The Diagnosis & Treatment of Acute Ischemic Stroke: New Frontiers in Managing ED Stroke Patients

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Global Objectives

- Improve ischemic stroke patient outcome
- Know how to effectively Rx stroke patients
- Understand current diagnostic strategies
- Be able to recommend latest treatments
- Improve Emergency Medicine practice

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Session Objectives

- Present a patient case
- Review Key Learning Points
- Discuss diagnostic options
- Explore treatment options
- Conclude with learning points for the practicing emergency physician

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A Clinical Case

- A 58 year old emergency physician has a stroke while attending a conference
- EMS brings the patient to you within 30 minutes, with right sided weakness, slurred speech, and visual field neglect
- You are in the ED at a tertiary center
- What tests and treatments can you give?

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ED Stroke Patient: EM Priorities

- Stabilization, initial exam (etiology)
- Neurological exam, calculate NIHSS
- Promptly obtain CT neuroimaging
- Determine nature of thromboembolism
- Provide advanced diagnostics
- Administer IV tPA or plan another Rx
- Interventional radiology
- Intra-arterial thrombolysis
- Cerebrovascular stent, clot retrieval

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ED Stroke Pt: Critical Questions

- Once the CT is performed, are you comfortable giving tPA within 3 hours?
- If the patient merits aggressive Rx, what would you do beyond 3 hours?
- Do any diagnostic tests enhance the ability to intervene with new therapies?
- What new therapies should we consider?
- Do these new options improve outcome?

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Neuroimaging in Stroke

- Patients with acute stroke
- Moderate to severe insult
- NIHSS ranges from 10-15, 16+
- Acute hemorrhage must be excluded
- Thrombolytic therapy a consideration
- Can pt selection be optimized?

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Key Concept

Stroke Pt Diagnostic Modalities

- The diagnostic modalities that are to be considered in the ED evaluation of stroke patients include: Cranial CT, CT angiography, MRI (including diffusion and perfusion weighting studies), MR angiography, cerebral angiography, carotid Doppler ultrasonography, and cardiac echocardiography.

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Key Concept

Initial Head CT in Acute Stroke

- The initial non-contrast CT is performed in order to determine the presence of intracranial hemorrhage, a space-occupying lesion, signs of cerebral edema, and/or evidence of a large middle cerebral artery distribution infarct or an infarct of many hours' duration.

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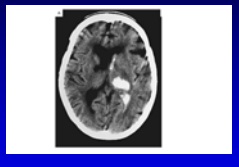
Non-Contrast Cranial CT

- Primary use is to rule out acute hemorrhage
  - Contraindications to the use of thrombolytic therapy
  - Identification of potential surgical candidates
- Limited sensitivity for the detection of acute cerebral ischemia signs (31-75%)



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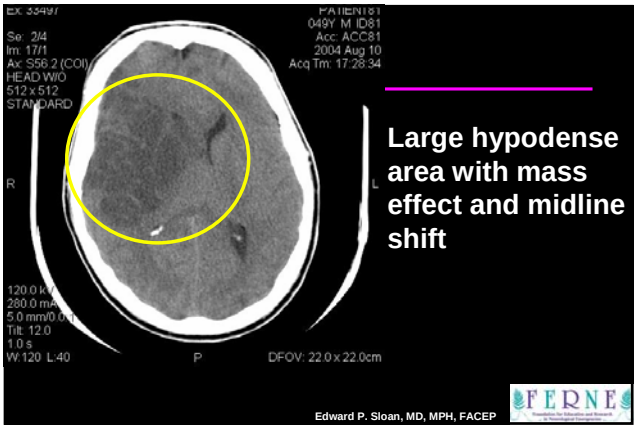
Ischemic Stroke CT Findings

- Decreased gray-white differentiation
  - Especially in the basal ganglia
- Loss of insular ribbon
- Effacement of sulci
- Edema and mass effect *
- Large area of hypodensity* (>1/3 MCA)

*May signify increased risk of hemorrhage with thrombolytic therapy



Key Concept

Stroke Pt Dx: CT vs. MRI

- Although MRI can detect hemorrhage acutely and can provide information regarding the stroke pathology via diffusion/perfusion mismatch data, CT is still currently indicated in ED stroke patients, given it availability and its ability to support decision making regarding acute IV tPA therapy.

Magnetic Resonance Imaging

- Multimodal MRI
- Demonstrates hyperacute ischemia
- Considered less reliable in identifying early parenchymal hemorrhage, but data suggests adequate blood detection ability
- What role does MRI play in diagnosis and management of the acute stroke pt?

MRI: Stroke Center Approaches

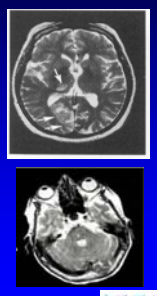
- CT acutely with follow-up MRI
  - Late delineation of stroke findings
- Both CT and MRI acutely
  - More expensive, time-consuming
  - Possible enhancements in therapy?
- MRI acutely
  - Is it a reasonable alternative?

What is Multimodal MRI?

- T1, T2 Imaging: Conventional weighted pulse sequences
- DWI: Diffusion-Weighted Imaging
- PWI: Perfusion-Weighted Imaging
- GRE: Gradient Recalled Echo pulse sequence (T2*-sensitive)
- FLAIR: Fluid-Attenuated Inversion Recovery images

T1 & T2 Weighted Pulse Sequences

- Sensitive for subacute and chronic blood
- Less sensitive for hyperacute parenchymal hemorrhage



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Diffusion-Weighted Imaging

- Ischemia decreases the diffusion of water into neurons
- Extracellular water accumulates
- On DWI, a hyperintense signal
- Present within minutes
- Irreversible damage delineated
- Non-salvageable tissue??

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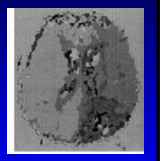
Perfusion-Weighted Imaging

- Tracks a gadolinium bolus into brain parenchyma
- PWI detects areas of hypoperfusion
  - Infarct core (DWI area) *AND*
  - Ischemic penumbra



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DWI/PWI Mismatch

- Subtract DWI signal (infarct core) from the PWI signal (infarct core and ischemic penumbra)
- DWI/PWI mismatch is the hypoperfused area that may still be viable (ischemic penumbra)

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DWI/PWI Mismatch

- Important clinical implications
- May identify the ischemic penumbra
- If there is a large mismatch, then reperfusion may be of benefit, even beyond the three hour tPA window
- If there is no mismatch, there may be little benefit to thrombolytic therapy, even within the three hour window

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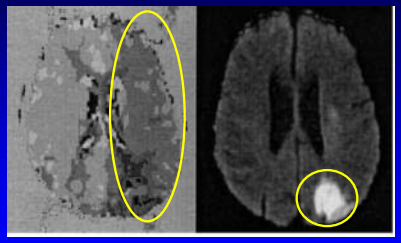
DWI/PWI Mismatch



- PWI hypoperfusion area
- DWI infarct core

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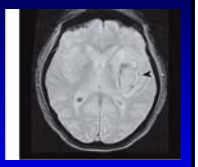
Gradient Recalled Echo (GRE) Pulse Sequence

- May be sensitive for hyperacute parenchymal blood
- Detects paramagnetic effects of deoxyhemoglobin & methemoglobin as well as diamagnetic effects of oxyhgb



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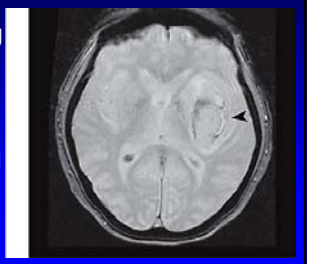
Gradient Recalled Echo (GRE) Pulse Sequence

- Core of heterogeneous signal intensity reflecting recently extravasated blood with significant amounts of oxyhgb
- Hypodense rim reflecting blood that is fully deoxygenated



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So what is the role of MRI in the ED evaluation of the stroke patient?

- Secondary?
  - Initial CT to rule out hemorrhage
  - Subsequent MRI to fully delineate ischemia, infarct and to follow treatment
- Primary?
  - Initial and possibly only imaging modality

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MRI in Acute Stroke Dx

- Primary MRI not current EM standard
- Logistical, timing issues exist
- MRI likely able to diagnose hemorrhage
- DWI/PWI mismatch a promising exam
- Tailored thrombolytic therapy??
- Improved patient outcome??

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Key Concept

Stroke Pt: Advanced Diagnostics

- Advanced diagnostic and therapeutic tests are indicated when the three hour IV tPA window has expired, if mechanical interventions or intra-arterial thrombolytic therapy is planned, or when the diagnosis of stroke or the etiology remains uncertain following the initial CT.

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Key Concept

Stroke Pt: Advanced Diagnostics

- Cerebral angiography, CTA, and MRA are utilized to detect the presence of intracranial or extracranial vascular occlusions and/or vascular abnormalities that assist in defining the etiology of the cerebrovascular accident.

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Key Concept

Stroke Pt: Advanced Diagnostics

- Cerebral angiography is the test that will be performed acutely in the setting of planned interventional radiography techniques that include cerebrovascular stenting, mechanical clot retrieval, or intra-arterial thrombolytic therapy.
- Angiography also is indicated for the detection of aneurysms after SAH.

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Clinical Settings: Diagnostics

- Inflammation, infection, vasculitis
- Carotid or vertebral artery dissection
- Dural venous sinus thrombosis
- Acute hemorrhage (SAH, ICH & IVH)
- TIA and small CVA
- Large, severe CVA

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Inflammation, Infection & Vasculitis

- CT contrast if mass lesion possible
- MRI more sensitive: lesion detection
- Examples:
  - Multiple lesions noted in MS
  - Lesions of herpes or WNV encephalitis
- MRI usually NOT indicated acutely

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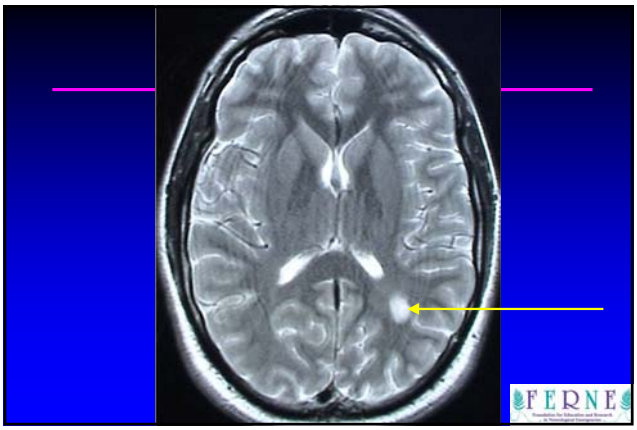

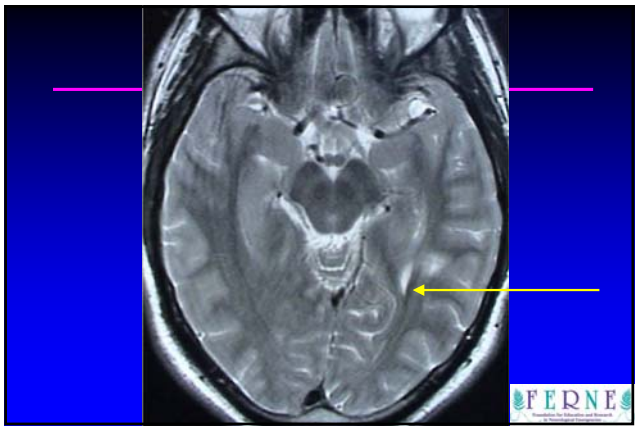

WNV Encephalitis MR Findings

- Inflamed portion of the temporal lobe, involving the uncus and adjacent parahippocampal gyrus, in brightest white on MR.

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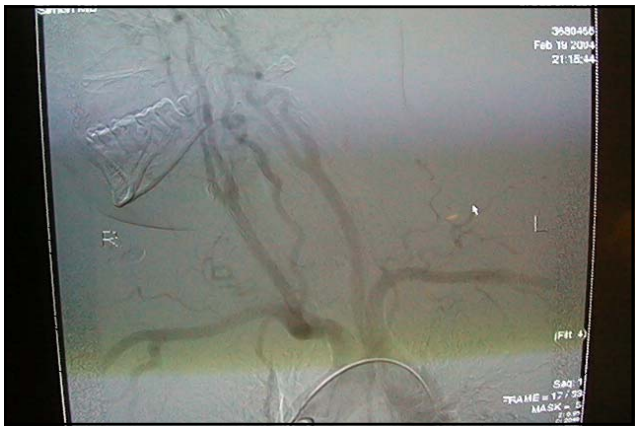
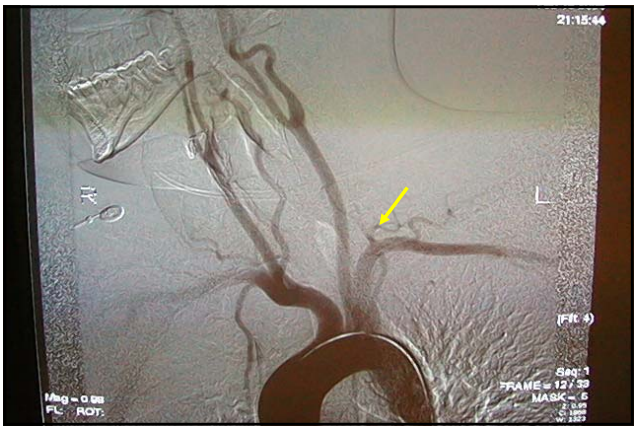
Carotid or Vertebral Artery Dissection

- Local hematoma, mass & occlusion
- Thromboemboli distally
- Angiography is the gold standard
- MRI will detect intramural hematomas
- MRA will detect lumen compromise
- CTA may be of value in the future

Severe Headache: Working Dx

- 38 yo wrestling coach, trauma, cephalgia
- Rule out basilar migraine and CVA
- Rule out vascular etiology
- CTA: suspected high grade stenosis R common carotid and subclavian origin
- Vertebral artery plaques, L vessel small





Dural Venous Sinus Thrombosis

- Major brain dural venous sinuses
- Lost cortical, deep venous drainage
- Multiple infarctions, hemorrhagic
- Dehydration, sepsis, pregnancy, coag
- Headache, vision changes, CVA, sz
- High mortality disease process

Dural Venous Sinus Thrombosis

- MRI, MR venography acutely
- MRI will show acute thrombus
- Contrast MRI will highlight vessel
- MR venography will exclude false +
- Anticoagulant therapy
- Repeat assessments non-invasive

Subarachnoid Hemorrhage

- Detection of aneurysm or AVM
- Decisions need to be made regarding:
  - Interventional radiology, coil placement
  - Neurosurgery, operative intervention
- Cerebral angiography optimal test
- CTA duplicates contrast
- MRA may not detect small aneurysms

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Subarachnoid Hemorrhage

- No cerebral angiogram acutely, unless:
- Interventional radiology is able to perform the angiogram and coil placement ASAP
- Neurosurgical operative intervention is to be performed immediately
- If performed in the ED, MRA or CTA may not obviate the need for cerebral angiography
- Useful in low risk pts?

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Acute Intracerebral Hemorrhage

- CT will detect hemorrhage, effects
- Contrast CT not indicated
- MRI also detects acute hemorrhage
- MRI detects chronic microbleeds
  - Small punctate hemosiderin lesions
  - Clinically silent, unknown significance
  - Increased ICH risk with tPA use?

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Stroke, Microbleeds, and ICH

- Didn't plenty of patients in the NINDS trials likely have undiagnosed microbleeds?
- If undetected, do they exist clinically?
- Do microbleeds actually impart risk?
- Are these predictive of symptomatic ICH?
- No need to perform MRI in order to manage risk prior to tPA use in ischemic stroke

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TIAs and Small Strokes

- Minimal or resolving symptoms
- Need to evaluate for future CVA risk
- Six questions:
  - Ischemic? Location?
  - Etiology? Probability of each etiology?
  - What tests? What treatments?
- Large and small vessel disease
- Cardioembolic source

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TIAs, Small CVAs: Large Vessel Dx

- Large vessel 15-20% of all strokes
- Extracranial (Likely large vessel cause)
  - 75%+ of large vessel disease location
  - Carotids, vertebrals, aorta
- Intracranial
  - 5-8% of strokes
  - CVD, dissection, vasculitis, spasm
  - Moya Moya Dx

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Large Vessel Extracranial Disease

- CT angiography
  - Will detect carotid artery occlusion
  - Sensitivity, specificity for stenosis OK
- MR angiography
  - Also good study to detect carotid occlusion
  - Comparable sensitivity and specificity
- Cerebral arteriography
  - Not needed given CTA, MRA use

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Large Vessel Intracranial Disease

- CTA and MRA both may be used
- Cerebral angiography may be optimal
- Suspect intracranial lesion when:
  - Young patients, no extracranial source
  - Failed antiplatelet therapy, recurrent TIAs or cortical strokes in a single vascular territory
  - Posterior stroke, negative cardiac evaluation
  - In pre-op eval for carotid endarterectomy

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TIAs, Small CVAs: Small Vessel Dx

- Lacunar infarcts
- 20% of all cerebral ischemic events
- DM, HTN, smoking
- Sub-cortical infarct, < 1.5 cm in size
- Occlusion of a penetrating end artery
- Basal ganglia, thalamus, internal capsule, brainstem locations

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TIAs, Small CVAs: Small Vessel Dx

- Evaluate as with large vessel disease
- Consider MRI, MRA, CTA when:
  - No risk factors
  - Atypical lacunar infarct syndrome
  - Lacune is in an atypical territory
  - Lacunar syndrome, no infarct on CT
- Testing NOT indicated acutely

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TIAs and Small CVAs

- Need to evaluate for future CVA risk
- Large and small vessel disease
- Cardioembolic source
- There is no indication for ED evaluation that includes MRI, MRA, or CTA
- These tests may be used electively in an ED observation protocol
- Not current ED standard of care

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Key Concept

Carotid Doppler, Echocardiography

- Although cardiac echocardiography and carotid Doppler evaluation will determine the etiology of suspected thromboembolic strokes, neither is clinically indicated in order to assess the utility of IV tPA in the ED.
- These tests may be useful in ED observation unit protocols for TIA pt evaluation prior to disposition

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Recommendations for the Emergency Physician

Stroke Pt: Advanced Diagnostics

- Utilize non-contrast CT as test of choice
- Look for hemorrhage, huge MCA lesion, diffuse cerebral edema (no IV tPA)
- Obtain cerebral angiography in critically ill patients for immediate intervention
- Consider CTA, MRA in patients in whom diagnosis or treatment plan uncertain
- TIA: Carotid Doppler, Cardiac Echo

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Key Concept

Stroke Pt Treatment Modalities

- The treatment modalities for ED stroke patients include: IV and intra-arterial thrombolysis with tPA or other thrombolytics, clot retrieval, cerebrovascular stenting, and operative intervention, including carotid endarterectomy or PFO repair

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Key Concept

Stroke Pt: Paired Interventions

- "Double play" is the term used to describe the use of a clot retrieval device followed by the use of intra-arterial tPA to avoid downstream clots from causing further CNS injury. A "triple play" is the above two interventions with carotid artery stenting provided for critical carotid artery stenosis.

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Key Concept

Stroke Pt: New Rx Indications

- These advanced therapies, although potentially beneficial to stroke patients, are neither universally available nor are the current standard of care. They are to be considered when available and feasible to provide, and when they are believed to represent an opportunity for improved stroke patient outcome.

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Intra-arterial Thrombolysis

- Numerous clinical series published
- Basilar artery stroke data suggests benefit
- Benefit with basilar infarct up to 12-24 hrs
- MRI diffusion/perfusion may aid in patent selection

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Intra-arterial Thrombolysis

- Two randomized trials – PROACT 1 & 2
- Prourokinase vs. heparin <6 hours
- MCA occlusions only
- Recanalization improved with IA lysis
- Mortality identical, outcomes variable
- Combined IV tPA and IA lysis not useful

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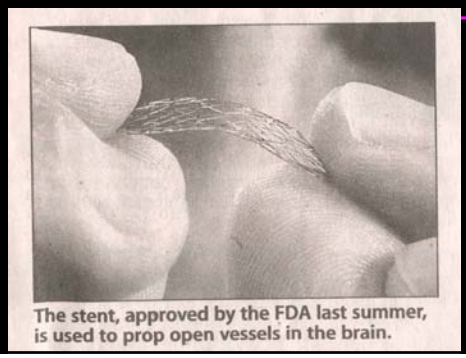
Cerebrovascular Stent



The stent, approved by the FDA last summer, is used to prop open vessels in the brain.

Cerebrovascular Stenting

- May preclude tPA use (less ICH)
- May follow balloon angioplasty
- Requires accessible single lesion (carotid artery)
- Vessel integrity an important issue
- Not a standard therapy in 2006

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Mechanical Clot Removal

- Follows carotid/cerebral angiography
- Neuroradiologist or neurosurgeon
- Window extended to 8 to 12 hours
- Intra-arterial thrombolysis may be given after clot removal in order to prevent emboli downstream (double play)

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Merci Trial: Clot Retrieval

- 151 pts, anterior strokes, Rx <8 hours
- With recanalization (46%)
  - Good outcome (46% vs. 10%)
  - Mortality improved (32% vs. 54%)
- ICH rate 7.8%
- Complications: SAH, device fx, emboli

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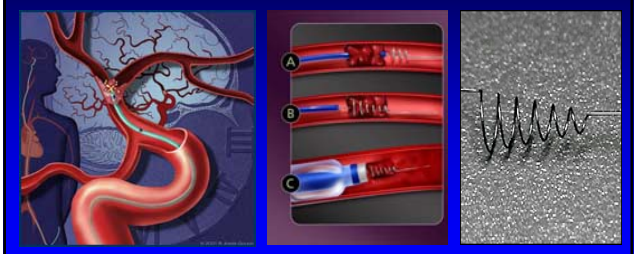
Clot Retriever



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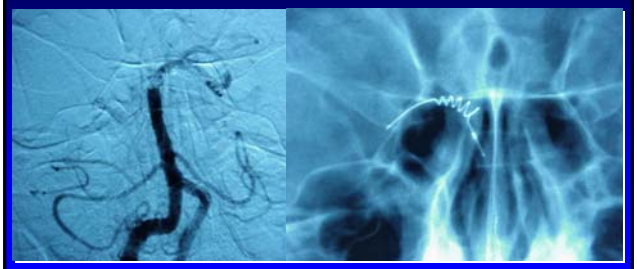
Clot Retriever



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Clot Retriever

Recommendations for the Emergency Physician

Stroke Pt Treatment Modalities

- Attempt to provide IV tPA as able
- Utilize these therapies beyond the 3 hour IV tPA window, or when feasible to provide
- Consider IA thrombolysis still experimental
- Discuss with your consultant which of these interventions can be performed, and in which optimal patient population

New Frontiers in Stroke Pt Management

Key Learning Points

- Non-contrast CT still the test of choice
- MRI may provide insight Re: thrombolysis
- IV tPA still is the treatment of choice
- Isolated IA thrombolysis experimental
- Mechanical interventions require extensive coordination and resource mobilization
- These new frontiers likely pursued fully in comprehensive stroke centers

Questions??

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