

# **Klasifikace subtypů ischemické CMP: TOAST, CCS a ASCO**

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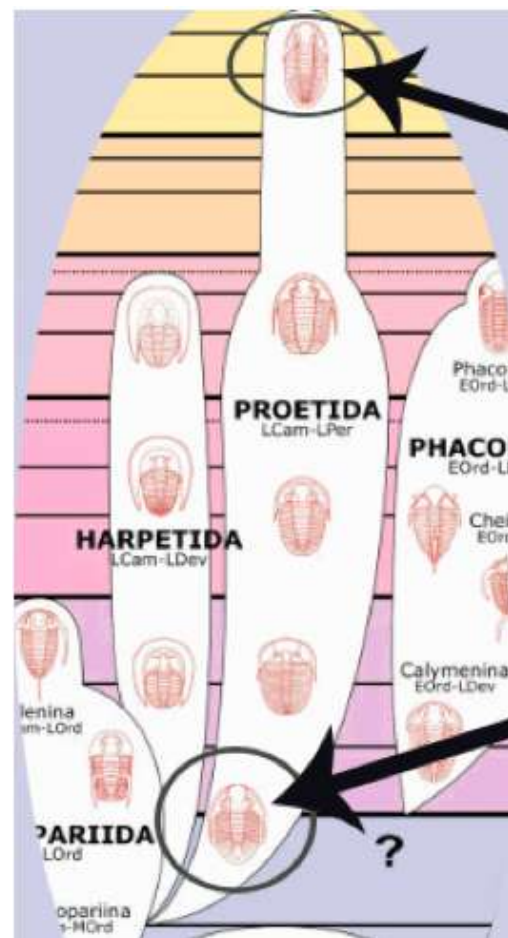
Neurologická klinika UK 2. LF a FN Motol

# Proč klasifikovat?

- Metodika multicentrických studií – přesnost vzájemné domluvy (hrušky s hruškami)
- Epidemiologie a prognostika
- Správná volba sekundární prevence

Předpoklad:

- Minimální diagnostický panel s jasnými definicemi kategorií



# Používané klasifikační systémy

- Stroke Data Bank (SDB, Harvard Stroke Registry, NINDS Stroke Data Bank) - **1978**
- Lausanne Stroke Registry and the Étude du profil Génétique de l'Infarctus Cérébral (GÉNIC) study – **1988**
- Oxfordshire Community Stroke Project (OCSP) – **1991**
- **TOAST** (Trial of ORG 10172 in Acute Stroke Treatment) – **1993**
- SSS-TOAST - **2005**
- **Causative Classification System (CCS)** - **2007**
- **ASCO** - **2009**

# TOAST subtype

**TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke**

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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
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TOAST, Trial of Org 10172 in Acute Stroke Treatment.

\*Possible or probable depending on results of ancillary studies.

# Klasifikace dle TOAST

- 2 stupně:
- **pravděpodobný (probable)** - klinický nález a vyšetřovací metody svědčí pro daný subtyp a ostatní subtypy byly vyloučeny
- **možný (possible)** – klinický nález a vyšetřovací metodiky naznačují subtyp, ale vyšetření není kompletně ukončeno

# TOAST – neurčená etiologie UND

- Zcela negativní nebo nekompletní vyšetření
- 2 a více možných příčin, kdy se lékař nedokáže definitivně rozhodnout
- Např.
  - FiS + 50% ipsilaterální ICA
  - Lakunární syndrom + 50% ipsilaterální ICA

# Causative Classification System (CCS)

- Podle váhy důkazu 3 kategorie:
- Evidentní (evident) – jediný možný mechanismus etiologie
- Pravděpodobný (probable) – více možných etiologických faktorů zároveň s rizikem CMP >2%/rok
- Možný (possible) - <2% roční riziko CMP, jednorázový rizikový faktor/situace nebo evidentní faktor, který nebyl kompletně dovyšetřen

# CCS

**Table** Causative stroke subtypes according to the Causative Classification of Stroke System (CCS)<sup>a</sup>

5 Subtype CCS	8 Subtype CCS	16 Subtype CCS
Supra-aortic large-artery atherosclerosis	Supra-aortic large-artery atherosclerosis	Supra-aortic large-artery atherosclerosis
		Evident, probable, possible
Cardioaortic embolism	Cardioaortic embolism	Cardioaortic embolism
		Evident, probable, possible
Small-artery occlusion	Small-artery occlusion	Small-artery occlusion
		Evident, probable, possible
Other uncommon causes	Other uncommon causes	Other uncommon causes
		Evident, probable, possible
Undetermined	Undetermined	Undetermined
	Unknown-cryptogenic embolism	Unknown-cryptogenic embolism
	Unknown-other cryptogenic	Unknown-other cryptogenic
	Unclassified	Unclassified
	Incomplete evaluation	Incomplete evaluation

# ASCO - metodika

## Stupeň kauzality

1. Rozhodně možná příčina indexové CMP
2. Kauzalita je nejasná
3. Něpravděpodobná příčina indexové CMP, ale rozhodně přítomen možný rizikový faktor

## Úroveň diagnostického průkazu

- A) Přímý průkaz standardní metodikou (gold standard)
- B) Nepřímý důkaz méně senzitivní nebo specifickou metodikou
- C) Slabý důkaz při nepřítomnosti specifické vyšetřovací metodiky

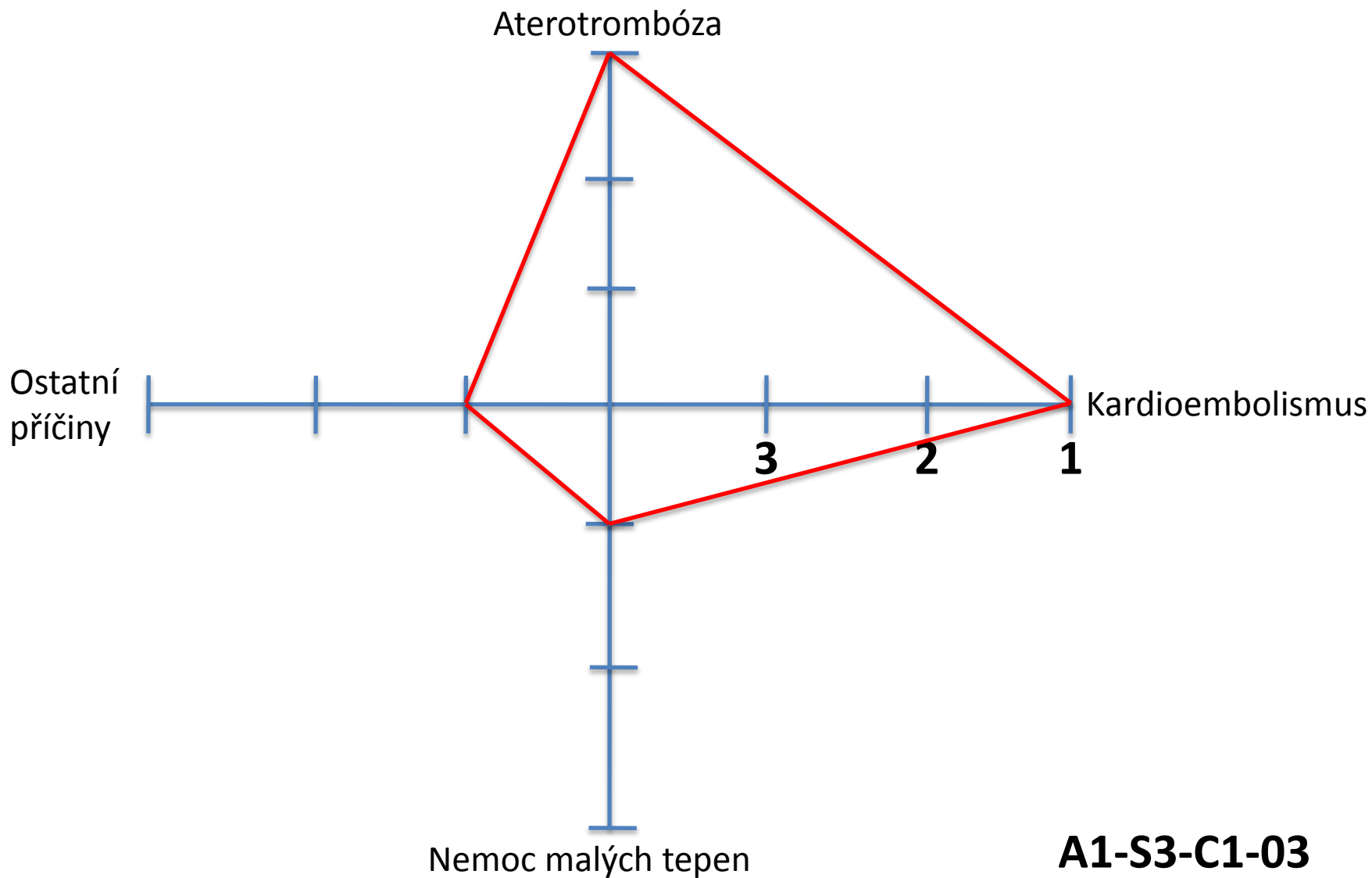
Hodnotíme 1, 2, 3 jak výše uvedeno, není-li rizikový faktor přítomen vůbec pak hodnotíme 0, při nedostatečném a nedokončeném vyšetřovacím programu hodnotíme 9.

# Modelový pacient

- Ipsilaterální stenóza ICA 70% (A1)
- Leukoaraióza, microbleeds (S3)
- FiS (C1)
- Trombocyty 700,000/mm<sup>3</sup> (O3)

**= A1-S3-C1-O3**

# ASCO - diagram



# ASCO – diagnostický panel – příklad kardioembolismus

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## *Ruling out a cardiac source of embolism:*

Minimum is negative ECG and auscultation by a cardiologist;

Maximum is negative ECG/telemetry/Holter ECG and negative TEE, negative cardiac CT/MRI, negative abdominal CT/MRI (search for old or simultaneous subdiaphragmatic visceral infarction).

## *Ruling out a PFO by best available technology:*

Microbubble injections with Valsalva maneuver;

With assessment by either TCD of the MCA or TTE (TTE usually allows a better Valsalva maneuver than under TEE).

In case of a negative TTE/TEE, if one doubts the quality of the technique used to search for microbubbles crossing, a confirmation can be obtained by TCD technique: negative results in both techniques is the gold standard for ruling out PFO.

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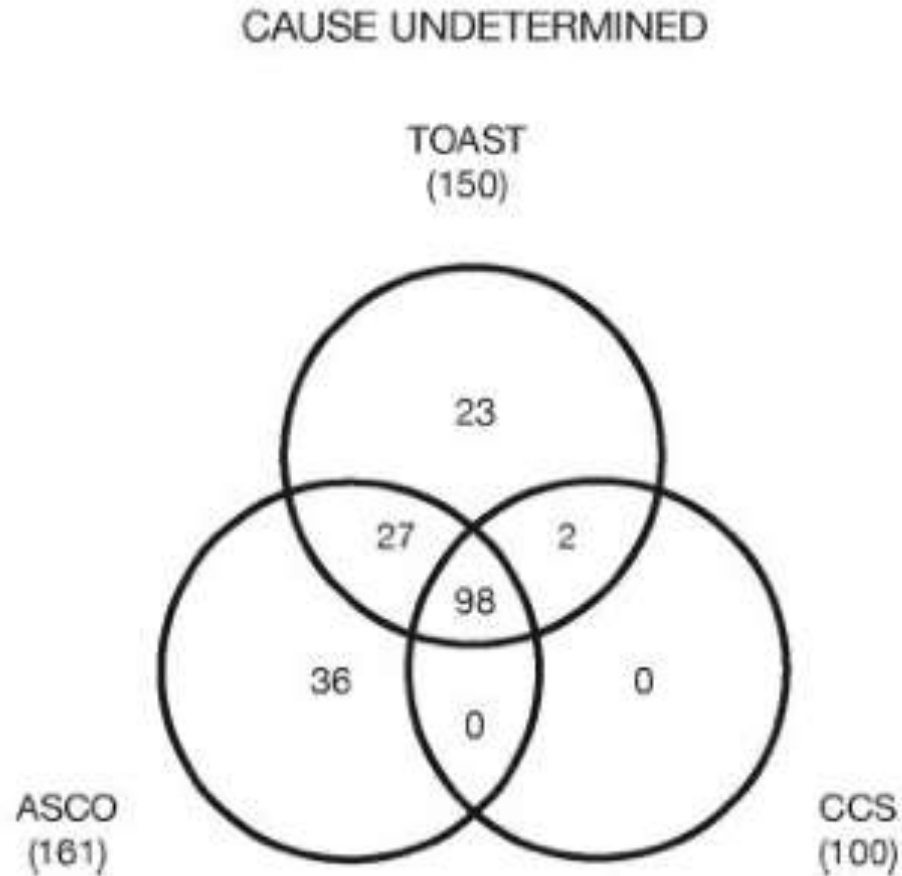
## **Cardiac disease**

- TEE for: valvular disease, atrial and aortic thrombus, atrial tumor or endocarditis;
- TTE for: left ventricle mural thrombus or endomyocardial fibrosis;
- Cardiac ultra-fast CT or MRI for some cardiac pathologies (intracardiac thrombi, a tumor, endomyocardial fibrosis);
- Pathology (autopsy evidence, macro- and microscopic demonstration of a cardiac source of embolism);
- ECG documentation for atrial fibrillation;
- Combined ECG and biologic (troponin) documentation for myocardial infarction; or pathology (autopsy evidence, macro- and microscopic demonstration of MI).

# Porovnání ASCO, CCS vs. TOAST

- Oproti TOAST – CCS:
  - méně pacientů s neurčenou etiologií (26.2% vs. 39.4%;  $P < 0.000001$ )
  - větší množství kardioembolických (o 6.9%;  $P = 0.004$ ), LVD (o 44.1%;  $P = 0.00006$ ), SVD (o 27.3%;  $P = 0.00006$ ) a s jinou určenou příčinou=OC (o 91.7%;  $P = 0.001$ )
- Oproti TOAST - ASCO (započetno grade 1):
  - méně SVD (o 29.1%;  $P = 0.007$ )
  - více LVD/aterotrombotické (o 17.6%;  $P = 0.03$ ).
- Korelace mezi klasifikacemi od dobré (kappa 0.61 TOAST/ASCO grade 1 small artery category) po výbornou (kappa 0.95 TOAST/CCS a ASCO grade 1/CCS CE/AT)
- Využití ASCO grades 1-3 u pacientů s neurčenou etiologií podle TOAST: LVD(73.3%), CE (31.3%), SVD (64.7%), OC (12%)

# Porovnání ASCO, CCS a TOAST



# Klasifikace – originální publikace

- TOAST – Adams HP et al. *Stroke* 1993;24;35-41.
- ASCO – Amarenco P et al. *Cerebrovasc Dis* 2009;27:502–508.
- CCS – Ay H et al. *Stroke* 2007, 38:2979-2984.

# Příloha – definice ASCO

Grades for atherothrombosis (A)	
1. Definitely a potential cause of the index stroke	<p>Atherothrombotic stroke defined as:</p> <ul style="list-style-type: none"><li>(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</li><li>(b) Any atherosclerotic stenosis &lt;70% in an intra-/or extracranial artery supplying the ischemic field with attached luminal thrombus diagnosed by level A or B evidence; or</li><li>(c) A mobile thrombus in the aortic arch; or</li><li>(d) Occlusion with imaging evidence of atherosclerosis in an intra-/or extracranial artery supplying the ischemic field.</li></ul>
2. Causality uncertain	<ul style="list-style-type: none"><li>(a) Patients with any atherosclerotic stenosis 70–99% in an intra-/or extracranial artery supplying the ischemic field diagnosed by level C evidence; or</li><li>(b) Any atherosclerotic stenosis &lt;70% in an intra-/or extracranial artery supplying the ischemic field with attached luminal thrombus diagnosed by level C evidence; or</li><li>(c) Aortic arch plaques &gt;4 mm in thickness without a mobile component.</li></ul>
3. Unlikely a direct cause of index stroke (but disease is present)	<ul style="list-style-type: none"><li>(a) Presence of carotid or vertebral artery plaque without stenosis; or</li><li>(b) Aortic arch plaque &lt;4 mm; or</li><li>(c) Stenosis (any degree) in a brain artery, contralateral to the brain infarction or in the opposite circulation (either posterior or anterior circulation); or</li><li>(d) History of myocardial infarction or coronary revascularization or peripheral arterial disease.</li></ul>

## 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.

## Grades for cardioembolism (C)

1. Definitely a potential cause of the index stroke	<p>Cardioembolic stroke – demonstration of:</p> <ul style="list-style-type: none"><li>(a) Mitral stenosis;</li><li>(b) Prosthetic heart valve;</li><li>(c) Myocardial infarction within the past 4 weeks;</li><li>(d) Mural thrombus in left cavities;</li><li>(e) Left ventricular aneurysm;</li><li>(f) Any documented history or permanent or transient atrial fibrillation or flutter with or without spontaneous echo contrast or left atrial thrombus;</li><li>(g) Sick sinus syndrome;</li></ul> <hr/> <ul style="list-style-type: none"><li>(h) Dilated cardiomyopathy;</li><li>(i) Ejection fraction &lt;35%;</li><li>(j) Endocarditis;</li><li>(k) Intracardiac mass;</li><li>(l) PFO plus in situ thrombosis;</li><li>(m) PFO plus concomitant PE or DVT preceding the brain infarction.</li></ul>
2. Causality uncertain	<ul style="list-style-type: none"><li>(a) PFO and ASA;</li><li>(b) PFO and concomitant DVT or PE (but not preceding the index stroke);</li><li>(c) Spontaneous echo contrast;</li><li>(d) Apical akinesia of the left ventricle and impaired ejection fraction (but &gt;35%);</li><li>(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;</li><li>(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).</li></ul>
3. Unlikely a direct cause of index stroke	<p>One of the following abnormalities: PFO, ASA, valvular strands, mitral annulus calcification, calcified aortic valve, nonapical akinesia of the left ventricle.</p>

## Grades for other causes (O)

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|---|--|
| 1. Definitely a potential cause of the index stroke (examples)      | (a) Arterial dissection by A or B evidence (table 3);<br>(b) Dolichoectasia with complicated aneurysm;<br>(c) Polycythemia vera, thrombocythemia $>800,000/\text{mm}^3$ ;<br>(d) Lupus erythematosus;<br>(e) Disseminated intravascular coagulation;<br>(f) Criteria for antiphospholipid antibody syndrome;<br>(g) Fabry's disease;<br>(h) Concomitant meningitis;<br>(i) Sickle cell disease;<br>(j) Ruptured cerebral aneurysm with or without demonstration of spasm in the territory of the brain infarct;<br>(k) Homozygote for hyperhomocystinuria. |
| 2. Causality uncertain  | (a) Arterial dissection diagnosed by level C evidence (see table 3; only suggestive history or clinical syndrome, e.g. isolated acute painful Horner's syndrome, or only history of previous dissection);<br>(b) Fibromuscular dysplasia.  |
| 3. Unlikely a direct cause of index stroke (but disease is present) | (a) Kinking or dolichoectasia without complicated aneurysm or plicature;<br>(b) Arteriovenous malformation or saccular aneurysm;<br>(c) Thrombocytosis $>450,000$ and $<800,000/\text{mm}^3$ ;<br>(d) Antiphospholipid antibodies $<100$ GPL units;<br>(e) Mild hyperhomocysteinemia heterozygote.   |