Admission mean arterial blood pressure, mm Hg	106	93, 121

Table 2 *Use of antihypertensive agents in management of patients with acute ischemic stroke according to prior antihypertensive treatment*

Antihypertensive management	Prior treatment, n = 79		No prior treatment, n = 75	
	n	%	n	%
Discontinued	6	7.6	—	—
Continued	40	50.6	—	—
Intensified	33	41.8	—	—
Initiated	—	—	27	36.0

Table 3 *Antihypertensive agents used in treatment of patients with acute ischemic stroke*

Class	At home*		During hospitalization†	
	n	%	n	%
ACE inhibitors or angiotensin II				
Receptor antagonists	36	31.0	60	30.3
β-Adrenergic antagonists	34	29.3	54	27.3
Calcium channel blockers	13	11.2	25	12.6
Diuretics	19	16.4	22	11.1
CNS-acting agents	6	5.2	15	7.6
Direct vasodilators	0	0.0	11	5.6
Combined αβ antagonists	4	3.5	7	3.5
α-Adrenergic antagonists	4	3.5	4	2.0

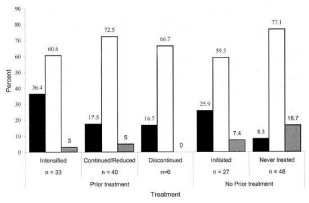
* No. treated with antihypertensive agents before hospitalization for acute ischemic stroke = 79, median interquartile range (IQR) = 1 (1, 2).
† No. treated with antihypertensive agents during hospitalization for acute ischemic stroke = 199, median (IQR) = 2 (1, 3).

The European Stroke Initiative Executive Committee and the EUSI Writing Committee

Table 8. Characteristics of selected antihypertensive drugs that may be used in acute stroke (modified from Kaplan [1990] and Ringleb et al. [1998])

Oral drugs	Dose	Onset min	Duration h	Adverse effects
Angiotensin-converting enzyme inhibitor				
Captopril	6–12.5 mg s.c.	15–30	4–6	decrease in cerebral blood flow orthostatic hypotension
Parenteral drugs				
Central sympaticolytic				
Clonidine	0.2 mg initial then 0.1 mg/h up to 0.8 mg	5–15	6–8	profound hypotension; caution if combined with diuretics
Vasodilators				
Nitroprusside	0.25–10 μg/kg min^{-1}	1–5		nausea, vomiting, muscle twiching, sweating, thiocyanate intoxication
Nitroglycerin	5–100 μg/kg min^{-1}	2–5		tachycardia, headaches, vomiting
Dihydralazin	6.5–20 mg i.v. bolus 1.5–7.5 mg/h	1–2	1–2	tachycardia, headaches
β-Blocker				
Propranolol	1–10 mg i.v.	1–2	3–6	β-blocker side-effects (e.g. bronchospasm, decreased cardiac output, bradycardia)
α/β-Blocker				
Labetalol	20–80 mg i.v. bolus 2 mg/min i.v. infusion	5–10	3–5	vomiting, postural hypotension, nausea, dizziness
α-Blocker				
Urapidil	10–50 mg i.v. bolus 9–30 mg/h	2–5	3	no serious side-effects
Central sympatholytic				
Clonidine	0.075 mg s.c.	5–10	3–5	initial blood pressure increase, sedation
The use of oral nifedipin is strongly discouraged.				

Cerebrovasc Dis 2003;16:311–337



July (2 of 2) 2004 NEUROLOGY 63

Table 9. Suggested antihypertensive treatment in acute ischaemic stroke (modified from Brott et al. [1994] and Ringleb et al. [1998]; availability of substances may vary between countries)

1	Systolic BP 180–220 mm Hg and/or diastolic BP 105–140 mm Hg	do not treat
2	Systolic BP ≥ 220 mm Hg and/or diastolic BP 120–140 mm Hg, on repeated measures	captopril 6.25–12.5 mg p.o./i.m. labetalol 5–20 mg i.v.[1] urapidil 10–50 mg i.v., followed by 4–8 mg/h i.v.[2] clonidine 0.15–0.3 mg i.v. or s.c. dihydralazine 5 mg i.v. plus metoprolol 10 mg
3	Diastolic BP ≥ 140 mm Hg	nitroglycerin 5 mg i.v., followed by 1–4 mg/h i.v. sodium nitroprusside 1–2 mg

BP = Blood pressure.
1 Avoid labetalol in patients with asthma, cardiac failure, severe conduction abnormalities and bradycardia.
2 In patients with unstable conditions and rapidly fluctuating BP, alternating urapidil/labetalol and arterenol may be used.

CONTROLUL GLICEMIEI

- Hiperglicemia ageavează prognosticul bolnavului cu AVC
- Glicemie> 10 mmol/l necesită insulinoterapie imediată
- Soluţii de repletie în terapia imediată: nu vor conţine glucoză!
- ATENŢIE: hipoglicemia poate avea simptomatologie de AVC acut!

CME

Use of antihypertensive agents in the management of patients with acute ischemic stroke

P.K. Lindenauer, MD, MSc; M.C. Mathew, MD, MPH; T.S. Ntuli, MPH; P.S. Pekow, PhD; J. Fitzgerald, MS, RN; and E.M. Benjamin, MD

NEUROLOGY 2004;63:318–323

BALANŢA HIDROELECTROLITICĂ

- NORMOVOLEMIE!!! Pt a menţine presiunile de perfuzie: cerebrală şi renală
- Balanţă uşor negativă în prezenţa edemului cerebral
- Nu soluţii hipotone! ATENŢIE: glucoza 5%!
- Dozare eletroliţi sanguini zilnic!

European Stroke Initiative Recommendations for Stroke Management – Update 2003

Recommendations (All Level IV)

1 Continuous cardiac monitoring is recommended in the first 48 h of stroke onset particularly in patients with: (a) previous known cardiac disease, (b) history of arrhythmias, (c) unstable blood pressure, (d) clinical signs/symptoms of heart failure, (e) abnormal baseline ECG and (f) infarct involving the insular cortex.
2 Oxygenation monitoring with pulse oxymetry is recommended.
10 Avoid and treat hypotension particularly in unstable patients by administering adequate amounts of fluids (see further on) and, when required, volume expanders and/or catecholamines (epinephrine 0.1–2 mg/h plus dobutamine 5–30 mg/h).
11 Monitoring of serum glucose levels is recommended, particularly in known diabetic patients.
12 Glucose solutions are not recommended due to the detrimental effects of hyperglycaemia.
13 Treatment of serum glucose levels > 10 mmol/l with insulin titration is recommended.
14 Immediate correction of hypoglycaemia is recommended by intravenous dextrose bolus or infusion of 10–20% glucose.
15 Treatment of body temperature ≥ 37.5 °C is recommended.
16 In case of fever, the search of a possible infection (site and actiology) is recommended, in order to start tailored antibiotic treatment.
17 Antibiotic, antimycetic or antiviral prophylaxis is not recommended in immunocompetent patients.
18 Monitoring and correction of electrolyte and fluid disturbances are recommended.
19 Hypotonic solutions (NaCl 0.45% or glucose 5%) are contra-indicated due to the risk of brain oedema increase consequent to reduction of plasma osmolality.

European Stroke Initiative Recommendations for Stroke Management – Update 2003

Recommendations

1 Low-dose subcutaneous heparin or low-molecular-weight heparins should only be considered for patients at high risk of DVT or pulmonary embolism (level II).
2 The incidence of venous thromboembolism may be reduced through early re-hydration and mobilisation and graded compression stockings (level IV).
3 Infections after stroke should be treated with appropriate antibiotics.
4 Aspiration pneumonia may not be prevented by nasogastric feeding (level IV).
5 Early mobilisation is helpful to prevent numerous complications after stroke including aspiration pneumonia, DVT and decubital ulcers (level IV).
6 Administration of anticonvulsants to prevent recurrent seizures is strongly recommended (level III).
7 Prophylactic administration of anticonvulsants to patients with recent stroke who have not had seizures is not recommended level IV).

European Stroke Initiative Recommendations for Stroke Management – Update 2003

Recommendations

1 Intravenous rtPA (0.9 mg/kg, maximum 90 mg), with 10% of the dose given as a bolus followed by an infusion lasting 60 min, is the recommended treatment within 3 h of onset of ischaemic stroke (level I).
2 The benefit from the use of intravenous rtPA for acute ischaemic stroke beyond 3 h after onset of the symptoms is smaller, but present up to 4.5 h (level I).
3 Intravenous rtPA is not recommended when the time of onset of stroke cannot be ascertained reliably; this includes persons whose strokes are recognised upon awakening (level IV).
4 Intravenous administration of streptokinase is dangerous and not indicated for the management of persons with ischaemic stroke (level I).
5 Data on the efficacy and safety of any other intravenously administered thrombolytic drugs are not available to provide a recommendation.
6 Intra-arterial treatment of acute MCA occlusion in a 6-hour time window using pro-urokinase results in a significantly improved outcome (level II).
7 Acute basilar occlusion may be treated with intra-arterial therapy in selected centres in an institutional protocol as experimental therapy or within a multicentre clinical trial (level IV).
8 Ancrod cannot presently be recommended for use in acute ischaemic stroke outside the setting of clinical trials.

European Stroke Initiative Recommendations for Stroke Management – Update 2003

Recommendations

1 Osmotherapy is recommended for patients whose condition is deteriorating secondary to increased ICP, including those with herniation syndromes (level IV).
2 Ventriculostomy or surgical decompression and evacuation of large cerebellar infarctions that compress the brain stem is justified (level III).
3 Surgical decompression and evacuation of a large hemispheric infarction can be a life-saving measure and survivors may have a residual neurological deficit that allows an independent life (level III).

European Stroke Initiative Recommendations for Stroke Management – Update 2003

Table 10. Possible remaining indications for heparin treatment after stroke

1 Stroke due to cardiac emboli with high risk of re-embolisation (artificial valves, AF, MI with mural thrombi, left atrial thrombosis)
2 Coagulopathies such as protein C and S deficiency, APC resistance
3 Symptomatic dissection of extracranial arteries
4 Symptomatic extracranial and intracranial stenoses
  a Symptomatic ICS prior to operation
  b Crescendo TIAs or stroke in progression
5 Sinus-venous thrombosis

APC = Activated protein C.