

Update On Acute Stroke Intervention

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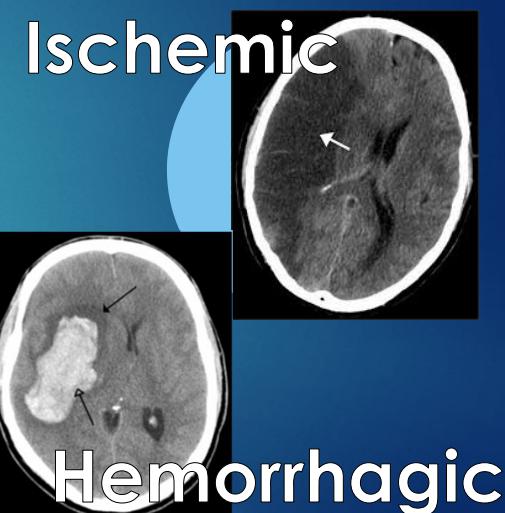
Objectives

- ▶ Know the basic classifications and etiologies of stroke
- ▶ Become familiar with methods of acute stroke assessment
- ▶ Learn the commonly used acute stroke interventions currently available and the recently published trials regarding their use
- ▶ Be able to discuss the method of action of various techniques
- ▶ Review acute stroke radiology studies
- ▶ Be aware of future directions in acute stroke treatment

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What is Stroke?

- ▶ Two types:
 - ▶ Ischemic – occlusion of an artery, loss of blood flow
 - ▶ Hemorrhagic – rupture of a vessel causing accumulation of blood within the brain producing deficits by mass effect or subsequent loss of perfusion
- ▶ Treatment, etiology and outcomes may be different depending on the type of stroke.



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Ischemic Stroke

Major Risk Factors for Stroke

- ▶ Hypertension*
 - ▶ Hyperlipidemia
 - ▶ Diabetes
 - ▶ Smoking
 - ▶ Atrial fibrillation
 - ▶ Heart & Carotid Artery Disease
 - ▶ Excessive alcohol/Illegal Drug Use
 - ▶ Age and Gender
 - ▶ Race & Ethnicity
 - ▶ Personal or family history of stroke

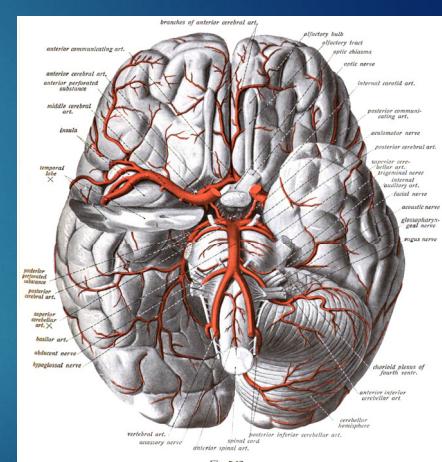
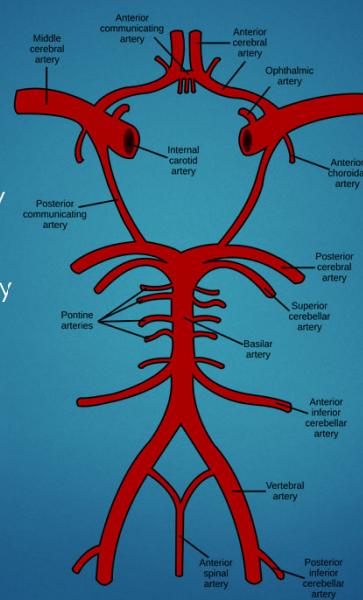


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Cerebral Vascular System

Large Vessels:

- ▶ Anterior Cerebral Artery
 - ▶ Middle Cerebral Artery
 - ▶ Posterior Cerebral Artery
 - ▶ Basilar artery
 - ▶ Vertebral artery
 - ▶ SCA, AICA, PICA

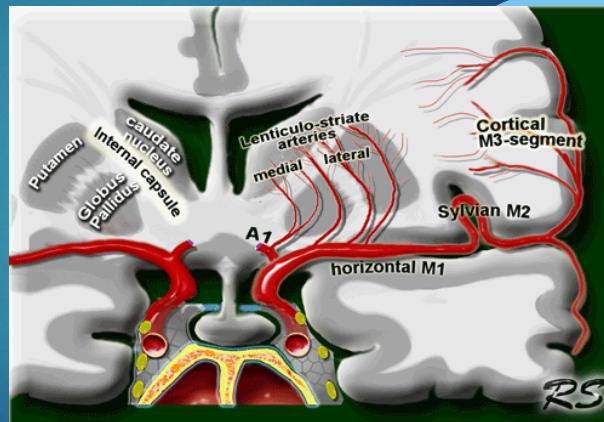


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Cerebral Vascular System

Small Vessels

- ▶ Lenticulostriate arteries
- ▶ Thalamoperforate arteries
- ▶ Brainstem perforators

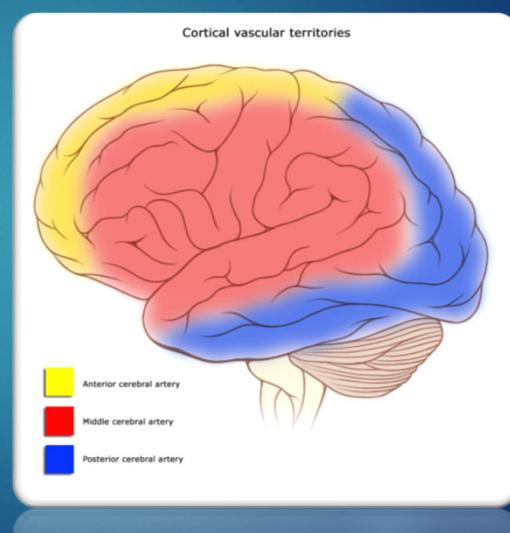


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Cortical Vascular Territories

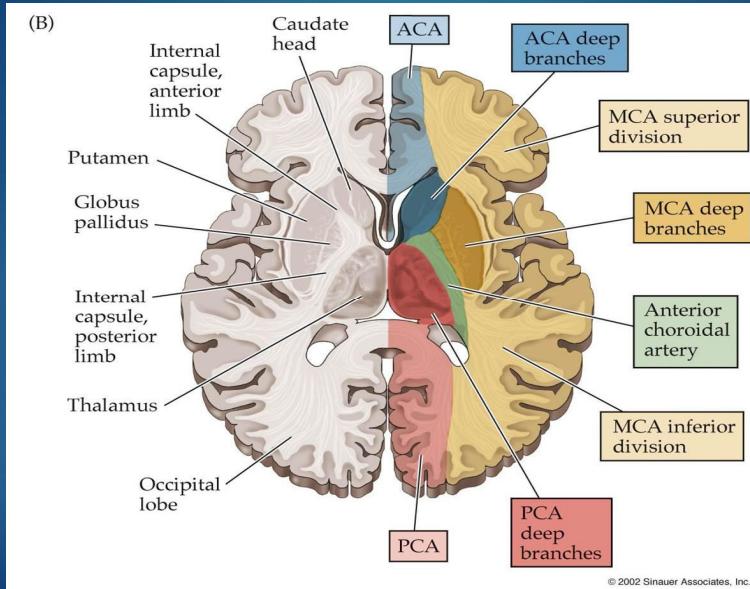
Large Vessel Distribution

- ▶ Anterior Cerebral Artery
- ▶ Middle Cerebral Artery
- ▶ Posterior Cerebral Artery



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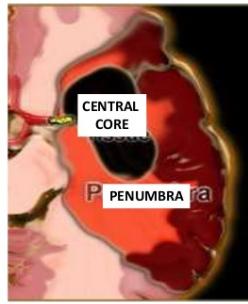
Vascular Territories & Distribution



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Ischemic Stroke Pathophysiology

CONSEQUENCES OF REDUCTION IN BLOOD FLOW DURING STROKE



- ▶ Penumbra is the zone of reversible ischemia around core infarction. This area is potentially salvageable in the first few hours after an ischemic stroke onset.

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Time Lost = Brain Lost

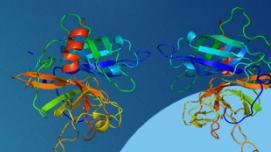


- ▶ During a stroke, 2 million neurons can die every minute.
- ▶ Strokes must be treated emergently. Every minute in delay of treatment affects functional outcome.

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What Have You Heard About IV Alteplase (tPA)?

- ▶ What is it?
 - ▶ Alteplase, a recombinant tissue-plasminogen activator (**r-tPA**)
 - ▶ Serine protease found naturally on the lining of blood vessels (endothelium)
 - ▶ Catalyzes conversion of plasminogen to plasmin, an enzyme that catalyzes the breakdown of proteins such as fibrin, a major component of blood clots
 - ▶ Goal is to initiate thrombolysis of clots present arterial circulation, specifically intracranial in the case of stroke.



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What Have You Heard About IV tPA?

- ▶ How is it used?
 - ▶ Suspected acute ischemic stroke within 3 to 4.5 hours from last seen normal.
 - ▶ Administered via peripheral IV line with an initial bolus followed by a 1 hour infusion, and the patient is monitored in an ICU-level of care for 24 hours followed by a CT to confirm no hemorrhagic conversion.
 - ▶ Using strict inclusion and exclusion criteria originally based on the National Institute of Neurologic Disorders and Stroke (NINDS) study for acute stroke in the 90s, subsequently revised after more recent trials, such as the European Cooperative Acute Stroke Study (ECASS).

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What Have You Heard About IV tPA?

- ▶ Exclusions 0-4.5 Hour Window
 - ▶ ONLY Absolute: Cerebral hemorrhage on CT scan or suspected SAH
 - ▶ Relative contraindications: Previous ICH or brain tumor, stroke or MI in past 3 month, major surgery in past 14 days, GI/GU bleeding in past 21 days, NIHSS <4, BP >185/105 mm Hg, anticoagulant use (warfarin with INR > 1.7 or newer oral in last 2 days), other bleeding coagulopathy, therapeutic heparin use within 48 hours or significantly elevated aPTT, platelets <100 k, symptoms related to hypoglycemia or post-ictal period, patient or family refusal.

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What Have You Heard About IV tPA?

► Risks?

- ▶ Bleeding
- ▶ Cerebral hemorrhage is the primary concern
 - ▶ Classification 1: **Symptomatic** Pt develops symptoms from hemorrhage, including worsening of stroke symptoms, NIHSS difference > 4 from initial NIHSS, new neurologic symptoms, coma, death.
 - ▶ Classification 2: **Asymptomatic** Pt develops secondary hemorrhage after administration of tPA, typically found incidentally on follow-up imaging.
- ▶ Overall mortality not significantly different across stroke patients treated with IV tPA versus conventional care in earlier studies.



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What Is Beyond IV Thrombolytics?

- ▶ Intra-arterial (IA) thrombolytics
- ▶ Endovascular clot disruption and retrieval
- ▶ Hemicraniectomy



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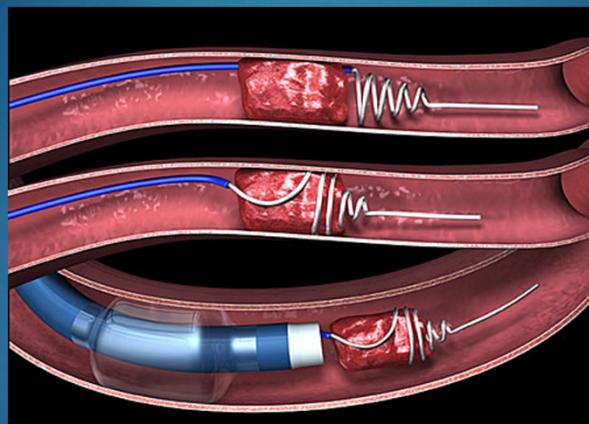
Intra-arterial (IA) Thrombolytic Therapy

- ▶ What is it?
 - ▶ Same tPA used peripherally, is administered via arterial catheter directly to the clot in the cerebral vasculature
- ▶ How is it used? With the advent of clot retrievers and stents, IA therapy is rarely used anymore.
 - ▶ Primary therapy : patients beyond IV tPA window, typically up to 6 hours
 - ▶ Adjunctive therapy: patients with continued severe deficit after IV tPA who have a persistent visualized occlusion on angiography.



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Endovascular Clot Disruption and Retrieval



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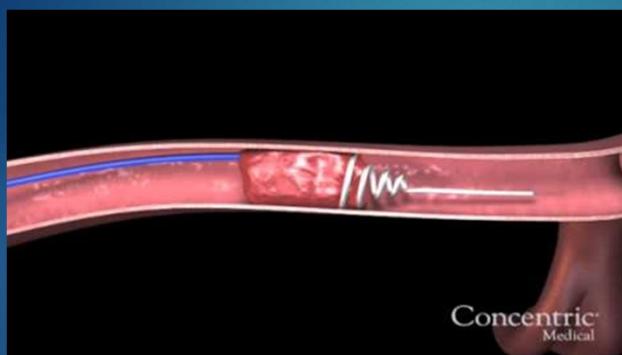
Endovascular Clot Retrieval

- ▶ What is it?
 - ▶ A device that is catheter-based and inserted into the clot in the brain and meant to disrupt and remove it (recanalization).
- ▶ How is it used?
 - ▶ Primary therapy: for patients beyond the window of IV tPA, up to 24 hours (Dawn Trial). Or, in the case of patients with coagulation/bleeding contraindications.
 - ▶ Adjunct therapy: for patients treated with IV tPA with persistent deficits and proximal artery occlusions seen on angiography.
 - ▶ Examples: MERCI, PENUMBRA, SOLITAIRE



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Endovascular Clot Retrieval

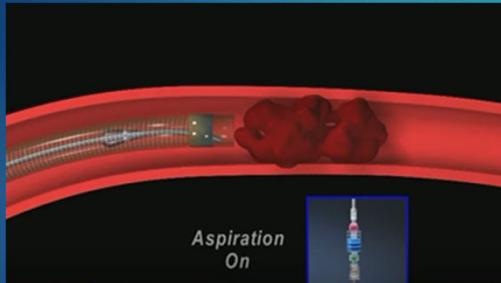


MERCI is the first FDA mechanical thrombectomy device designed as a corkscrew -shaped distal catheter to remove large clots from intracranial vessels.

MERCI Clot Retrieval Animation- You Tube
[SSMDePAUL](#)
<https://www.youtube.com/watch?v=MGX7deuFkhc>

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Endovascular Clot Retrieval



- Penumbra System is mechanical thrombectomy device designed to aspirate large intracranial vessels in acute ischemic stroke.

Penumbra Stroke System
[ChicagoEndovascular](#)
<https://www.youtube.com/watch?v=ajcqsAr6K2A>

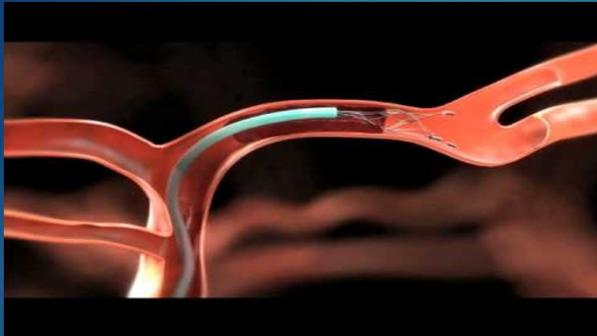
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Endovascular Stent Retrievers

- Similar concept, approach and indications/usage as other endovascular devices except it opens a wire mesh within the clot to recanalize while clot is retrieved.



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Solitaire FR Revascularization is a mechanical thrombectomy device to restore blood flow and retrieve clot in patients experiencing an acute ischemic stroke

Solitaire™ FR Revascularization Device Animation

StrokeCareNow Network

<https://www.youtube.com/watch?v=eFVT9T47CFI>

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Endovascular Therapies

- ▶ Overall, these modalities are used typically in conjunction with one another.
- ▶ IV tPA is recommended to be given prior to attempting clot retrieval if no contraindication to thrombolytics.
- ▶ Involves use of contrast media for angiography, making this challenging for patient with allergies or renal issues but may still will proceed regardless of renal function .
- ▶ Complications associated with procedure in addition to those for stroke and thrombolytic therapy.

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Encouraging Early Trials with Mechanical Thrombectomy Within 6 Hours of Symptom Onset

Five published clinical trials announced positive outcomes for endovascular therapies in stroke management of large vessel occlusion.

- ▶ MRCLEAN – Dec 2014
- ▶ ESCAPE – Feb 2015
- ▶ SWIFT-PRIME – Feb 2015
- ▶ EXTEND-IA – Feb 2015
- ▶ REVASCAT- Sept 2015

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Mechanical Thrombectomy Within 6 Hours: Conclusions from Early Trials

- ▶ Compared to older studies, faster times of reperfusion of occluded artery suggests earlier time to reperfusion is associated with better outcome.
- ▶ For acute ischemic stroke with proximal artery occlusion, endovascular therapy within 6 hrs of onset is associated with an improved functional outcome at 3 months, without increase in mortality
- ▶ Produced higher rates of function independence (mRS) at 90 days
- ▶ No significant increase in symptomatic ICH with endovascular treatments

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Pitfalls for Acute Stroke Interventions

- ▶ Currently, ALWAYS consider IV tPA first
- ▶ Cannot use endovascular therapies if there is no target
 - ▶ Must have CT angio evidence of occlusion, typically up to proximal M2, basilar or PCA P1/P2 segment for retriever.



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Pitfalls for Acute Stroke Intervention Continued

- ▶ Is patient not eligible for IV tPA? They may still be eligible for clot retrievers!
 - ▶ Can still use with bleeding risks associated with IV tPA, such as anticoagulants, recent surgeries, bleeding diatheses, etc.
- ▶ Consent (even verbal) should NOT delay IV tPA. TIME IS BRAIN.
 - ▶ Institutionally dependent. UF Health Jacksonville/Brown (RIH) required documented VERBAL consent or two physician consensus.
 - ▶ A physician may act in the best interest of a patient not capable of consenting and without reasonable availability of proxy for consent.
 - ▶ Most recently proposed recommendations suggest against need for consent, though it would always be a good idea to discuss with patient/family, if they are available and capable.

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Modified Rankin Scale (mRS)

- ▶ A standardized rating scale for functional disability
- ▶ Commonly used in stroke literature as an outcome measure, typically at intervals over 90 day period after event

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

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Mechanical Thrombectomy Extended to 6-24 Hours in DAWN and DEFUSE 3 Trials

- ▶ Advanced imaging with CT Perfusion, MRI/MR Perfusion to select patients extends thrombectomy benefits to 6-24 hours from symptom onset changing the paradigm for management of acute ischemic stroke.
- ▶ Both trials show large benefit with favorable functional outcome at 90 days with modified Rankin scale (mRS) score of 0-2.

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- ▶ They treated acute stroke within 24 hours of time last seen normal, with high stroke severity (NIHSS ≥10) with "clinical imaging mismatch" criteria based on CTA, CTP, utilizing RAPID software, and with treatment criteria based on age (> or < 80 yrs), and volume of "core" on perfusion imaging.
- ▶ **49% compared to 13% ("standard" care, control)** with favorable functional outcome at 90 days, modified Rankin scale (mRS) score of 0-2 (no disability to mild disability with functional independence)
- ▶ The "number needed to treat" of 2.8, meaning 1 in every 2.8 people would have a favorable outcome from treatment. This is GREAT!
- ▶ Endovascular therapy for 6-16 hrs based on core size to penumbra (<70 ml), No NIHSS requirement.
- ▶ No minimum severity, no age limit, based on core size to penumbra (<70 ml, 1.8 ratio), utilizing RAPID software with CTA/CTP.
- ▶ **45% compared to 17% ("standard care", control)** with favorable functional outcome at 90 days, mRS 0-2.
- ▶ Echoes the DAWN trial in outcome, but was **MORE INCLUSIVE**. Nearly 40% of patients treated would not have met criteria based on DAWN trial

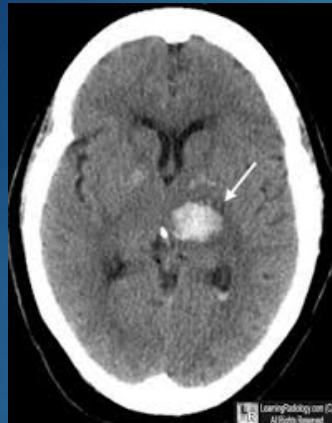
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Acute Radiology Studies in Stroke

- ▶ Non-contrast CT head (NCCT)
- ▶ CT angiogram (CTA) of head and neck carotid
- ▶ Magnetic resonance imaging (MRI) brain wo contrast
- ▶ CT brain perfusion with contrast

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Non-contrast CT Head



Hemorrhagic strokes are denser (white) on CT

- ✓ Acute stroke evaluation - Is this patient a IV tPA candidate?
CT is usually the first diagnostic study in a suspected acute stroke for decision of management. Primary goal is to exclude a hemorrhagic stroke.

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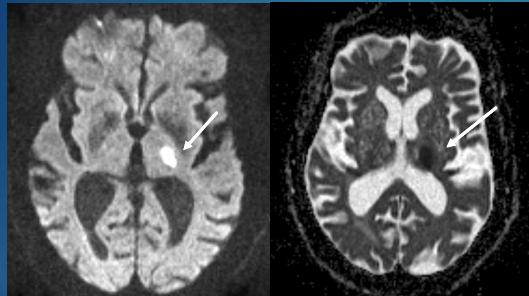
CTA or MRA Head and Neck Carotid



- ✓ Acute stroke evaluation- Is there arterial stenosis or major occlusion in the head or Neck carotid amendable for IV tPA or endovascular intervention?
CTA or MRA on intracranial vessels assist with detection of vascular occlusions in the head and neck carotid.

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MRI Brain



DWI

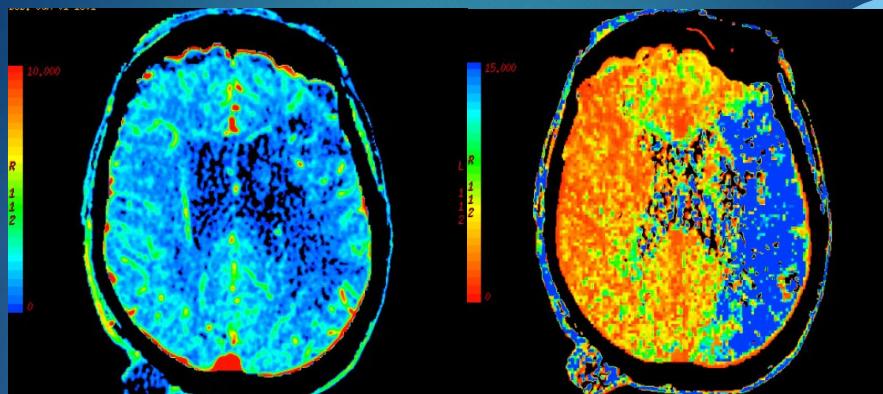
ADC

- white area on DW
- black area on corresponding ADC

- ✓ Acute stroke evaluation- Identify location and size of an acute ischemic stroke. MRI shows brain integrity, identifies acute ischemic lesions, and approximates core size of infarct. Hyper-acute MRI has less views and can be completed in about 10 minutes.

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CT Perfusion



- ✓ Acute stroke evaluation - Is penumbra salvageable?
Using contrast, vasculature is mapped to show patterns of ischemic core and penumbral region.

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WATCHING THE CLOCK

By AMERICAN HEART ASSOCIATION NEWS

Under new treatment guidelines, people having mild strokes can now be considered for a medication given within several hours to help dissolve a clot. Clot-snaring devices can also now be used up to 24 hours after the start of a stroke in some patients with clots blocking a large vessel in the brain.

Source: American Heart Association/American Stroke Association
Published: Jan. 24, 2018

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Prehospital Stroke Management and Systems of Care

1.5 Hospital Stroke Teams

Stroke centers should have:

- Organized protocol for emergent evaluation of suspected stroke
- Designated acute stroke team
- Among patients receiving IV alteplase:
 - Primary goal:** door to needle time of 60 minutes or less in ≥50% of cases
 - Secondary goal door-to-needle time of 45 minutes or less in ≥50% of cases may be reasonable

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Emergency Evaluation

2.2 Brain Imaging




Advanced Imaging:

- Vascular and perfusion imaging should not delay alteplase treatment
- Use of imaging to select AIS cases for alteplase treatment with uncertain symptom duration is not recommended
- For patients who meet criteria for endovascular treatment, it is reasonable to proceed with CTA
 - Clinical prediction of LVO is imprecise.
 - NIHSS is best instrument, but even cut-point of ≥ 6 will miss cases of LVO
 - No need to wait for creatinine

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Stroke Alert – Identification

Stroke Identified – Stroke alert paged out (received by all those involved with care)

- ▶ In the field (EMS)
- ▶ ED (triage, nurse, provider)
- ▶ Symptom onset during presentation

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Stroke Alert – Initial Evaluation

Initial Evaluation

- ▶ National Institute of Health Stroke Scale (NIHSS) by physician
 - ▶ Takes about 3-5 minutes
 - ▶ Abbreviated and standardized neurologic examination
 - ▶ Higher score indicates severity of symptoms. Greater than 4 considered inclusion criteria for IV tPA, but can treat for lower score with debilitating symptoms (isolated language, single extremity weakness, spatial neglect, visual loss, etc).
- ▶ Lab work (BMP, PT/INR, PTT, CBC).
- ▶ Only Glucose must precede IV tPA to rule out hypoglycemia. Stroke alert patients are exempt from lab requirements prior to CT contrast administration (**Policy #RAD-03-019**)
- ▶ EKG, Chest XR should not delay tPA.

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From the time of IV tPA administration, nursing documents vital signs and neurologic assessment on the Post Stroke Assessment (PSAT) in real time in EPIC. This is now the “focused neuro exam” flow sheet. A BPA will pop up during the 24 hours after bolus, as a reminder for the assessments.

- ▶ Every 15 minutes for 2 Hours
- ▶ Every 30 minutes for 6 hours
- ▶ Every hour for 16 hours



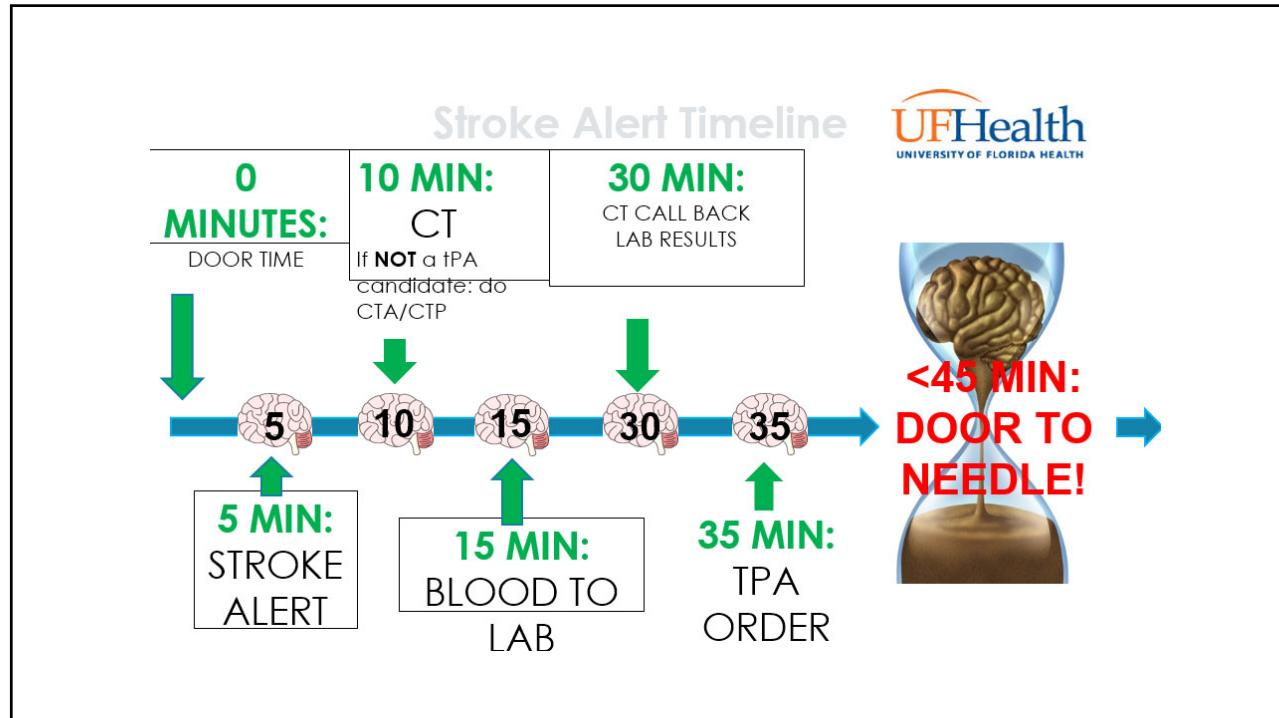
✓ If you have any questions regarding stroke, feel free to contact the Stroke Coordinator or Nurse Educator

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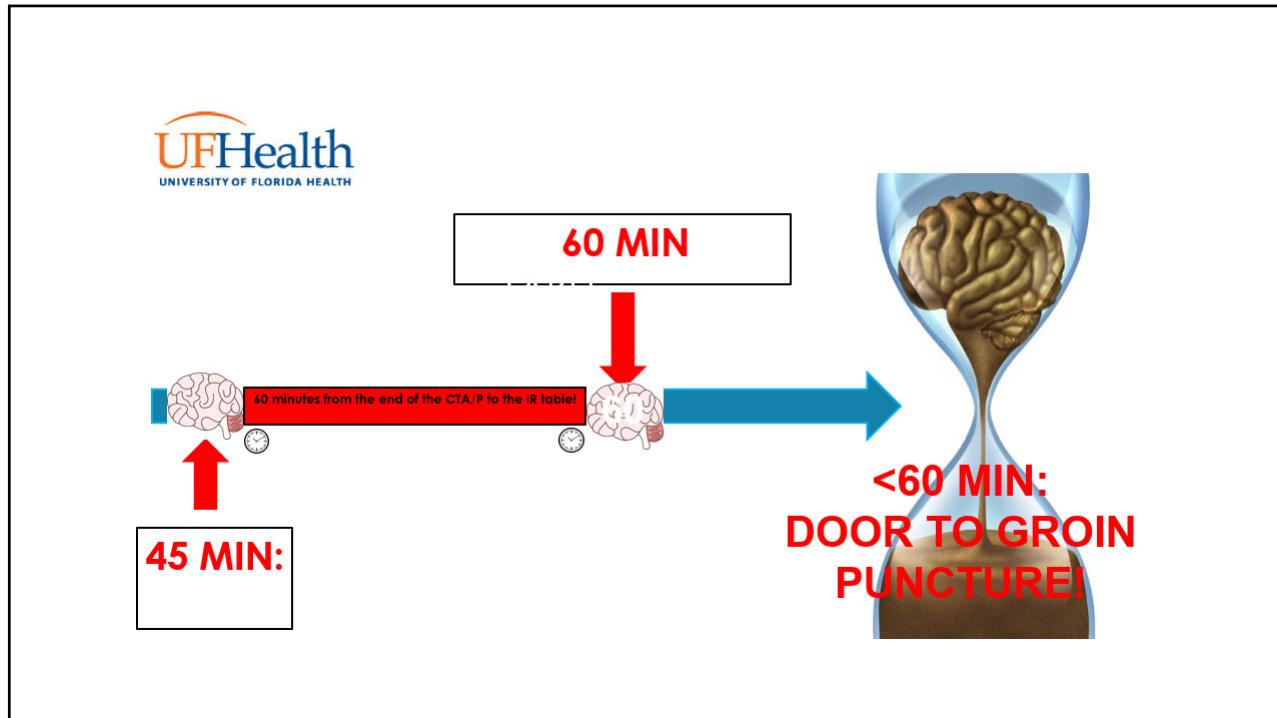
Stroke Alert – Treatment Pathway

- ▶ IV tPA vs IV tPA + intervention
 - ▶ NIHSS score of <6: IV tPA alone (if meets criteria)
 - ▶ NIHSS score of 6 or greater: IV tPA plus intervention (if meets criteria)

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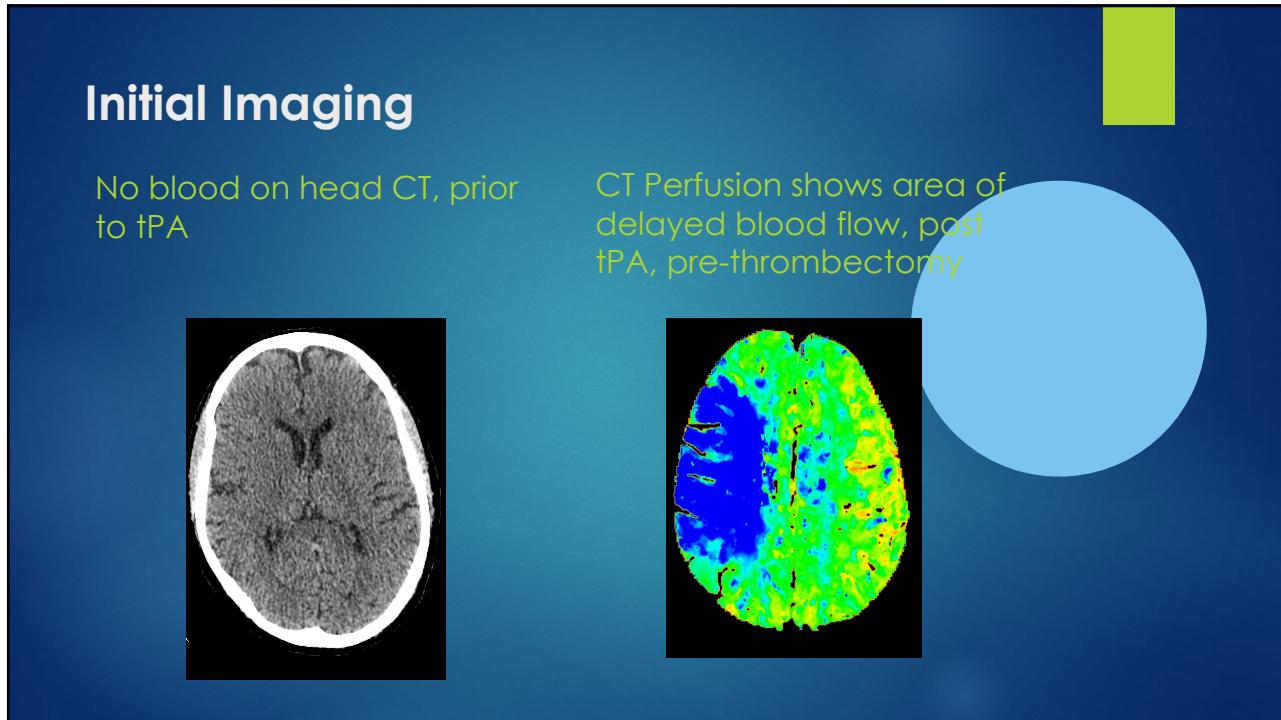


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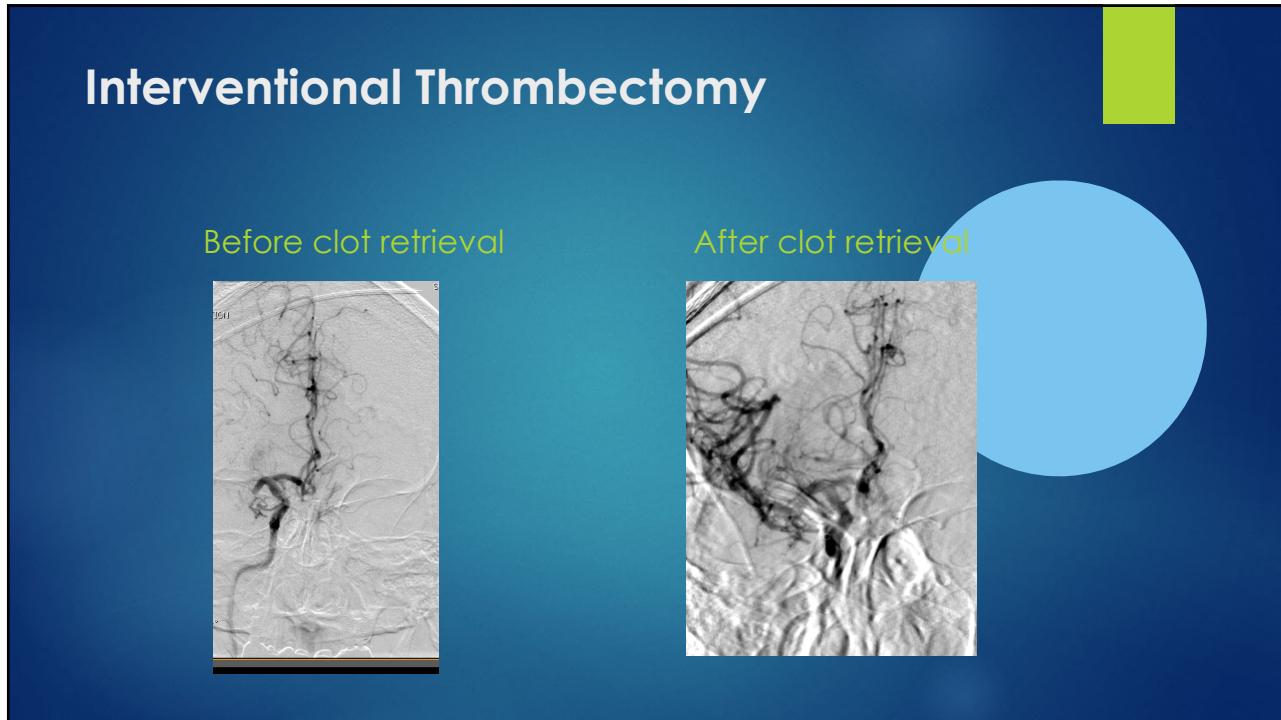
Case Study: Adult Male

- ▶ Last Time Seen Normal (LTSN) was 12:30
- ▶ Arrival to ED by EMS, 15:53; stroke alert upon arrival
- ▶ NIHSS score= 6
- ▶ CT head 16:00
- ▶ tPA order 16:10
- ▶ tPA bolus 16:18
- ▶ CTA/CTP 16:22
- ▶ Groin Puncture 17:31
- ▶ Reperfusion 19:05

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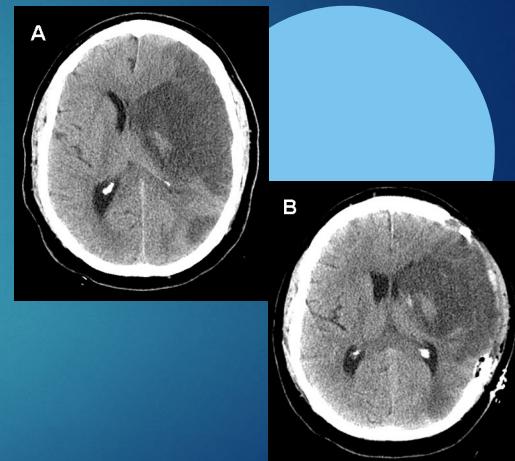
Hemicraniectomy

What is this?

- ▶ Surgical decompressive therapy for malignant stroke
- ▶ Commonly used in MCA territory, but posterior decompression can also be done in cerebellar or brainstem infarcts.
- ▶ Controlled herniation of the edematous brain
- ▶ Based on DESIMEL (2007), Hamlet (2009) and DESTINT II (2015) TRIALS

How it is used:

- ▶ Within 48 hours on onset
- ▶ Preferably in non-language dominant hemisphere
- ▶ Significant mass effect present



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- ▶ [Sequential-Design, Multicenter, Randomized, Controlled Trial of Early Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarction \(DECIMAL Trial\)](#)
- ▶ Patient **under age 55** with a malignant MCA stroke who receive hemicraniectomy within a mean of **20.5 hours** have significantly better outcomes at 6 and 12 month and less death compare to those who do not receive hemicraniectomy.

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(DECIMAL Trial) (2007)

- ▶ **Background and Purpose**—There is no effective medical treatment of malignant middle cerebral artery (MCA) infarction. The purpose of this clinical trial was to assess the efficacy of early decompressive craniectomy in patients with malignant MCA infarction.
- ▶ **Methods**—Conducted in France a multicenter, randomized trial involving patients between **18 and 55 years of age** with malignant MCA infarction to compare functional outcomes with or without decompressive craniectomy.
- ▶ A sequential, single-blind, triangular design was used to compare the rate of development of moderate disability (modified Rankin scale score <3) at 6 months' follow-up (primary outcome) between the 2 treatment groups.

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(DECIMAL Trial) 2007

- ▶ **Results**—After randomization of **38 patients**, the data safety monitoring committee recommended stopping the trial because of slow recruitment and organizing a pooled analysis of individual data from this trial and the 2 other ongoing European trials of decompressive craniectomy in malignant MCA infarction. Among the 38 patients randomized, the proportion of patients with a modified Rankin scale score < 3 at the 6-month and 1-year follow-up was 25% and 50%, respectively, in the surgery group compared with 5.6% and 22.2%, respectively, in the no-surgery group ($P=0.18$ and $P=0.10$, respectively). There was a 52.8% absolute reduction of death after craniectomy compared with medical therapy only ($P=0.0001$).
- ▶ **Conclusions**—In this trial, early decompressive craniectomy increased by more than half the number of patients with moderate disability and very significantly reduced (by more than half) the mortality rate compared with that after medical therapy.

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Hemicraniectomy after middle cerebral artery infarction with life-threatening Edema trial (HAMLET)

- ▶ Patients with a hemispheric infarct and massive space-occupying brain edema have a poor prognosis. Despite maximal conservative treatment, the case fatality rate may be as high as 80%, and most survivors are left severely disabled. Non-randomized studies suggest that decompressive surgery reduces mortality substantially and improves functional outcome of survivors. This study was designed to compare the efficacy of decompressive surgery to improve functional outcome with that of conservative treatment in patients with space-occupying supratentorial infarction

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Hemicraniectomy after middle cerebral artery infarction with life-threatening Edema trial (HAMLET)

- ▶ Dutch, randomized, control trial -2009
- ▶ Randomized 64 pts up to **60 years old with large MCA infarct to hemicrania vs best medical management** up to 4 days of stroke onset.
- ▶ Based on this study, surgical decompression **within 4 days** for the treatment of malignant MCA is no better than best medical therapy for good functional outcome at 1 year but does significantly reduce case fatality rate.
- ▶ As part of meta analysis it did improve functional outcome compared to medical therapy when done within **2 days** and where good outcome is defined as an MRS of 0-3.

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DESTINY II TRIAL- 2014

- ▶ **Hemicraniectomy in Older Patients with Extensive Middle-Cerebral-Artery Stroke**
- ▶ **BACKGROUND**
- ▶ Early decompressive hemicraniectomy reduces mortality without increasing the risk of very severe disability among patients 60 years of age or older with complete or subtotal space-occupying middle-cerebral-artery infarction.
- ▶ **METHODS**
- ▶ Randomly assigned 112 patients **61 years of age or older (median, 70 years; range, 61 to 82)** with malignant middle-cerebral-artery infarction to either conservative treatment in the intensive care unit (the control group) or hemicraniectomy (the hemicraniectomy group); assignments were made within **48 hours** after the onset of symptoms. The primary end point was survival without severe disability (defined by a score of 0 to 4 on the modified Rankin scale, which ranges from 0 [no symptoms] to 6 [death]) 6 months after randomization.

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DESTINY II TRIAL- 2014

- ▶ **RESULTS**
- ▶ **Hemicraniectomy** improved the primary outcome; the proportion of patients who survived without severe disability was 38% in the hemicraniectomy group, as compared with 18% in the control group (odds ratio, 2.91; 95% confidence interval, 1.06 to 7.49; **P=0.04**). This difference resulted from lower mortality in the surgery group (33% vs. 70%). No patients had a modified Rankin scale score of 0 to 2 (survival with no disability or slight disability); 7% of patients in the surgery group and 3% of patients in the control group had a score of 3 (moderate disability); 32% and 15%, respectively, had a score of 4 (moderately severe disability [requirement for assistance with most bodily needs]); and 28% and 13%, respectively, had a score of 5 (severe disability). Infections were more frequent in the hemicraniectomy group, and herniation was more frequent in the control group.
- ▶ **CONCLUSIONS**
- ▶ Hemicraniectomy increased survival without severe disability among patients 61 years of age or older with a malignant middle-cerebral-artery infarction. The majority of survivors required assistance with most bodily needs.

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Questions

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