Stroke Types and Etiologies

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Disclosures

Genentech – Speaker Bureau and Consulting



Stroke Types

- Ischemic stroke (TIA)
- Intracerebral hemorrhage
- Subarachnoid





Placebo-controlled RCT blinded study of LMW heparinoid given within 24hrs after ischemic stroke



TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

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

TOAST, Trial of Org 10172 in Acute Stroke Treatment. *Possible or probable depending on results of ancillary studies.

- Based on clinical, imaging, and lab assessments
- Probable vs possible determinations

Ischemic Stroke Classification Cardioaortic embolism

- 1. Atrial fibrillation
- 2. Low left ventricular ejection fraction



Middle-cerebral artery clot

and facunar inchamic inforsts.

TABLE 3. TOAST Classification of High- and Medium-Risk Sources of Cardioembolism

High-risk sources Mechanical prosthetic valve Mitral stenosis with atrial fibrillation Atrial fibrillation (other than lone atrial fibrillation) Left atrial/atrial appendage thrombus Sick sinus syndrome Recent myocardial infarction (<4 weeks) Left ventricular thrombus Dilated cardiomyopathy Akinetic left ventricular segment Atrial myxoma Infective endocarditis Medium-risk sources Mitral valve prolapse Mitral annulus calcification Mitral stenosis without atrial fibrillation Left atrial turbulence (smoke) Atrial septal aneurysm Patent foramen ovale Atrial flutter Lone atrial fibrillation Bioprosthetic cardiac valve Nonbacterial thrombotic endocarditis Congestive heart failure Hypokinetic left ventricular segment Myocardial infarction (>4 weeks, <6 months) TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Clues to cardioembolic etiology

- Symptoms palpitations
- Signs irregular heart beat or pulse
- Explosive onset of stroke symptoms/signs
 - Maximal at onset
- Patterns of stroke symptoms/signs not localizing to a single vascular distribution



Work-up for cardioembolic stroke

- Bedside examination
- Telemetry
- Transthoracic echocardiography
- Transesophageal echocardiography
- Cardiac MRI
- Implanted loop recorder

Atrial fibrillation and stroke

Condition	Points
Prior stroke	2
CHF	1
HTN	1
DM	1
>75 years old	1



CHADS score	Yearly risk for stroke
0	1.9%
1	2.8%
2	4.0%
3	5.9%
4	8.5%
5	12.5%
6	18.2%

Low EF and risk of stroke

TABLE 2. LV Function in Stroke Patients and Control Subjects

	Stroke Patients, n (%)	Control Subjects, n (%)	Unadjusted OR (CI)*	Adjusted OR† (CI)
Normal LV function	205 (75.9)	274 (95.1)		
LV dysfunction				1
Any degree	65 (24.1)	14 (4.9)	6.21 (3.39-11.37)	3.92 (1.93-7.97)
Mild	29 (10.7)	7 (2.4)	5.54 (2.38-12.89)	3.96 (1.56-10.0)
Moderate/severe	36 (13.3)	7 (2.4)	6.87 (3.00–15.75)	3.88 (1.45-10.39)

*95% CI; †adjusted for age, gender, atrial fibrillation, diabetes mellitus, arterial hypertension, hypercholesterolemia, current smoking, coronary artery disease, clinical CHF, and LV mass index.

Ischemic Stroke Classification Large vessel

- Atherothrombosis 1.
 - >50% stenosis or occlusion 2
- Artery-to-artery embolism 2.





Clues to large artery etiology

- Monocular visual loss
- Cortical signs
- Fluctuating deficits
- Hemodynamic response



Work-up for large artery etiology

- CTA neck
- CTA head
- MRA neck with contrast
- MRA head
- TCD
- CUS
- Catheter angiogram
- Homocysteine
- Lipoprotein A
- Lipid panel

Consider cost, risk, what your question is, false positive and false negative rates

Ischemic Stroke Classification Small vessel thrombosis







Clues to small artery etiology

- Classic syndromes
- Lack of cortical signs/symptoms



Work-up for small artery etiology

- Brain imaging
- Requires intracranial vessel imaging to exclude large artery stenosis



Ischemic Stroke Classification

2.

1.

- 3.
- 4.
- 5.
- **Hyperviscosity** 6.
- TTP 7.
- Moyamoya 8.
- Post-procedural 9.

Must exclude large artery disease and cardioembolic source



BC S Stud

Clues to specific "other" etiologies

- Young, trauma, neck pain preceding deficits
 Dissection
- Localizing headache with progressive severity, which may be worse supine
 - Venous sinus thrombosis
- Low grade fever, night sweats, weight loss with elevated WBC
 - Hyperviscosity from acute myelogenous leukemia
- Headache and confusion on a background of autoimmune disease
 - Vasculitis
- Sickle cell disease, headache, progressive strokes
 - Moyamoya

Ischemic Stroke Classification Cryptogenic

- We looked for a cause and couldn't find one
- 2. We found two or more possible etiologies
- 3. The work-up was incomplete



	Subtype			
Features	Large-artery atherosclerosis	Cardioembolism	Small-artery occlusion (lacune)	Other cause
Clinical				D
Cortical or cerebellar dysfunction	+	+	-	+/-
Lacunar syndrome	1.77	~	+	+/-
Imaging				
Cortical, cerebellar, brain stem, or subcortical infarct >1.5 cm	+	+	10	+/-
Subcortical or brain stem infarct <1.5 cm	100	<u>8</u>	+/	+/-
Tests				
Stenosis of extracranial internal carotid artery	+	20	8 <u>0</u> 1	-
Cardiac source of emboli	3 <u>0-</u> 37	+	8 <u>0</u>	-
Other abnormality on tests			100	+

TABLE 2. Features of TOAST Classification of Subtypes of Ischemic Stroke

TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Causative Classification System for Ischemic Stroke (CCS)

evaluation	(check all that an	(vla
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a.	There is prior history of ischemic stroke, transient ischemic attack, or transient monocular blindness from the territory of index artery within the month preceding the index stroke
b.	Prior clinical events described in 1a are exclusively a cluster of repetitive and stereotypic lacunar transient ischemic attacks that started within the week preceding the index stroke
C.	The patient presents with a lacunar syndrome
d.	There is evidence of concurrent systemic embolism

2. Imaging evaluation of the brain (check all that apply)

- a. Brain imaging has not been done (CT or MRI)
- b. Brain imaging is negative for the presence of acute brain infarct or perfusion deficit consistent with clinical symptoms
- C. There is a lacunar infarct as defined by a single acute infarct within the territory of penetrating arteries in the brainstem, deep gray matter, or internal capsule that is ≤20 mm in its greatest diameter and there is no known focal pathology in the parent artery at the site of the origin of the penetrating artery
- d. There are multiple acute and subacute ischemic lesions in either right and left anterior or anterior and posterior circulations or both, in the absence of non-embolic occlusion or near occlusive stenosis of all relevant vessels
- e. There are acute unilateral internal watershed infarcts
- f. There are multiple temporally separate infarcts exclusively within the territory of the clinically relevant artery

Causative Classification System for Ischemic Stroke (CCS)



- b. There is stenotic or occlusive vascular disease judged to be due to atherosclerosis in clinically-relevant arteries
 - i. 🛛 Intracranial arteries
 - ii. 🛛 Extracranial arteries
- c. The atherosclerotic plaque described in 3b has features consistent with thrombus formation, ulceration, near-occlusive stenosis or non-chronic occlusion
- d. There is an atherosclerotic plaque causing mild stenosis in the absence of any detectable plaque ulceration or thrombosis in clinically-relevant extracranial or intracranial artery. There is also a prior history of two or more ischemic stroke, transient ischemic attack, or transient monocular blindness from the territory of index artery, at least one event within the last month
- e. There is angiographic evidence of abrupt cut-off consistent with a blood clot within the clinically relevant and otherwise angiographically normal appearing intracranial artery

f. There is vascular imaging evidence that the clinically relevant occluded intracranial artery has been completely recanalized

Causative Classification System for Ischemic Stroke (CCS)

4. Cardiac evaluation (check all that apply)

- a. Cardiac evaluation has not been done
- b. Cardiac evaluation reveals a high-risk source (check all that apply)
- i. Left atrial thrombus
- ii. Left ventricular thrombus
- iii. Atrial fibrillation
- iv. Paroxysmal atrial fibrillation
- v. Sick sinus syndrome
- vi. Atrial flutter
- vii. Recent myocardial infarction
- viii. D Mitral stenosis or rheumatic valve disease
- ix. Bioprosthetic and mechanical heart valves
- x. Chronic myocardial infarction together with low ejection fraction <28%
- xi. Dilated cardiomyopathy
- xii. Non bacterial thrombotic endocarditis
- xiii. 🗌 Infective endocarditis
- xiv. D Papillary fibroelastoma
- xv. 🛛 Left atrial myxoma
- xvi. Detent foramen ovale and concurrent systemic embolism

Causative Classification System for Ischemic Stroke (CCS)

- C. Cardiac evaluation reveals a low- or uncertain-risk source (check all that apply)
 - i. Mitral annular calcification
 - ii. D Patent foramen ovale
- iii. Atrial septal aneurysm
- iv. Atrial septal aneurysm and patent foramen ovale
- v. Left ventricular aneurysm without thrombus
- vi. Left atrial smoke
- vii. Congestive heart failure with ejection fraction <30%
- viii. Complex atheroma in the ascending aorta or proximal arch
- ix. 🛛 Apical akinesia
- x. 🛛 Wall motion abnormalities (hypokinesia, akinesia, dyskinesia) other than apical akinesia
- xi. Hypertrophic cardiomyopathy
- xii. Left ventricular hypertrophy
- xiii. Left ventricular hypertrabeculation/non-compaction
- xiv. 🗌 Other

Causative Classification System for Ischemic Stroke (CCS)

- Evaluation for diagnosis of other (uncommon) causes of stroke (check all that apply)
- a. Acute arterial dissection in relevant arteries
- b. Cerebral vascular abnormalities in the relevant artery
- c. Cerebral vasculitis
- d. Cerebral venous thrombosis
- e. Acute disseminated intravascular coagulation
- f. Drug-induced stroke
- g. Fibromuscular dysplasia
- h. Heparininduced thrombocytopenia type II
- i. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
- j. Hyperviscosity syndromes
- k. Hypoperfusion syndromes
- I. latrogenic causes
- m. Partially thrombosed cerebral aneurysm in a clinically relevant artery
- n. MELAS
- 🗌 o. Meningitis
- p. Migraine-induced stroke
- g. Moyamoya disease
- r. Primary antiphospholipid antibody syndrome
- s. Primary infection of the arterial wall
- t. Sickle cell disease
- u. Sneddon's syndrome
- v. Thrombotic thrombocytopenic purpura Hemolytic uremic syndrome
- w. Segmental vasoconstriction or vasospasm
- x. Abnormalities of thrombosis and hemostasis
- y. Other causes

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Causative Subtype	Phenotypic Subtype
A. Supra-aortic large artery evident atherosclerosis:	
possible	Large Artery Cardiac Embol
B. Cardio-aortic embolism: evident	(LAA) (CE
probable possible	
C. Small artery occlusion: evident	
probable possible	IIUPII
D. Other causes: evident	Lacunar
possible	Infarction (uncommon (LI) Cause
E. Undetermined causes: unknown - cryptogenic embolism	major minor absent
unknown - unknown -	
other incomplete unclassified	







Why do we care about TOAST?

Impact on management

- Anticoagulation prevents recurrent stroke in atrial fibrillation/cardioembolic stroke
- Carotid artery revascularization prevents recurrent stroke in extracranial large artery stroke
- Impact on prognosis
 - Mortality is highest for cardioembolic stroke
 - Mortality lowest with small vessel infarctions
 - Recurrent stroke highest after cardioembolic stroke
- Clinical trial standardization

Cases to determine TOAST



NH

- 82yo RH BF with prior stroke resulting in non-use of RLE s/p sudden onset of L HP & R gaze with NIHSS 16 at OSH.
- Treated with IV tPA and shipped to TMC where NIHSS 18.



MRI upon arrival from OSH

Standard work-up

- Telemetry Afib
- TTE EF 55-60%, DD indeterminant, severe LAE, PFO with L -> R shunting, RAE
- Vascular imaging R MCA occluded, extracranial ICAs open on MRA
- TEE severe continuous spontaneous echo contrast in LA and LAA with reduced velocity and no discrete thrombus

TOAS To A Combolic

DR

- 57yo RH WM with OSA and HTN s/p acute word-finding difficulty after swimming
- Symptoms preceded by neck pain on L side
- Numbness and incoordination R hand
- Presented outside of the window for tPA



TO/Other - dissection

Final PEARLS

- Consider TEE for:
 - Embolic appearing strokes, LAE, atrial fibrillation to determine indication for bridging, young patients without another cause

Add contrast to MRI for:

 Suspicion of demyelinating disease, autoimmune disease, neoplastic disease, atypical presentation or distribution of stroke

Hypercoagulability labs

- Arterial APLAs, FVIII, vWF antigen, HIT (if exposed), homocysteine (and MTHFR if elevated), lipoprotein A
- Add venous for R->L shunt, venous sinus thrombosis, or familial stroke - ATIII, Protein C/S, FVL, prothrombin gene mutation
- Brain biopsy and/or CSF examination for suspected small vessel vasculitis

Intracranial VS Intracerebral hemorrhage

Definition –Blood in the parenchyma of the brain

- Not to be confused with intracranial hemorrhage
 - Epidural hematoma = EDH
 - Subdural hematoma = SDH
 - Subarachnoid hemorrhage = SAH
 - Intracerebral hemorrhage = ICH
 - Intraventricular hemorrhage = IVH







Normal CT Scan Slice of Brain





Intracerebral Hemorrhage (bright white area) CT Scan Slice of Brain

Intracerebral hemorrhage (ICH)

- headache, nausea, and vomiting
- Iethargy or confusion
- sudden weakness or numbness of the face, arm or leg, usually on one side
- Ioss of consciousness
- temporary loss of vision
- seizures



Why the depressed level of consciousness?

Unlike acute ischemic stroke...

- Immediate space-occupying lesion
- Little time to equilibrate pressures
- Rise in intracranial pressure
- Obstruction to flow of CSF \rightarrow hydrocephalus



Causes of ICH

- Hypertension
- Anticoagulation
- ► AVM
- Aneurysm
- Head trauma
- Amyloid angiopathy
- Bleeding disorders
- Tumors
- Drug usage
- Spontaneous
- Hemorrhagic conversion
 - Reperfusion injury
 - Early anticoagulation
 - Venous infarct





Other causes: bleeding into tumor, hypocoagulable state, hemorrhagic infarction, latrogenic, and trauma

Other causes:

- Moyamoya
- Sickle cell disease
- Eclampsia or postpartum vasculopathy
- Infection
- Vasculitis

Predilection sites for ICH



- A) <u>Penetrating cortical branches</u> → lobar ICH (20-50%), of ACA, MCA, PCA
- B) <u>Basal ganglia</u> (40-50%), lenticulostriate branches of the MCA
- C) <u>Thalamus</u> (10-15%), thalamogeniculate branches of the PCA
- D) <u>Pons</u> (5-12%), paramedian branches of the basilar artery
- E) <u>Cerebellum</u> (5-10%), penetrating branches of the cerebellar arteries

Symptoms

Depends on the location of the hemorrhage

- A) <u>Penetrating cortical branches</u> looks like cortical infarct involving ACA, MCA, or PCA
- B) <u>Basal ganglia</u> contralateral hemiparesis
- C) <u>Thalamus</u> contralateral hemisensory, often with hemiparesis and field cut
- D) <u>Pons</u> often comatose, pupillary changes, quadriplegic

E) <u>Cerebellum</u> – nausea and vomiting, ataxia, reduced level of consciousness if mass effect

Clinical Manifestations

Acute focal neurlogical deficit

 Asymmetric weakness/numbness, incoordination/ataxia, vision change, abnormal speech

Signs of increased ICP

- Headache, vomiting, decrease LOC
- Can occur acutely with IVH (acute obstructive hydrocephalus)
- $\blacksquare>90\%$ will present with BP >160/100

Dysautonomia

 Central fever, hyperventilation, hyperglycemia, tachycardia/bradycardia

Symptoms more typical of ICH than ischemic stroke

- How can you tell the difference between ICH and ischemic stroke?
 - Younger patients
 - Occur while awake (only 15% upon awakening)
 - Headache (40% vs 17% in ischemic stroke)
 - Elevated blood pressure (SBP > 200)
 - Reduced level of consciousness (about 50%)
 - Vomiting (more with posterior fossa ICH)
 - Seizures (more common with lobar ICH)

Most importantly...

- Noncontrast CT scan
- LOUISIANA
 EMERGENCY RESPONSE NETWORK



CTA in ICH

Underlying vascular anorActive bleeding? Oozing





Clues to specific etiologies of ICH

- Elderly, progressive cognitive dysfunction, and lobar hemorrhage
 - Amyloid angiopathy MRI GRE typically with cerebral microbleeds
- Headache, seizures, focal deficits in young to middle-aged person
 - AVM
- Weight loss, smoking history, cough, bone pain
 - Hemorrhagic metastasis lung, breast, melanoma, renal cell, medullary thyroid, uterine

Subarachnoid hemorrhage

- sudden onset of a severe headache (often described as "worst headache of their life")
- popping or snapping sensation in head
- nausea and vomiting
- stiff neck
- transient loss of vision or consciousness
- seizures



Most common causes of SAH:

- Aneurysm: a balloon-like bulge or weakening of an arterial wall.
 - Most common locations are: AComm, PComm, & MCA
- Arteriovenous malformation (AVM): a congenital defect, which consists of a tangle of abnormal arteries and veins with no capillaries in between.
- Dural AVF
- Head trauma: fractures to the skull and penetrating wounds (gunshot) can damage an artery and cause bleeding
- "Benign" perimesencephalic SAH

Work-up of SAH

- CT: The first test performed is a CT scan.
- CTA
- Lumbar puncture (L3/4 or L4/5): blood in CSF
- Angiogram
- MRI/MRA scan



Vasospasm and treatment

- A common complication of SAH is vasospasm, which is a narrowing (spasm) of an artery that may occur 3-14 days following a SAH.
- Vasospasm narrows the artery and reduces the blood flow to the region of the brain that artery feeds.
- If left untreated, vasospasm can cause a stroke.
- To control vasospasm, patients are given the drug nimodipine for 14-21 days.
- Treated with Triple-H therapy:
 - Hypertension, Hypervolemia, Hemodilution





Severe vasospasm

After treatment

Case 1. 47yo Asian woman

- Had dinner with son. Complained of rightsided headache.
- Had bowel movement after which she screamed and then lost consciousness. 21:15
- > 911 called by son. Arrived at TMC 21:37
- **BP** 153/91
- GCS = 6T (E1, V1, M4)
- Went to CT scanner
- Son gave history no medical problems and no medications





What do you do?



Call Stroke Activation

- Intubate
- HOB 30
- Hyperventilate (pCO2 28–32)
- Cardene gtt to keep SBP <180</p>
- Mannitol to treat hernation
- STAT neurosurgery consult
- Reverse coagulopathy if present

Work-up included angiogram

- Why?
 - Young
 - No obvious etiology
 - Atypical location



- Post-op
- ▶ GCS = 10T
 E3, VT, M6
- Required PEG and trach
- 8 months later
 - Independent with ambulation
 - Independent with ADLs
 - Conversational in native language









After multiple embolization procedures





Arteriovenous Malformations -AVM

CT findings c/w structural lesions:

- presence of subarachnoid or intraventricular hemorrhage
- abnormal intracranial calcification
- prominent vascular structures
- site (eg, perisylvian hemorrhage).
- Among younger (mean 49yo) pts 44 with these CT findings, 38 underwent angiography
 - + findings in 32 of the 38 cases (84%)
 - AVMs in 23 patients; aneurysms in 9





Halpin SF et al. Prospective evaluation of cerebral angiography and computed tomography in cerebral haematoma. *J Neurol Neurosurg Psychiatry*. 1994;57: 1180–1186.

These are easy



Not as obvious?



Angiography

AHA guidelines

 Not required for older, hypertensive patients who have ICH in the basal ganglia, thalamus or brainstem and in whom CT findings <u>do not</u> suggest a structural lesion

Case. 82yo woman with sudden decrease in consciousness

- Baseline legally blind and nearly deaf
- Headache for 2 days prior to abrupt decline
- GCS = E2, V3, M5 = 10
- 90cc R temporal ICH with IVH and hydrocephalus
- ICH score = 3
- Could not swallow or stay awake
- PEG placed; modifed Rankin score 5
- Family opted for hospice



69yo woman presents to OSH with left sided weakness

- GCS = 15, NIHSS = 14
- 88cc ICH with IVH and hydrocephalus
- EVD placed to decompress ventricles
- D/C to inpatient rehab with NIHSS = 4
- RTC 6 months later with NIHSS = 2





70yo man transferred from OSH after CT scan

- Presented with CP and tx ACS including ASA, Plavix, eptifibatide infusion, heparin
- Developed headache and "blurred vision"
- Headache worsened 3 days later, prompting the CT scan
- Diagnosis?



Thank you.

Questions?

