



Frequent causes of stroke

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Aims

To

- know the difference between risk factor and etiology
- build up advanced knowledge on the three most frequent aetiologies of ischaemic stroke



Risk factor

Definition: A risk factor is any characteristic of a person (such as age), a situation (such as the severity of a traumatic event), or a person's environment (such as family life) that increases the likelihood that that person will eventually develop a disorder.

Or

a characteristic statistically associated with, although not necessarily causally related to, an increased risk of morbidity or mortality, *e.g.*, smoking as a risk factor for heart disease.



Results from "Google search" for risk factor

Prevalence (PV) und relative risks (RR) for modifiable risk factors for stroke

RF	PV(%)	RR
Diabetes mellitus	7.3	1.8-6.0
Dyslipidämia	25	- 2.0
Smoking	25	1.8
Alcohol abuse	5-7	1.6
Atherosclerotic carotid art. disease	2-8	2.0
Coronary heart disease	8.4	1.73
Hypertension (age!)	20-60	4-1 !
Atrial fibrillation (age!)	0.5-8.8	2.6-4.5
Hypercoagulability	-27	1.9
Sickel cell disease	<0.25	200-400



Patient, 62-jährig

JL: am Morgen beim Zähneputzen plötzlicher Schwindel, Zusammensacken

RF: arterielle Hypertonie

SA: intermittierend unregelmässiger Puls

FA: Mutter Status nach zerebrovaskulärem Insult

Medikamente: Indapamid, Acetylsalicylsäure, Fludapamid



Patient 62-jährig

Neurostatus (H +90Min.):

Déviaton conjugée nach rechts

Fazialisparese links

Hypästhesie, Plegie der oberen und unteren Extremität links

Hemianopsie nach links

Anosognosie

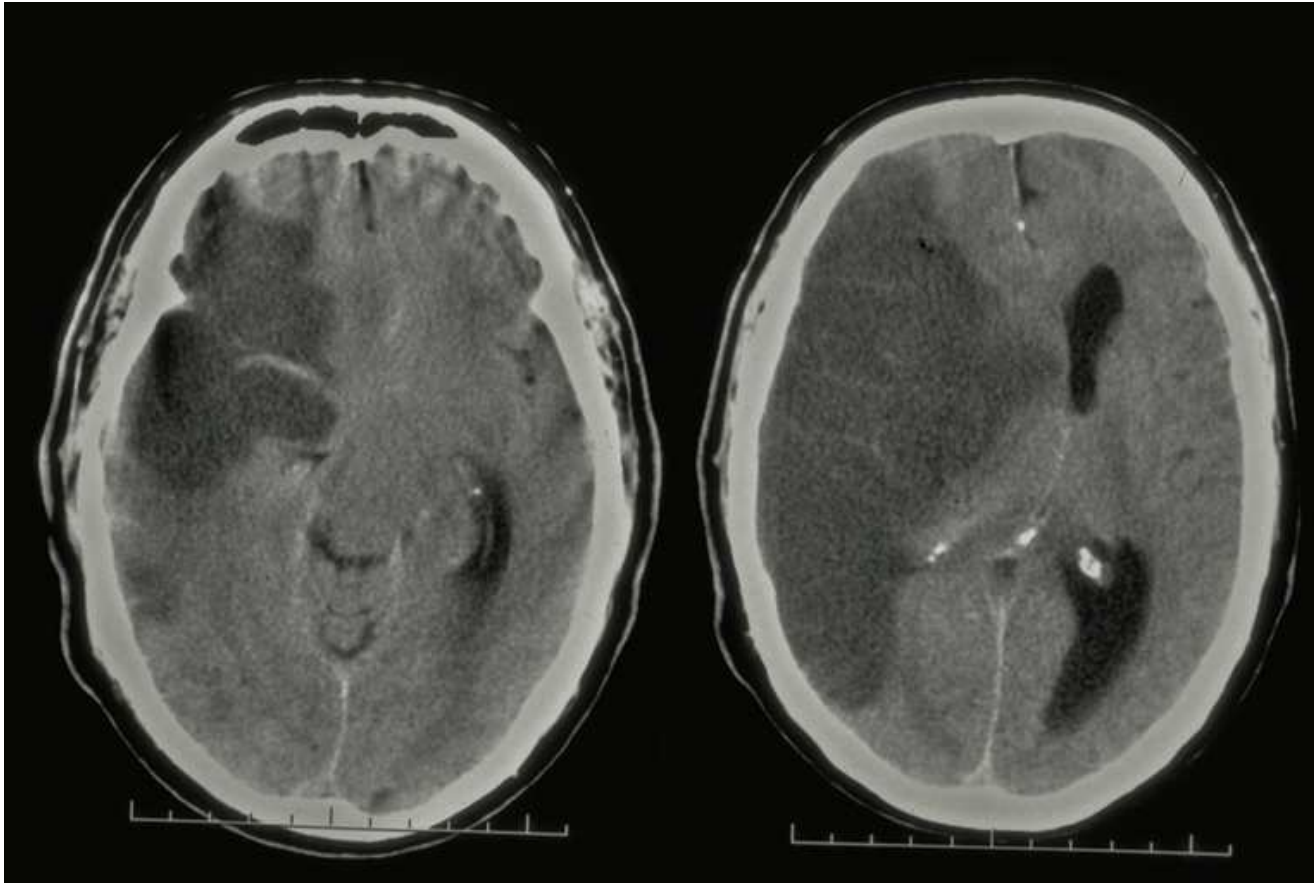
NIHSS: >20



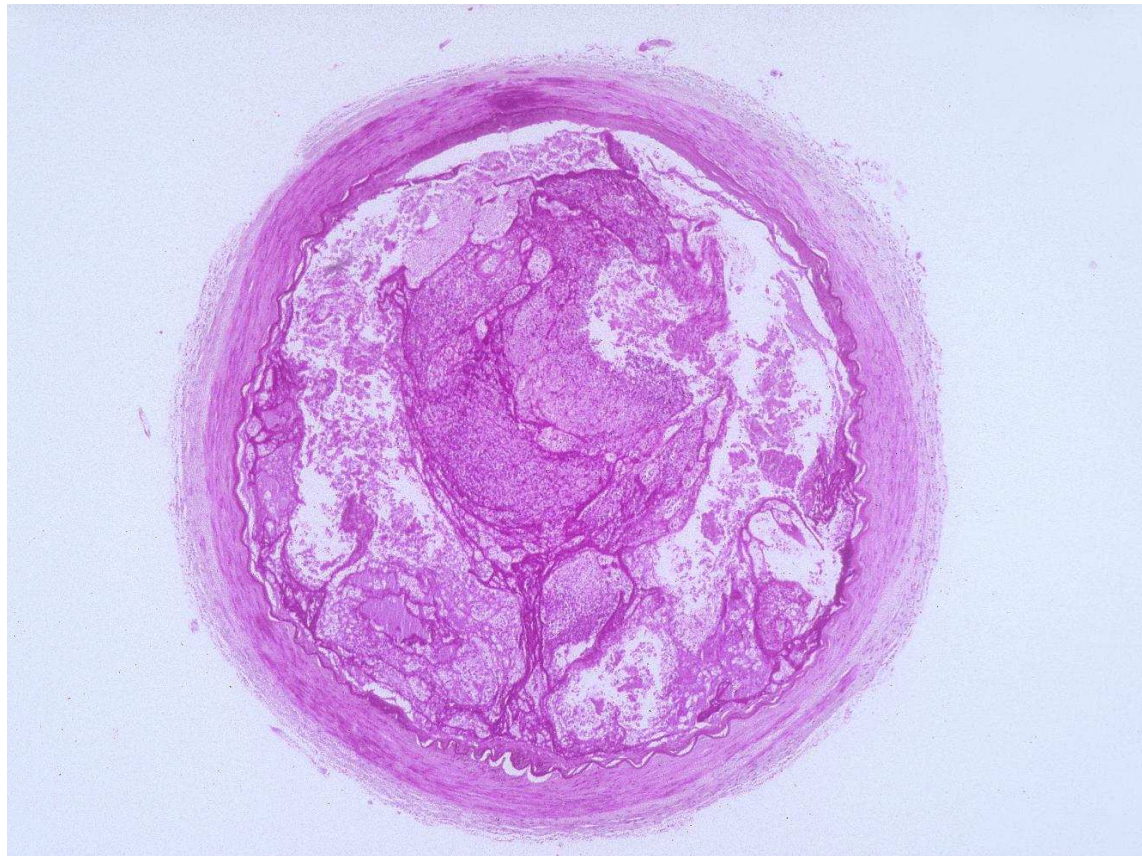
Acute occlusion of the middle cerebral artery (M1)



Subacute occlusion of the middle cerebral artery after 48 hours



Embololic occlusion of the middle cerebral artery (Neuropathologie Basel, AR, MT)



«TOAST» criteria – «conventional»

- Large-artery atherosclerosis (embolus/thrombosis)*
- Cardioembolism (high-risk/medium-risk)*
- Small-vessel occlusion (lacune)*
- Stroke of other determined etiology*
- Stroke of undetermined etiology
 - a. Two or more causes identified
 - b. Negative evaluation
 - c. Incomplete evaluation

ASCO criteria – «new»

A: for **a**therosclerosis

S: for **s**mall vessel disease

C: for **c**ardiac source

O: for **o**ther cause

graded 1, 2, or 3.

1 definitely a potential cause of the index stroke

2 causality uncertain

3 unlikely a direct cause of the index stroke

Level of evidence: A(strong),B,C (weak)

Lit: Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Hennerici MG. New approach to stroke subtyping: the A-S-C-O (phenotypic) classification of stroke. Cerebrovasc Dis. 2009;27(5):502-8.

Arterial suply of the brain

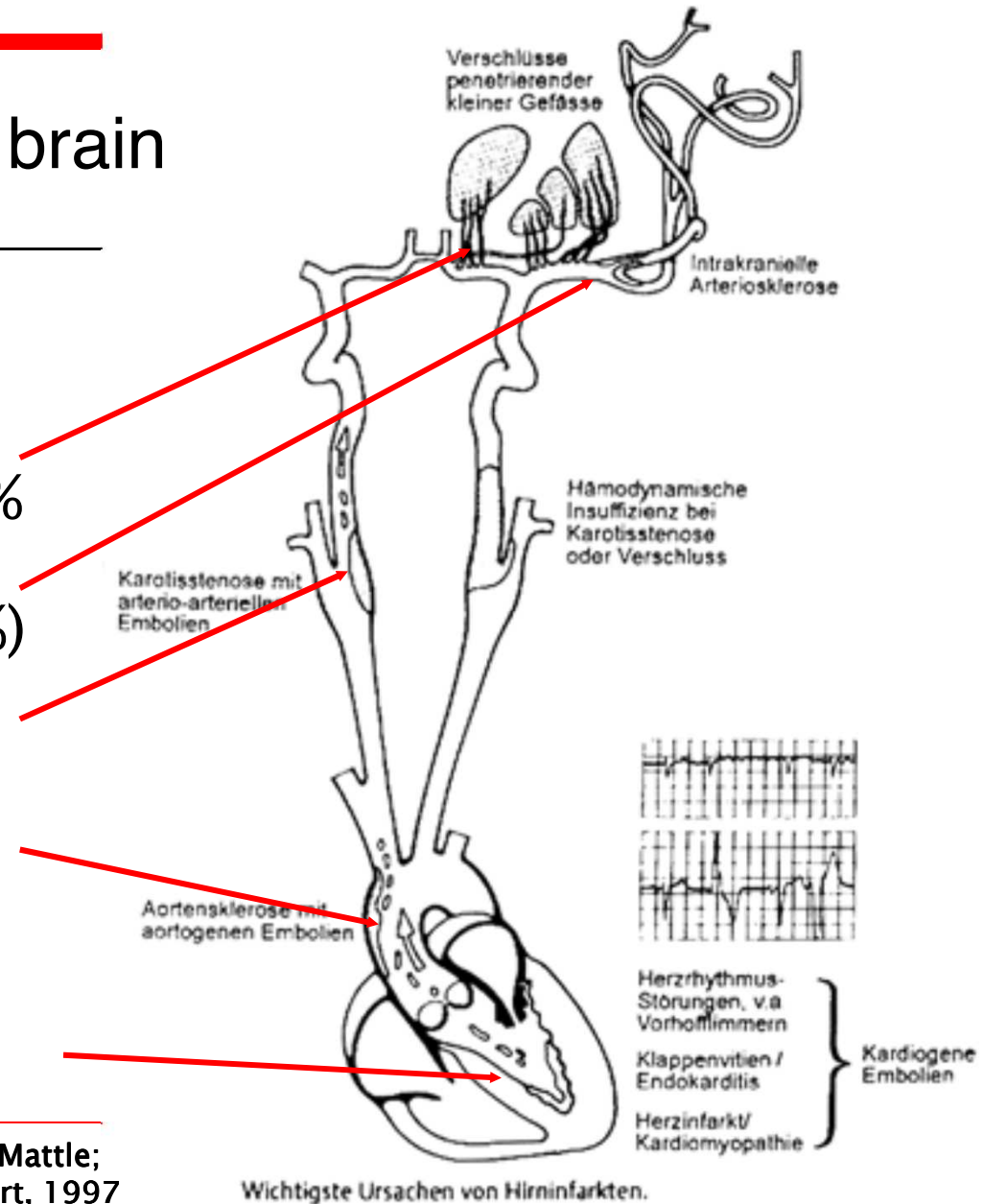
Small vessel dis. ca.30%

atherothrombosis(<5%)

Throboemboli from
arteriosclerotic dis.

Cardiogenic embolism
30%

© M. Mumenthaler, H. Mattle;
Thieme Verlag, Stuttgart, 1997



Case I: male 84 years

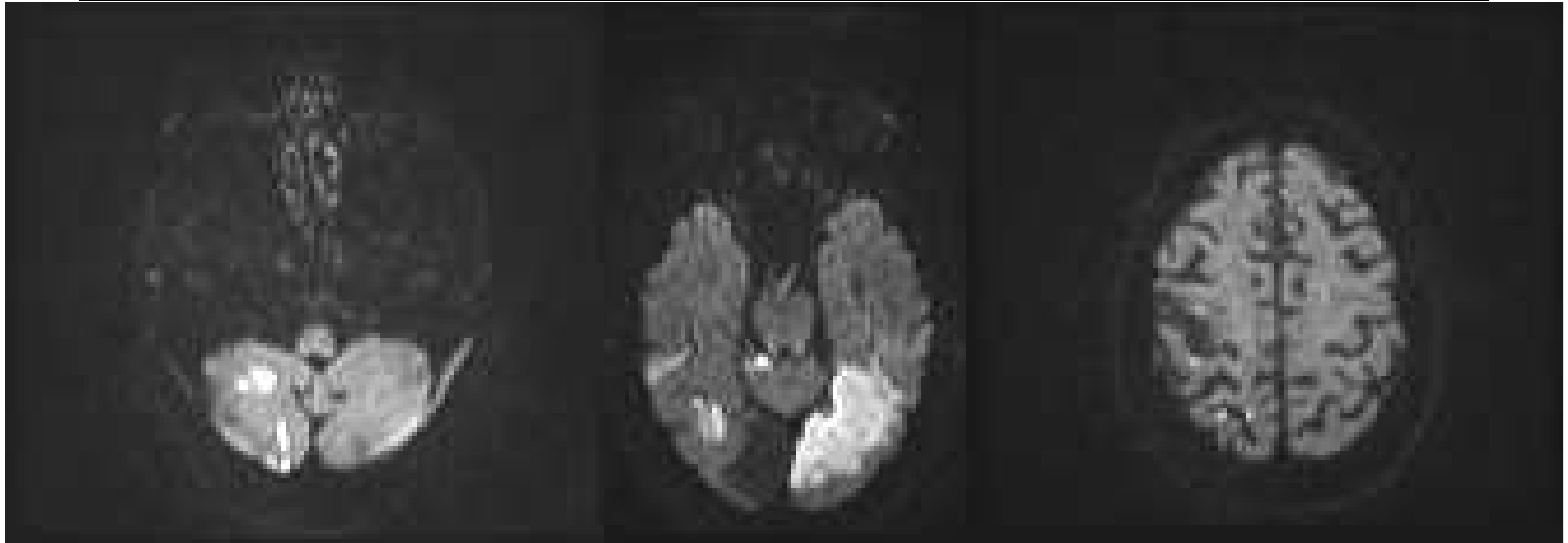
Case history: Dizziness, facial palsy (bilateral), dysarthria, sudden blindness (left eye; right eye blind before stroke)

NIHSS on admission: 8 points

- 1a. Level of Consciousness: alert; 0 points
- 1b. LOC questions: answers both questions correctly; 0 points
- 1c. LOC commands: performs both tasks correctly; 0 points
- 2. Best gaze: **partial gaze palsy**; 1 point
- 3. Visual: **bilateral hemianopsia** (cortical blindness); 3 points
- 4. Facial Palsy: normal; 0 points
- 5a. Motor arm right: **drifts down before 10 seconds**; 1 point
- 5b. Motor arm left: no drift; 0 points;
- 6a. Motor leg right: no drift; 0 points
- 6b. Motor leg left: no drift; 0 points
- 7. Limb ataxia: **present in right arm**; 1 point
- 8. Sensory: normal; 0 points
- 9. Best language: no aphasia; 0 points
- 10. Dysarthria: **severe dysarthria**; 2 points
- 11. Extinction and Inattention: no abnormality; 0 points



Case I: male 84 years



MRI DWI

A3 S 3 C1 O3

Holter-ECG showed paroxysmal atrial fibrillation



ASCO: Cardiogenic stroke

Grades for cardioembolism (C)

1. Definitely a potential cause of the index stroke	Cardioembolic stroke – demonstration of: (a) Mitral stenosis; (b) Prosthetic heart valve; (c) Myocardial infarction within the past 4 weeks; (d) Mural thrombus in left cavities; (e) Left ventricular aneurysm; (f) Any documented history or permanent or transient atrial fibrillation or flutter with or without spontaneous echo contrast or left atrial thrombus; (g) Sick sinus syndrome; (i) Ejection fraction <35%; (j) Endocarditis; (k) Intracardiac mass; (l) PFO plus in situ thrombosis; (m) PFO plus concomitant PE or DVT preceding the brain infarction.
2. Causality uncertain	(a) PFO and ASA; (b) PFO and concomitant DVT or PE (but not preceding the index stroke); (c) Spontaneous echo contrast; (d) Apical akinesia of the left ventricle and impaired ejection fraction (but >35%); (e) Only suggested by history of myocardial infarction or palpitation and multiple repeated brain infarcts on both sides or in both the anterior and posterior circulation; (f) Only suggested by abdominal CT/MRI or autopsy demonstration of the presence of systemic infarction (e.g. kidney, splenic, mesenteric) or lower limb embolism (in addition to the index stroke).
3. Unlikely a direct cause of index stroke	One of the following abnormalities: PFO, ASA, valvular strands, mitral annulus calcification, calcified aortic valve, nonapical akinesia of the left ventricle.

al

e Unit

Clinical and imaging findings indicating cardioembolic stroke mechanism

- Abrupt onset of stroke symptoms, particularly in AF with lack of preceding TIA and severe first-ever stroke.
- Striking stroke severity in the elderly (NIH-Stroke Scale ≥ 10 ; age ≥ 70 years)
- Previous infarctions in various arterial distributions
- Multiplicity in space ($\frac{1}{4}$ infarct in both the anterior and posterior circulation, or bilateral)
- Multiplicity in time ($\frac{1}{4}$ infarct of different age)
- Other signs of systemic thromboembolism (e.g. edge-shaped infarctions of kidney or spleen; Osler splits; Blue toe-syndrome)
- Territorial distribution of the infarcts involving cortex, or subcortical 'large lenticulostriate infarct' (see Figures 1 and 2)
- Hyperdense MCA sign (as long as without severe ipsilateral internal carotid stenosis)
- Rapid recanalization of occluded major brain artery (to be evaluated by repetitive neurovascular ultrasound)

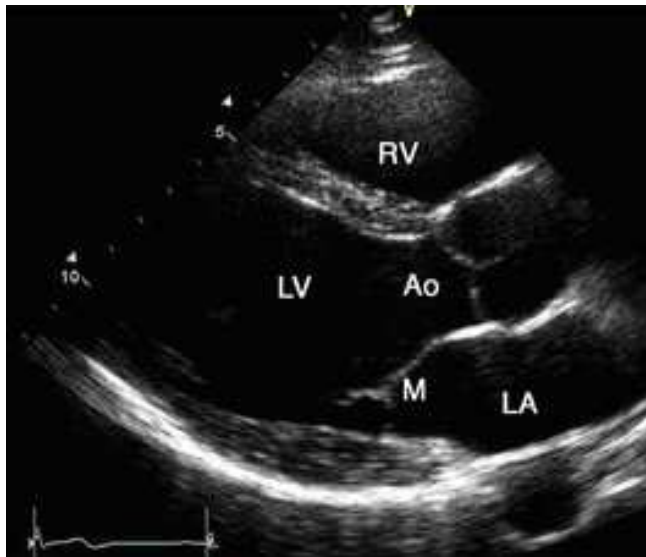


Cardiac evaluation 1



European Journal of Echocardiography (2010) 11, 461–476
doi:10.1093/ejehocard/jeq045

RECOMMENDATIONS



Recommendations for echocardiography use in the diagnosis and management of cardiac sources of embolism

European Association of Echocardiography (EAE) (a registered branch of the ESC)

Mauro Pepi^{1*}, Arturo Evangelista², Petros Nihoyannopoulos³, Frank A. Flachskampf⁴, George Athanassopoulos⁵, Paolo Colonna⁶, Gilbert Habib⁷, E. Bernd Ringelstein⁸, Rosa Sicari⁹, and Jose Luis Zamorano¹⁰ on behalf of the European Association of Echocardiography



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Potential cardioembolic sources

Major risk sources

Atrial fibrillation
Recent myocardial infarction
Previous myocardial infarction (LV aneurysm)
Cardiomyopathies
Cardiac masses
 Intracardiac thrombus
 Intracardiac tumours
 Fibroelastoma
 Marantic vegetations
Rheumatic valve disease (mitral stenosis)
Aortic arch atheromatous plaques
Endocarditis
Mechanical valve prosthesis

Minor or unclear risk sources

Mitral valve prolapse
Mitral annulus calcification

Calcified aortic stenosis

Atrial septal aneurysm

Patent foramen ovale

Giant Lambl's excrescences



Transthoracal echocardiography in myocardial infarction

- single most useful diagnostic test in the evaluation of patients following
- acute myocardial infarction
- the extent of LV and right ventricular systolic dysfunction
- status of heart valves, and pericardium
- identifying LV thrombus
- and the addition of contrast may increase diagnostic accuracy.
- Note: TOE has little to offer in the detection of LV thrombus



Echocardiographic predictors of embolic risk in AF

TTE is clinically indicated in patients with AF

- to detect an underlying pathology affecting management or therapeutic decisions (ischaemic heart disease, valvulopathy, cardiomyopathy, or reduced ventricular function);
- before cardioversion of atrial flutter (since this arrhythmia is often a marker of severe heart disease);
- to indicate, guide and follow-up invasive surgical procedures, such as substrate AF ablation (RF or surgical) or LAA closure.

The addition of TOE in patients with AF is indicated:

- in guiding short-term anticoagulated cardioversion.
 - in clinically selected cases (pre-ablation of AF and pre-closure LAA, suspected aortic arch atherosclerosis, recurrence of embolism during correct anticoagulation);
 - in determining the risk for future embolism (study of LAA function)
-

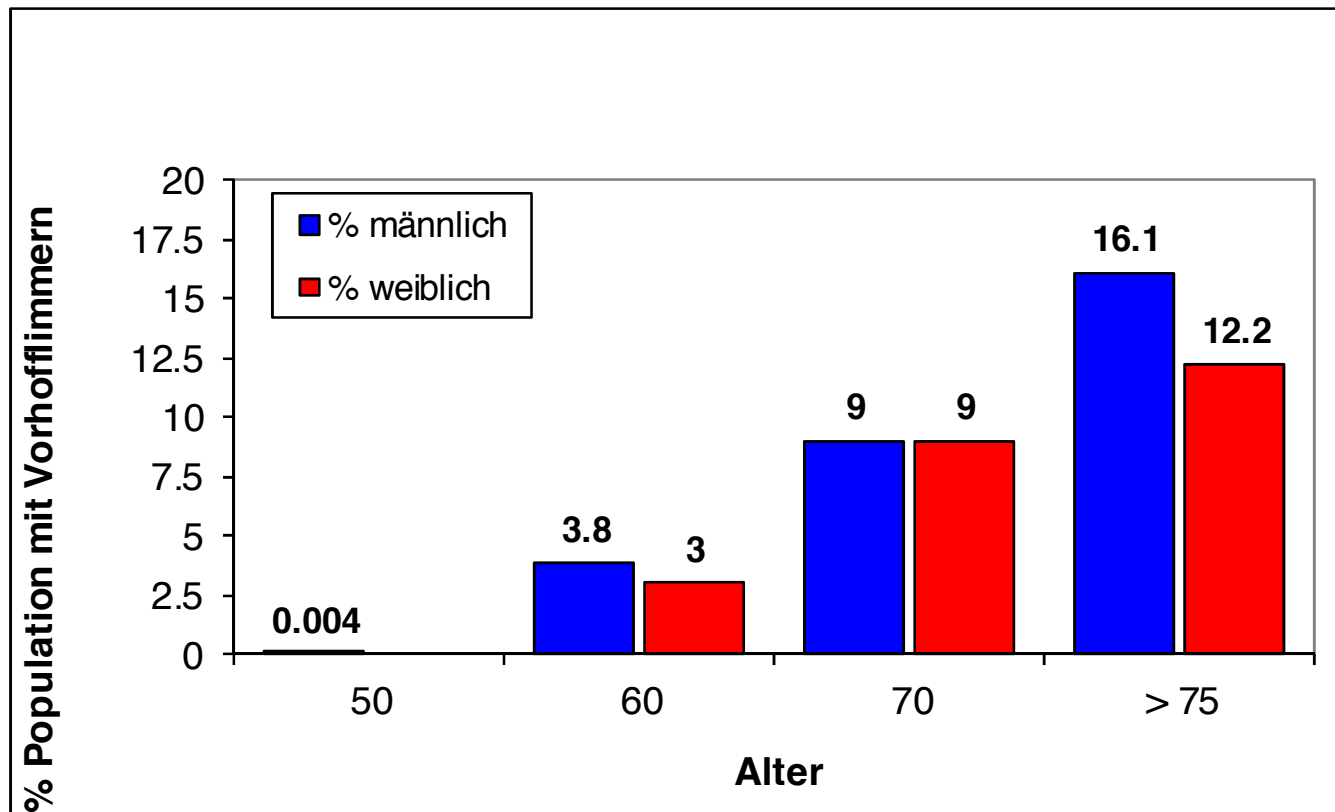


Transoesophageal echocardiography PFO

- Paradoxical embolism through a PFO is a rare cause
- In the absence of a demonstrable elevation of right atrial pressure, caution should be exercised to incriminate PFO in unexplained neurological events.
- In absence of more likely causes, paradoxical embolism through a PFO may be assumed in the following circumstances:
 - Young age. Over the age of 55 years, the likelihood of atherosclerotic disease or occult paroxysmal AF as a source of embolism is far higher than that of paradoxical embolism through a PFO.
 - The presence of an atrial septal aneurysm additional to a PFO is associated with a marked increase in recurrent unexplained neurologic events.
 - Large provokable right-to-left shunts have shown a stronger association with unexplained neurological events than small. More than 20 bubbles have been cited to indicate a 'large PFO'.

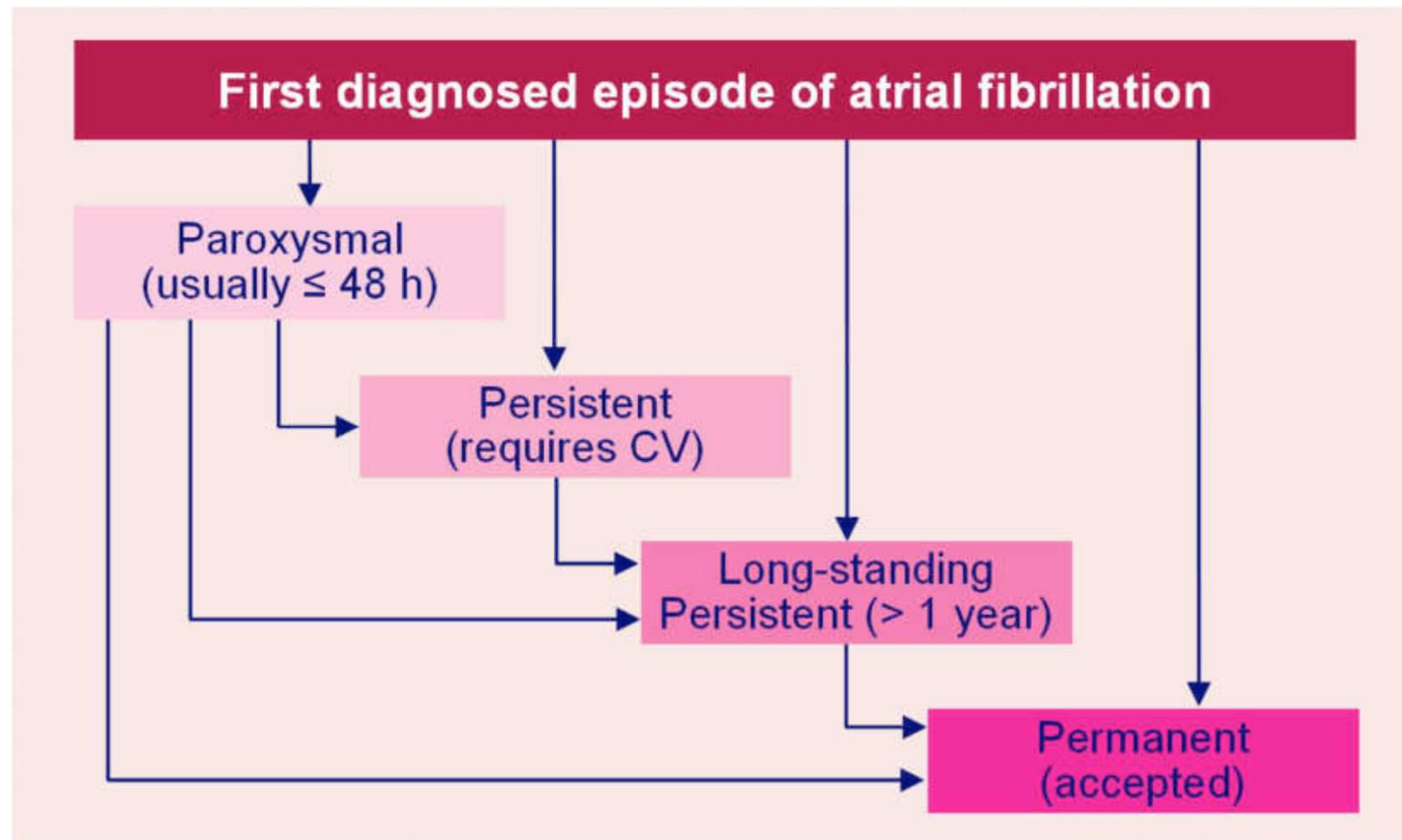


Prevalence of atrial fibrillation and age



Ezekowitz MD, Cohen IS, Gurlick CG. The Left Atrium In: Ezekowitz MD, ed.
Systemic Cardiac Embolism. New York: Marcel Dekker 1994:294

AF classification



AF – CHA₂DS₂VASc–Score

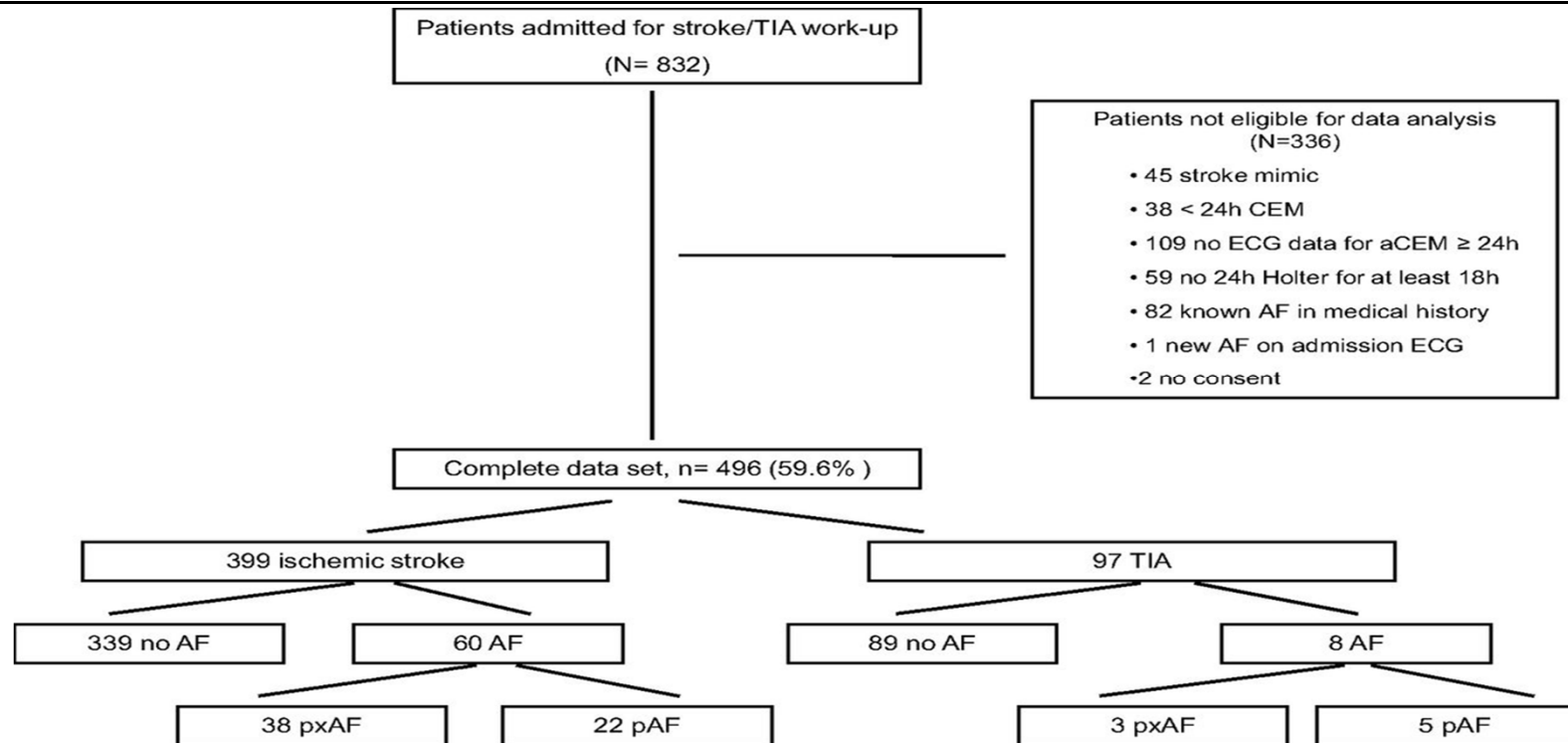
Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75 ans	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease*	1
Age 65-74	1
Sex category [i.e. femal sex]	1
Maximum score	9

AF – CHA₂DS₂VASc–Score

CHA ₂ DS ₂ -VASc score	Patients (n = 7329)	Adjusted stroke rate (%/y)
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

Role of the electrocardiogramm: Continuous Stroke Unit

Electrocardiographic Monitoring Versus 24-Hour Holter Electrocardiography for Detection of Paroxysmal Atrial Fibrillation After Stroke



Paroxysmal AF was documented in 41 of 496 patients (8.3%). Of these, Holter detected pxAF in 34.1%; CEM in 65.9%; automated CEM in 92.7%.



Case II: female 78 years

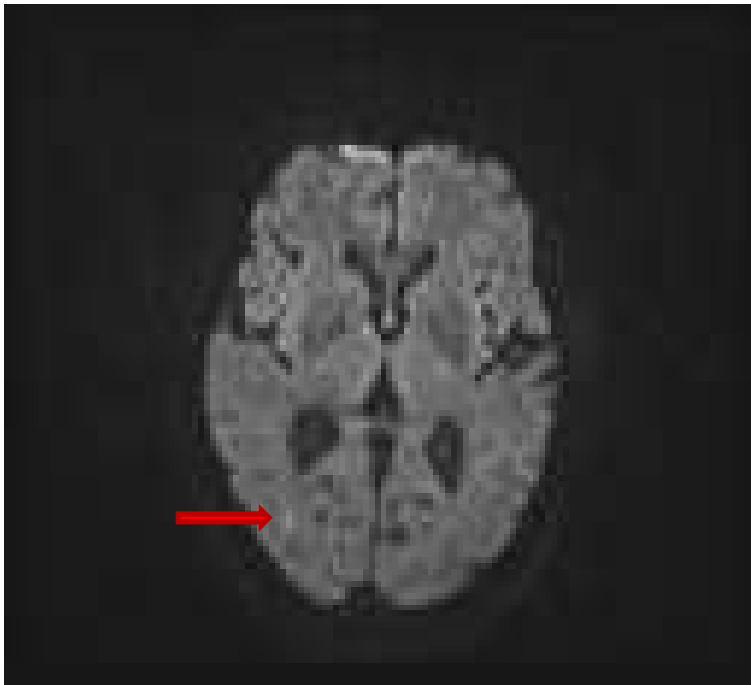
Case history: During lunch patient stops speaking, tries to speak but without forming words, comprehension of simple commands, no paresis, no decreased level of consciousness, LH

NIHSS on admission: 4 points

- 1a. Level of Consciousness: alert; 0 points
- 1b. LOC questions: **answers neither questions correctly**; 2 points
- 1c. LOC commands: performs both tasks correctly; 0 points
- 2. Best gaze: normal; 0 points
- 3. Visual: no visual loss; 0 points
- 4. Facial Palsy: normal; 0 points
- 5a. Motor arm right: no drift; 0 points
- 5b. Motor arm left: no drift; 0 points;
- 6a. Motor leg right: no drift; 0 points
- 6b. Motor leg left: no drift; 0 points
- 7. Limb ataxia: absent; 0 points
- 8. Sensory: normal; 0 points
- 9. Best language: **severe aphasia**; 2 points
- 10. Dysarthria: normal; 0 points
- 11. Extinction and Inattention: no abnormality; 0 points



Case II: female 66 years



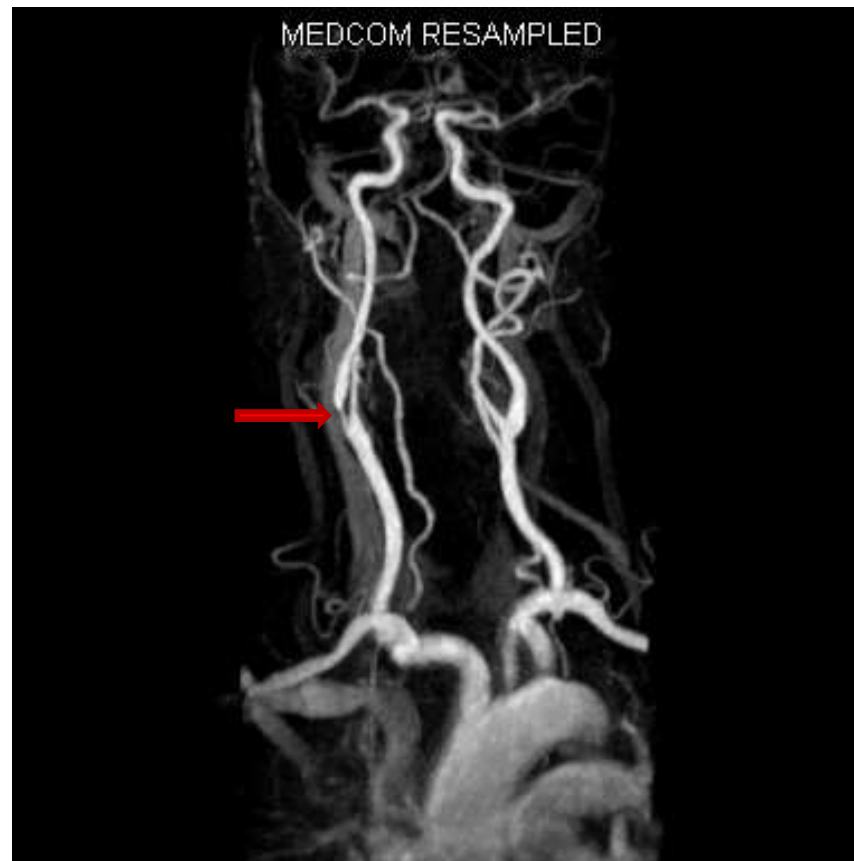
MRI DWI



MRI ADC

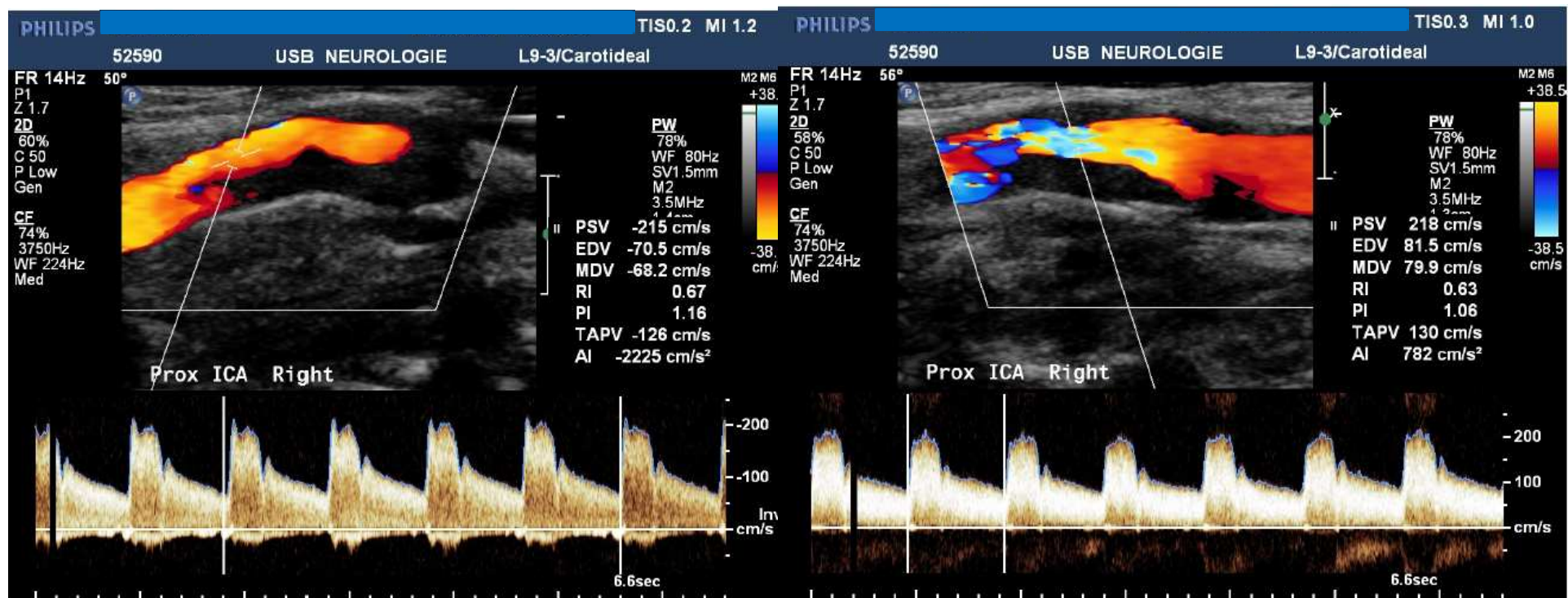


Case II: female 66 years



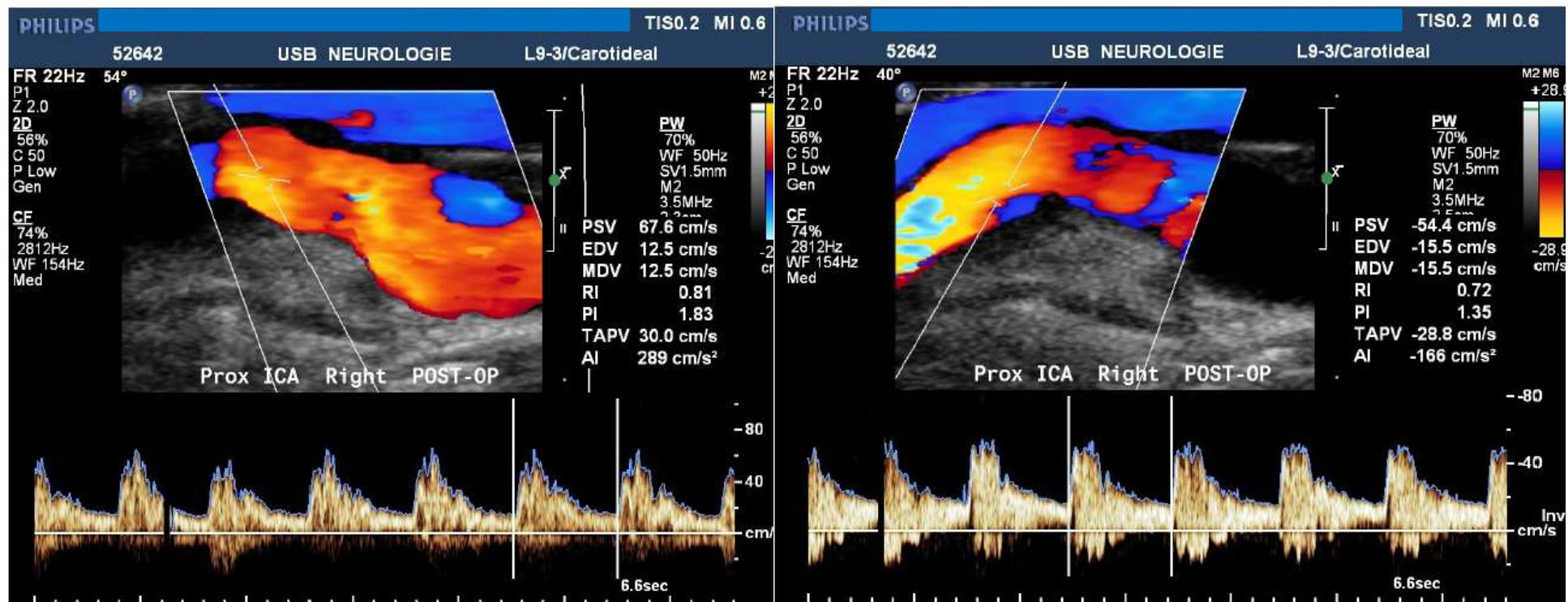
MRI Angio

Case II: female 66 years



A1 S3 C3 O3

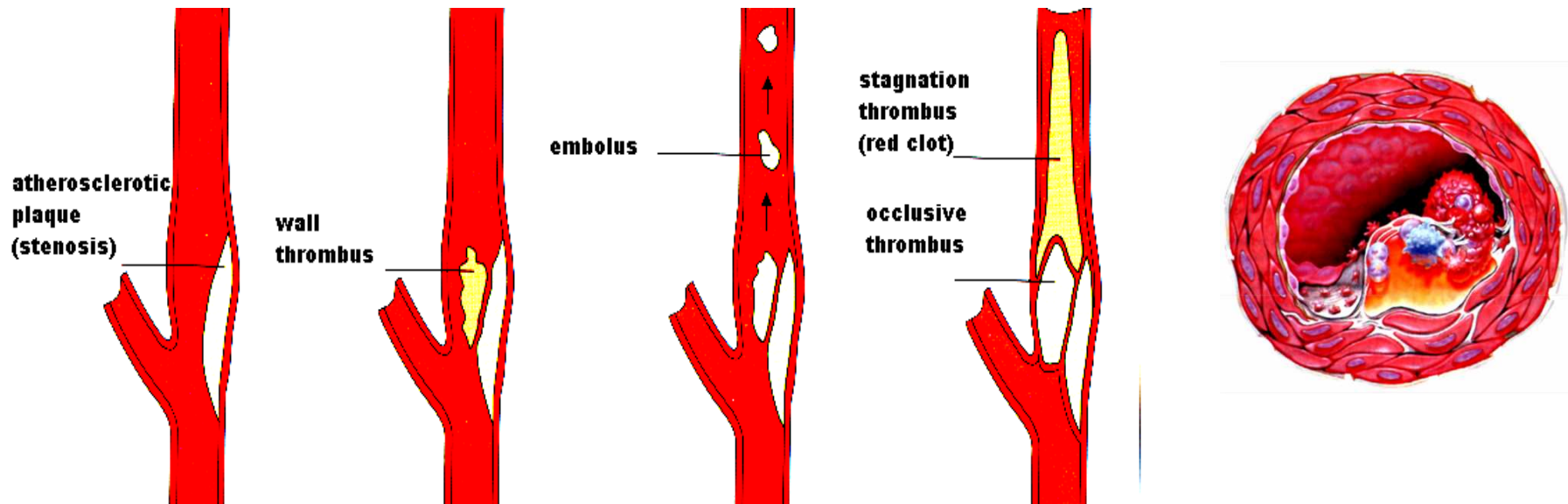
Case II: female 66 years



Post-OP

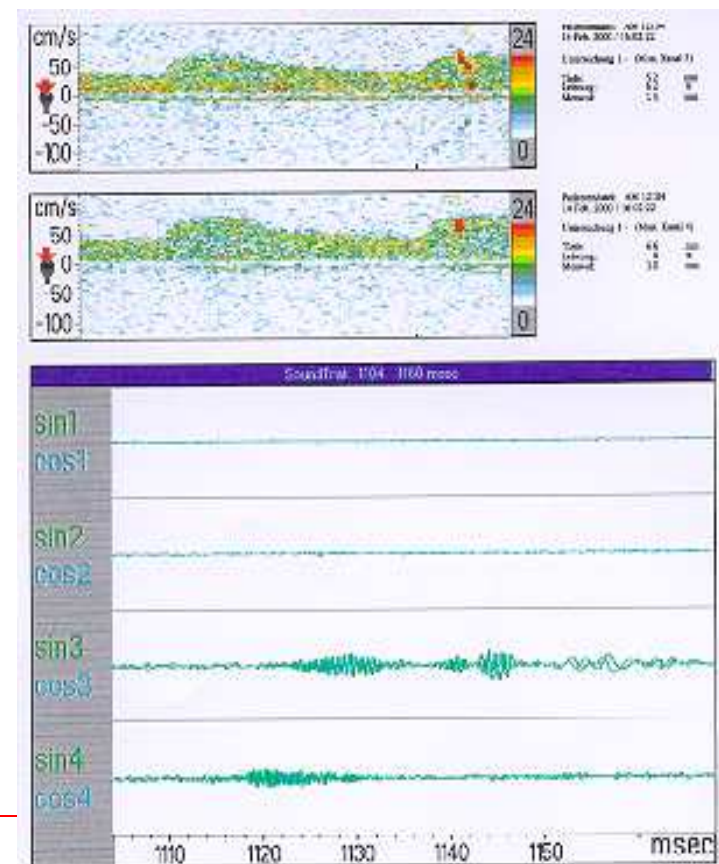
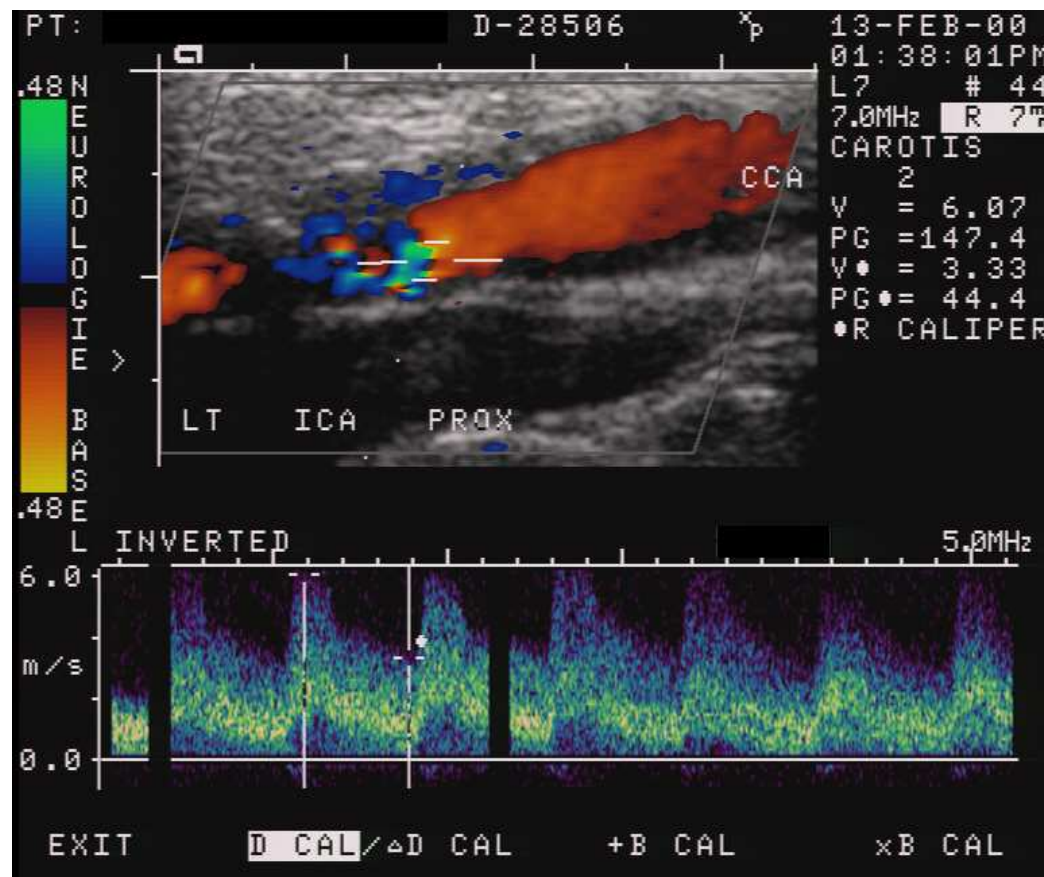


Carotid artery arteriosclerosis



Mostly extracranial!

Symptomatic carotid disease with high grade stenosis – emboli detection



ASCO Arteriosclerotic vessel disease

Grades for atherothrombosis (A)

1. Definitely a potential cause of the index stroke	Atherothrombotic stroke defined as: (a) Patients with any atherosclerotic stenosis 70–99% in an intra-/or extracranial artery supplying the ischemic field diagnosed by level A or B evidence; or (b) Any atherosclerotic stenosis <70% in an intra-/or extracranial artery supplying the ischemic field with attached luminal thrombus diagnosed by level A or B evidence; or (c) A mobile thrombus in the aortic arch; or (d) Occlusion with imaging evidence of atherosclerosis in an intra-/or extracranial artery supplying the ischemic field.
2. Causality uncertain	(a) Patients with any atherosclerotic stenosis 70–99% in an intra-/or extracranial artery supplying the ischemic field diagnosed by level C evidence; or (b) Any atherosclerotic stenosis <70% in an intra-/or extracranial artery supplying the ischemic field with attached luminal thrombus diagnosed by level C evidence; or (c) Aortic arch plaques >4 mm in thickness without a mobile component.
3. Unlikely a direct cause of index stroke (but disease is present)	(a) Presence of carotid or vertebral artery plaque without stenosis; or (b) Aortic arch plaque <4 mm; or (c) Stenosis (any degree) in a brain artery, contralateral to the brain infarction or in the opposite circulation (either posterior or anterior circulation); or (d) History of myocardial infarction or coronary revascularization or peripheral arterial disease.

Lit: Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Hennerici MG. New approach to stroke subtyping: the A-S-C-O (phenotypic) classification of stroke. Cerebrovasc Dis. 2009;27(5):502-8.

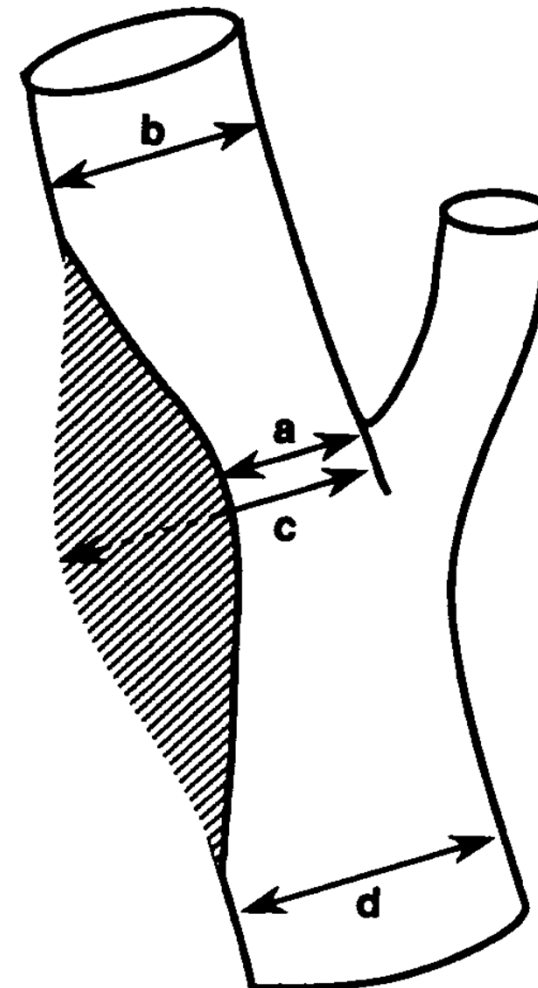
Elevated risk of cerebral embolism in carotid disease

Three main features

- Degree of stenoses
- Ulceration
- Intraluminal Thrombus formation

a - d

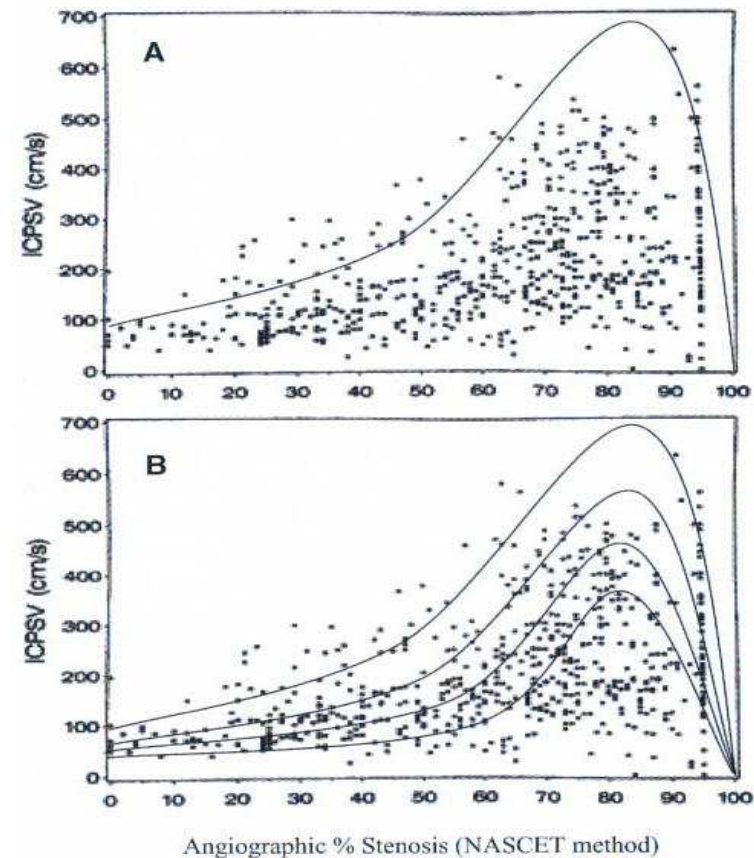
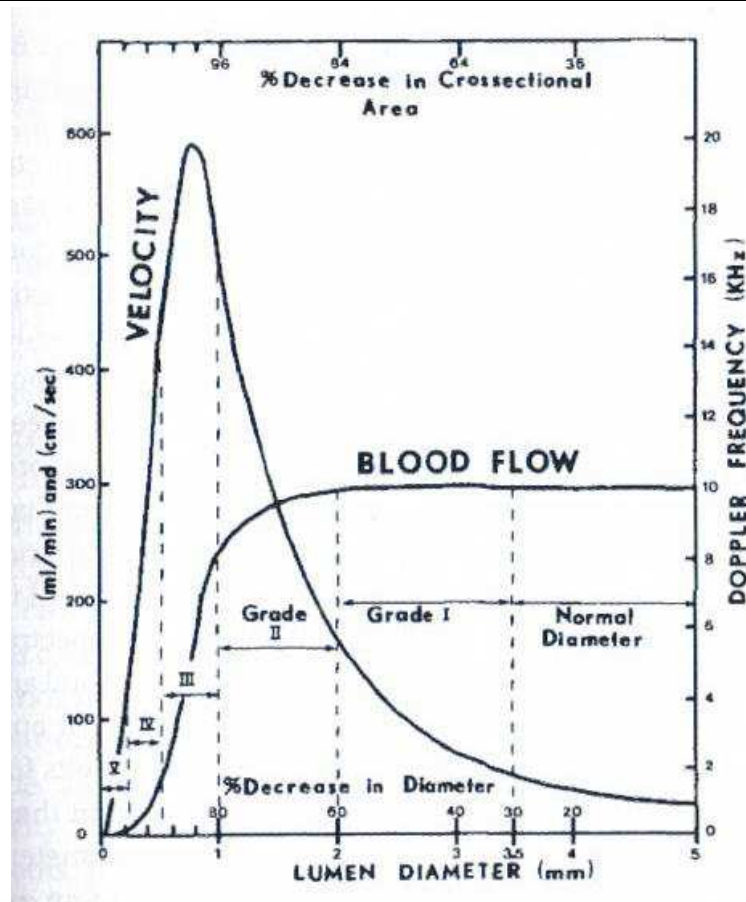
$$\% \text{Stenose} = (1 - S/N) \times 100$$



Ätsspital

Neurologische Klinik & Stroke Unit

Stenosegrad und Blutströmungs-geschwindigkeit „Spencerkurve“ und die „Realität“



Lit.: Spencer et al., Stroke 1979;10:326

Lit.: Eliasiw et al., Stroke 1995;27:1747 (Nascet)

Grading carotid stenosis

> 50%

PSV >120-125 cm/sec

Sens. 75-96%, Spez. 68-94%

>70%

PSV > 210 cm/sec

> 80%

(PSV >> 250 cm/sec)

EDV >105-135 cm/sec

Sens. 72-90%, Spez. 71-99%



Lit.: De Bray, Consensus, Cerebrovasc Dis 1995;5:414 u.a.

Cardiogenic vs. arteriosclerotic?

aetiology	cardio. n=256	artio. n=113
fractionated paralysis of OE	29%	50%
aphasia	52%	29%
Ataxia	7%	16%
VF disorder	46%	34%

Extinction, sensory symptoms

oculomotoric disorders, dysarthria :

n.s



Timsit Stroke 1992 NINDS

Case III: female 74 years

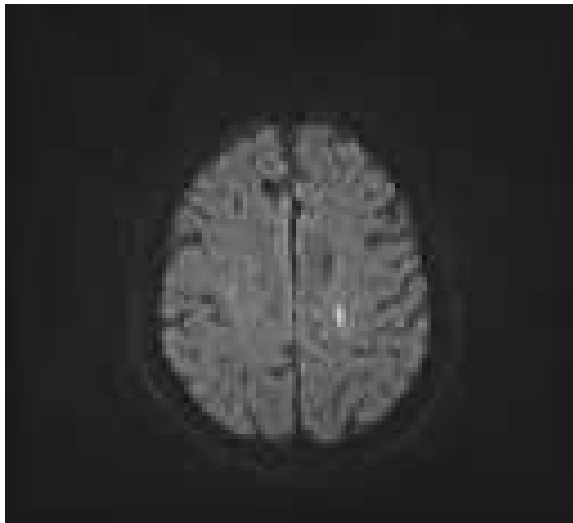
Case history: over two days slightly progressive paresis of the right arm and the right leg

NIHSS on admission: 3 points

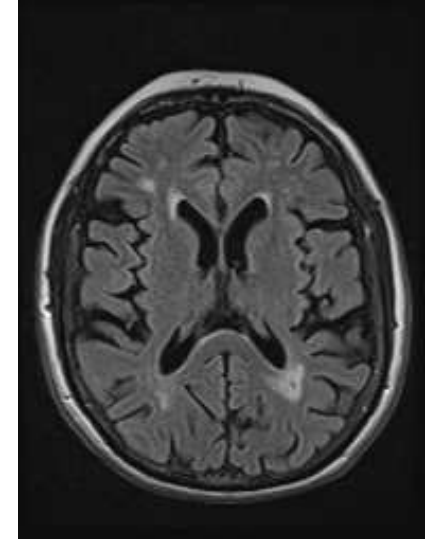
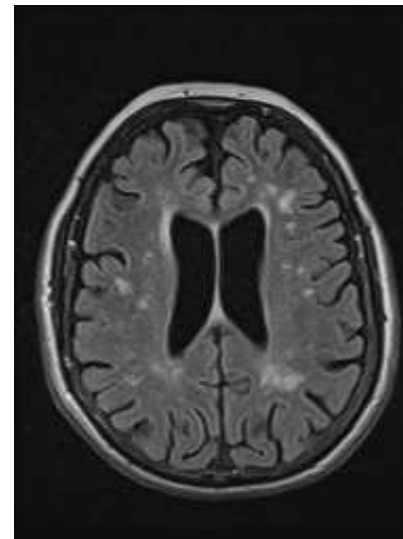
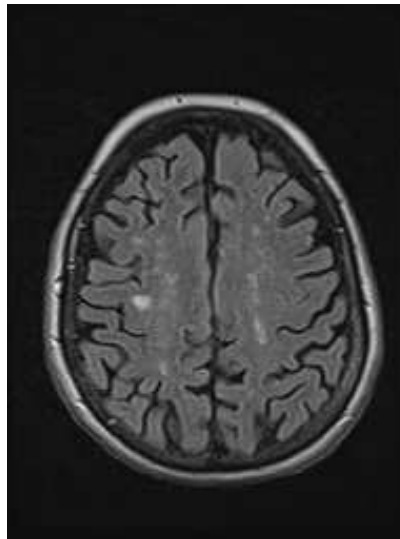
- 1a. Level of Consciousness: alert; 0points
- 1b. LOC questions: answers both questions correctly; 0points
- 1c. LOC commands: performs both tasks correctly; 0 points
- 2. Best gaze: normal; 0 point
- 3. Visual: no visual loss; 0 points
- 4. Facial Palsy: normal; 0 points
- 5a. Motor arm right: **drifts down before 10 seconds**; 1 point
- 5b. Motor arm left: no drift; 0 points;
- 6a. Motor leg right: **some effort against gravity**, leg falls to bed by 5 seconds; 2 points
- 6b. Motor leg left: no drift; 0 points
- 7. Limb ataxia: absent; 0 points
- 8. Sensory: normal; 0 points
- 9. Best language: no aphasia; 0 points
- 10. Dysarthria: normal; 0 points
- 11. Extinction and Inattention: no abnormality; 0 points



Case III: female 74 years



MRI DWI



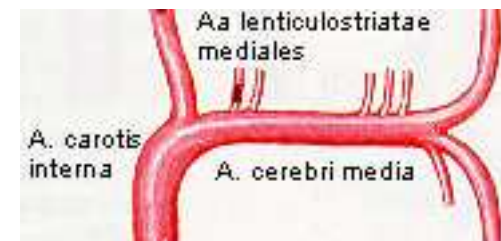
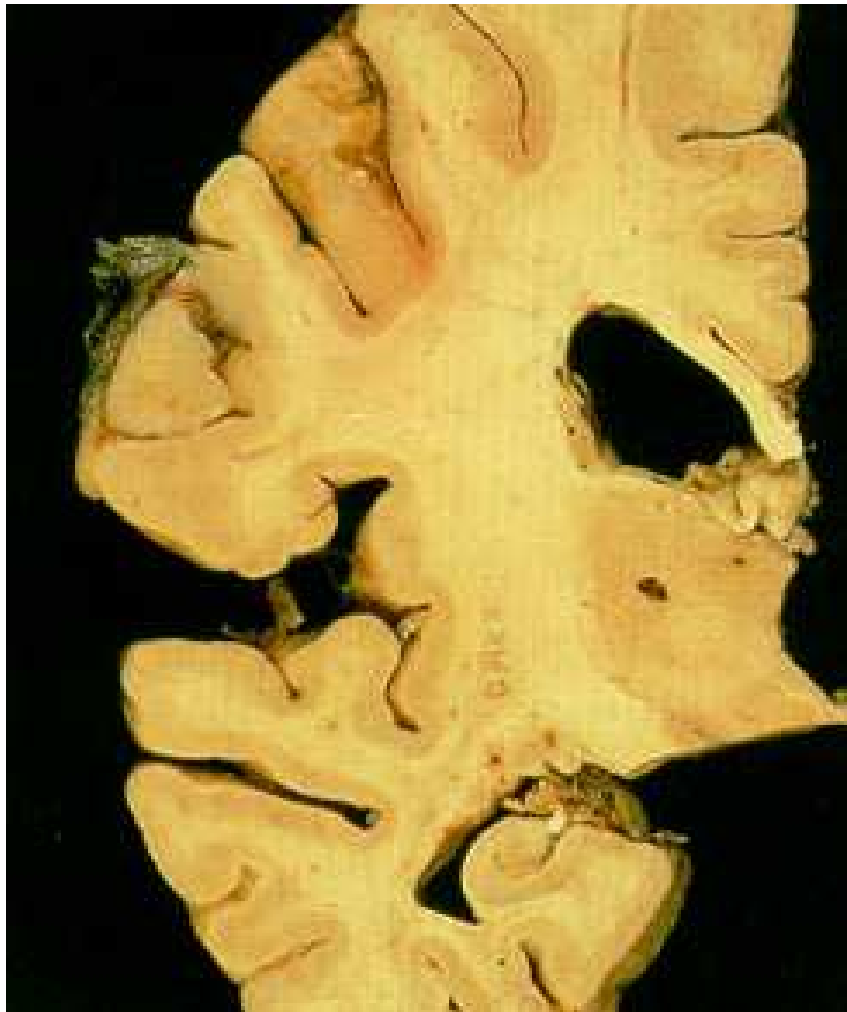
MRI FLAIR

Medical history: metabolic syndrome

A3 S1C3O3



Small vessel disease – deep lacunar infarction



R.N. Rosenberg Atlas of Clinical
Neurology on CD-ROM

Small vessel disease with subcortical arteriolosclerotic encephalopathy (causing dementia)



JJ160139, m 61 jährig, Hypertonie

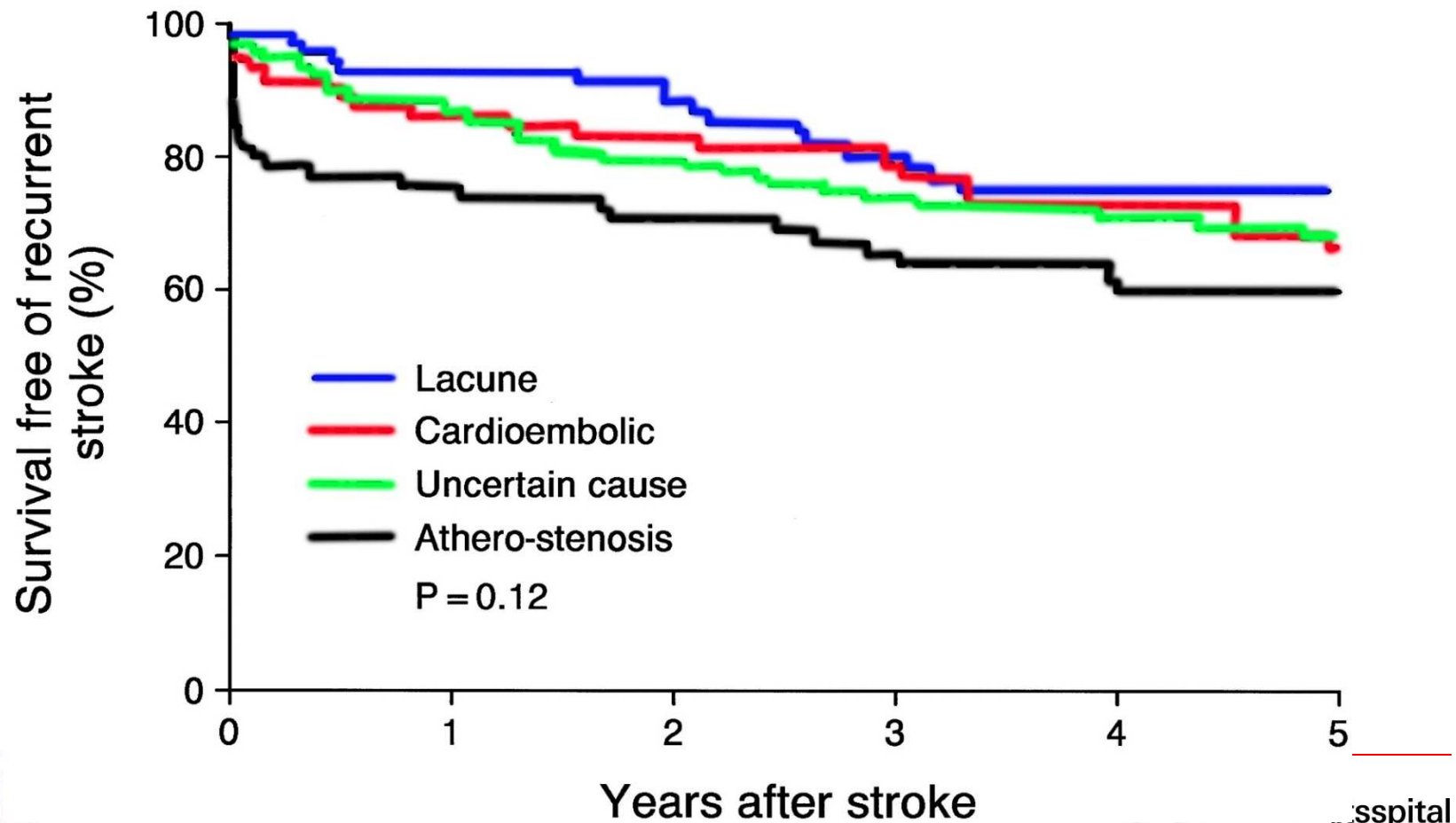
ASCO Small vessel disease

Grades for small vessel disease (S)

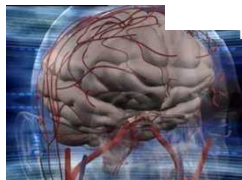
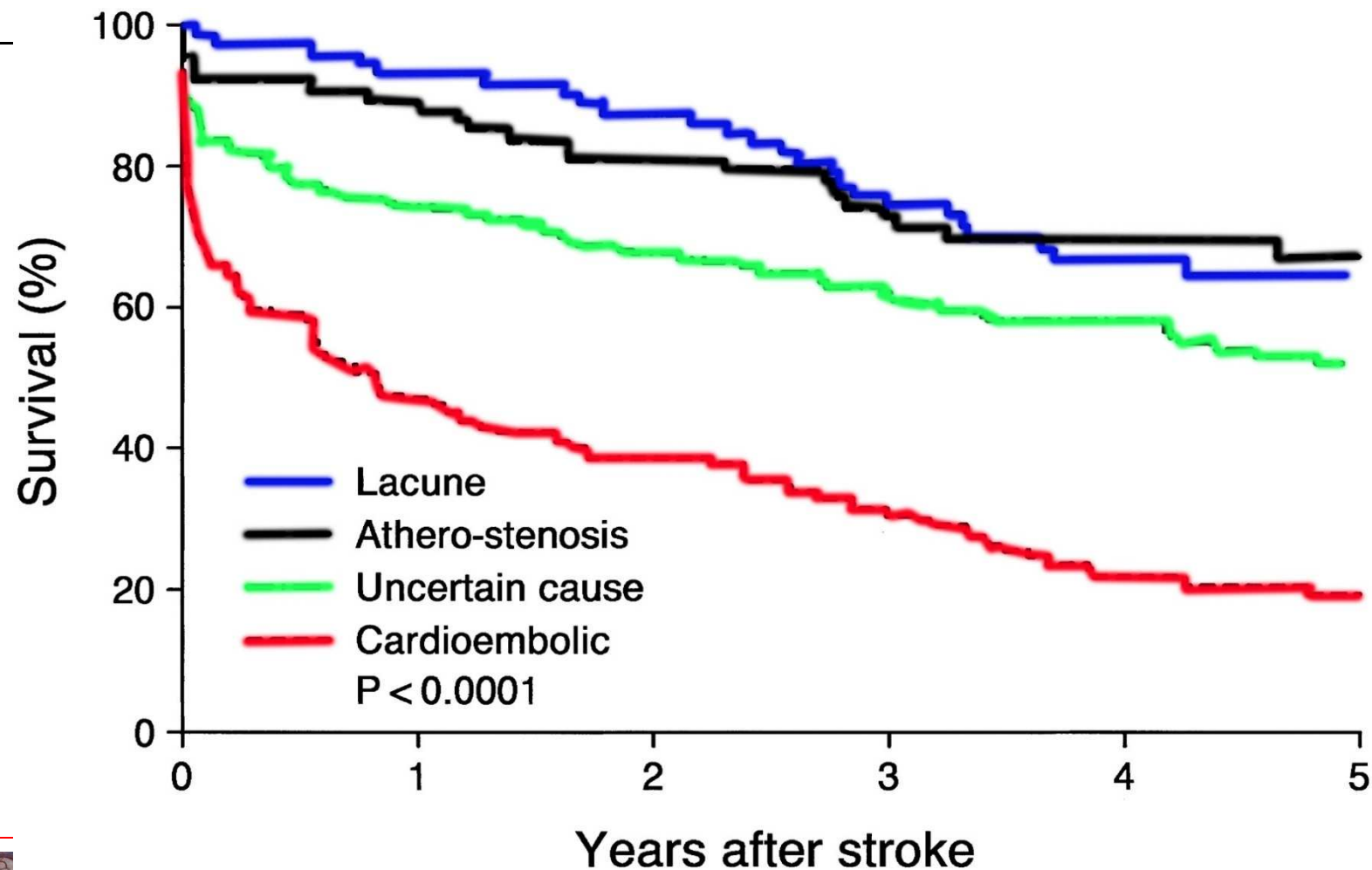
1. Definitely a potential cause of the index stroke	Association of: (a) Deep branch artery stroke: small, deep infarct with diameter <15 mm on MRI (or CT) in the territory corresponding to symptoms; and either (b) One or several old or silent lacunar infarcts in territories different from the index stroke; or (c) Leukoaraiosis on MRI (or CT), microbleeds on MRI (gradient echo imaging), dilatation of the perivascular spaces on MRI (or CT); or (d) Recent repeated similar TIAs – when they preceded the brain infarct by 1 month or less and attributable to the same territory as the subsequent BI (which increase the prediction for lacunar stroke from 57 to 80%, and are therefore supportive).
2. Causality uncertain	(a) Single, deep branch artery stroke; or (b) Clinical syndrome suggestive of deep branch artery stroke with no MRI/CT evidence of stroke (clinical syndrome suggestive of a deep branch artery stroke – classic lacunar syndromes: pure motor hemiparesis, pure sensory syndrome, ataxic hemiparesis, dysarthria clumsy-hand syndrome, and sensorimotor syndrome; or other ‘nonlacunar’ clinical syndromes. e.g. hemichorea, hemiballism, isolated dysarthria, etc.).
3. Unlikely a direct cause of index stroke (but disease is present)	Leukoaraiosis on MRI (or CT), and/or microbleeds on MRI (gradient echo imaging), and/or dilatation of perivascular spaces on MRI (or CT), and/or one or several lacunar infarcts (silent or old) in territories different from the index stroke.

Lit: Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Hennerici MG. New approach to stroke subtyping: the A-S-C-O (phenotypic) classification of stroke. Cerebrovasc Dis. 2009;27(5):502-8.

Recurrent stroke in relation to initial Stroke etiology



Survival in relation to initial Stroke etiology



Petty et al. Stroke 2000;31: 1062

Diagnostic investigations for ischaemic stroke

mandatory	From case to case
Neurological exam internal med. exam	Holter ECG, ECG-Monitoring
CT or MRI (DD Ischaemia, bleeding SAH, stroke mimic.)	24h Blood-pressure
Brain vessel ultrasound	Special lab tests (vasculitis, coagulation disorders)
Labor	
ECG	
Echocardiography (in case of pericardial infarction)	

Conclusions

- 60-80% of strokes are aetiologically related to
 - small vessel disease,
 - arteriosclerosis ,
 - or cardioembolism
- Investigate to make the right therapeutic choice
- Check for all 3 aetiologies
 - **stroke of undetermined aetiology ≠ unknown aetiology!**
 - **use ASCO - grading**

