# Stroke Guidelines Update 2018

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# Disclosures

- Dr. Adams has provided no disclosures.

# Objectives

- Discuss the common clinical presentations of stroke (ischemic and hemorrhagic)
- Review basic neuroanatomy
- Discuss acute stroke interventions
- Discuss Evaluation of Stroke
- Discuss Management & Secondary Prevention

## CLASS (STRENGTH) OF RECOMMENDATION

**CLASS I (STRONG)** — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

**CLASS IIa (MODERATE)** — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

**CLASS IIb (WEAK)** — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

**CLASS III: No Benefit (MODERATE)** — **Benefit = Risk**
*(Generally, LOE A or B use only)*

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

**CLASS III: Harm (STRONG)** — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

## LEVEL (QUALITY) OF EVIDENCE‡

**LEVEL A**
- High-quality evidence‡ from more than 1 RCTs
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

**LEVEL B-R (Randomized)**
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

**LEVEL B-NR (Nonrandomized)**
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

**LEVEL C-LD (Limited Data)**
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

**LEVEL C-EO (Expert Opinion)**

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

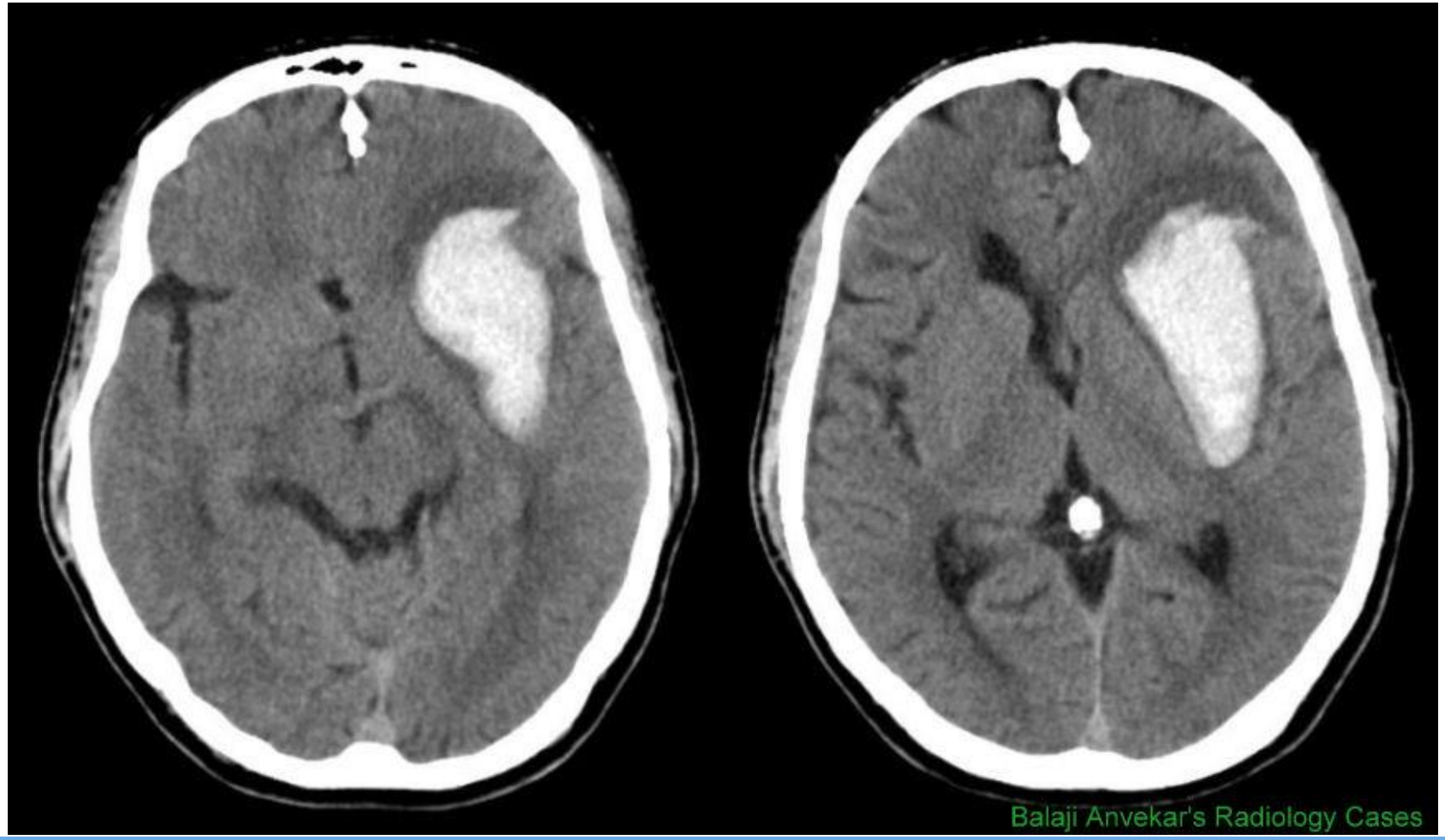
COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

# HEMORRHAGIC STROKE

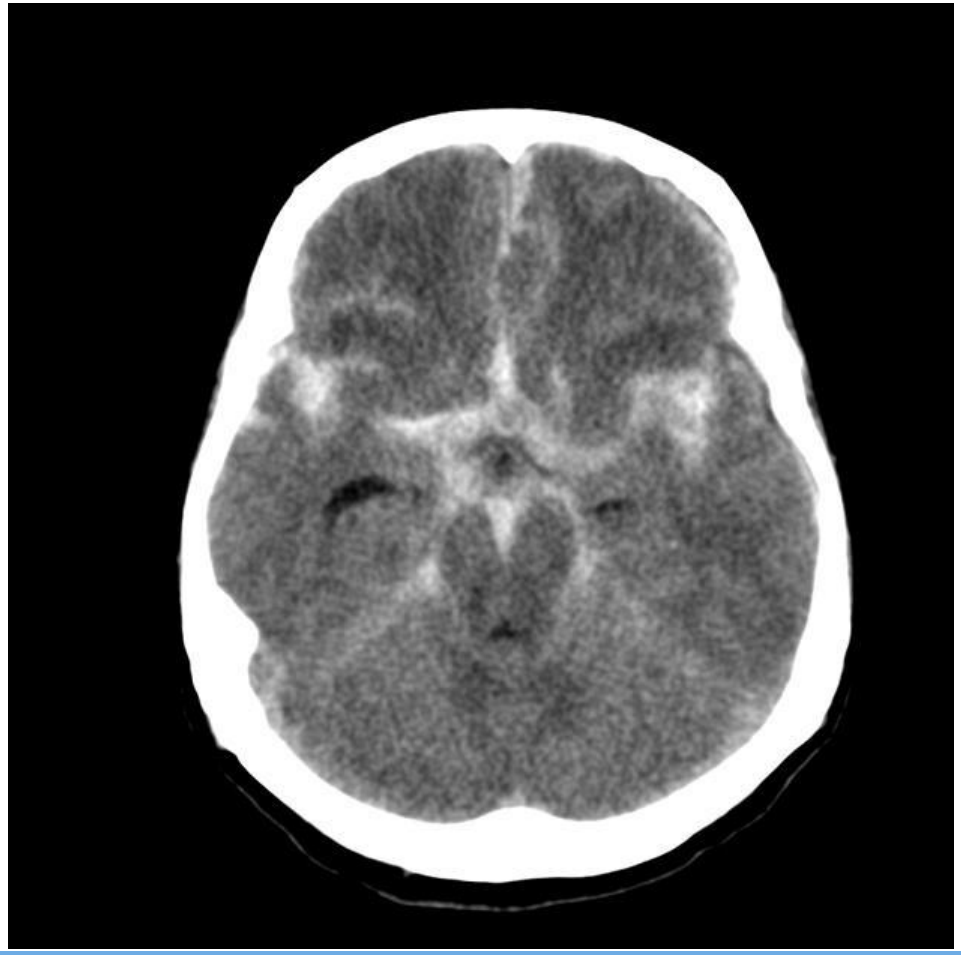
# Clinical Presentation-Hemorrhagic

- ICH
  - Abrupt onset focal neurologic symptoms, often have **headache**, **nausea/vomiting** common, **progressive deficits** (as bleed increases in size)
- SAH
  - Abrupt onset "**worst headache of life**", often impaired consciousness
  - Neurologic deficits can be focal or global depending on where the hemorrhage occurred

# Intracranial Hemorrhage



# Subarachnoid Hemorrhage



# Management of ICH

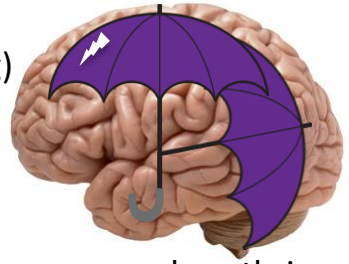
- Coagulopathy reversal
  - On warfarin:
    - INR >1.4: give Vit K + PCC
      - PCC may be better than FFP (IIb)
  - On Heparin
    - Protamine Sulfate (IIb)
  - On Rivaroxaban, Apixaban, or Dabigatran
    - FEIBA or other PCC or NovoSeven (IIb)
  - On antiplatelets
    - Platelet transfusion is of unclear benefit (IIb)
  - On nothing
    - Don't give anything unless they have a documented coagulopathy, in which case replace what they're missing (I)
- Blood Pressure
  - If BP >150 then consider lowering to <140 which is safe and can improve outcomes (IIa)
- Seizures
  - Treat them if they happen (I)
  - No role for prophylaxis (III)
- Edema and increased ICP
  - Don't give steroids (III)

Stroke. 2015;46:2032–2060

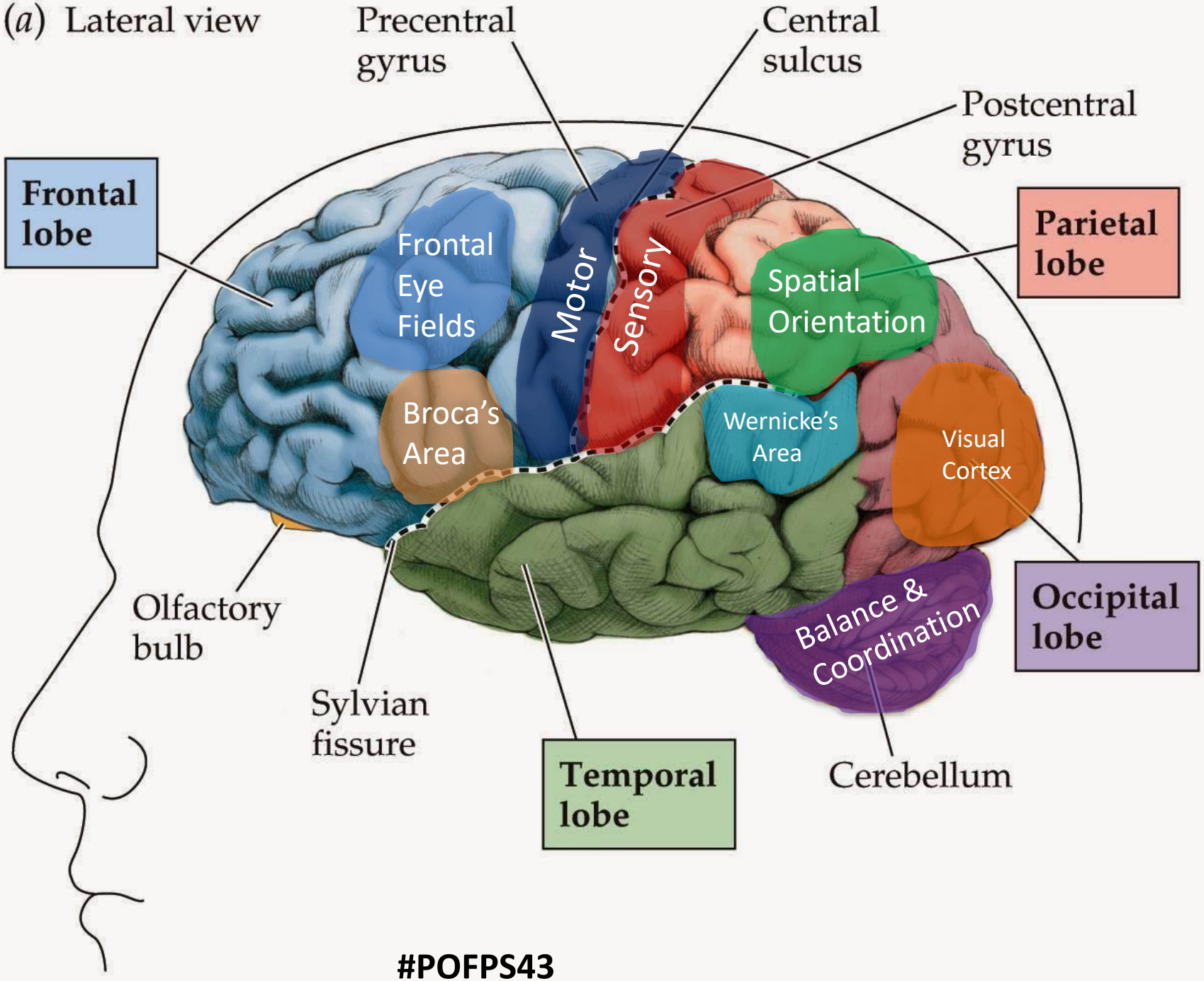
# ISCHEMIC STROKE

# Clinical Presentation-Ischemic

- Ischemic Stroke
  - Abrupt onset, typically no pain (headache *rare*), typically **maximal symptoms at onset**
  - **Symptoms may vary depending on location of ischemia**
  - Anterior Circulation
    - Symptoms
      - Weakness, aphasia, sensory loss, neglect, gaze preference, dysarthria, visual loss
      - Unilateral presentation
        - » Cortical Stroke = differential weakness (e.g. arm>>leg)
        - » Subcortical Stroke = non-differential (face=arm=leg)



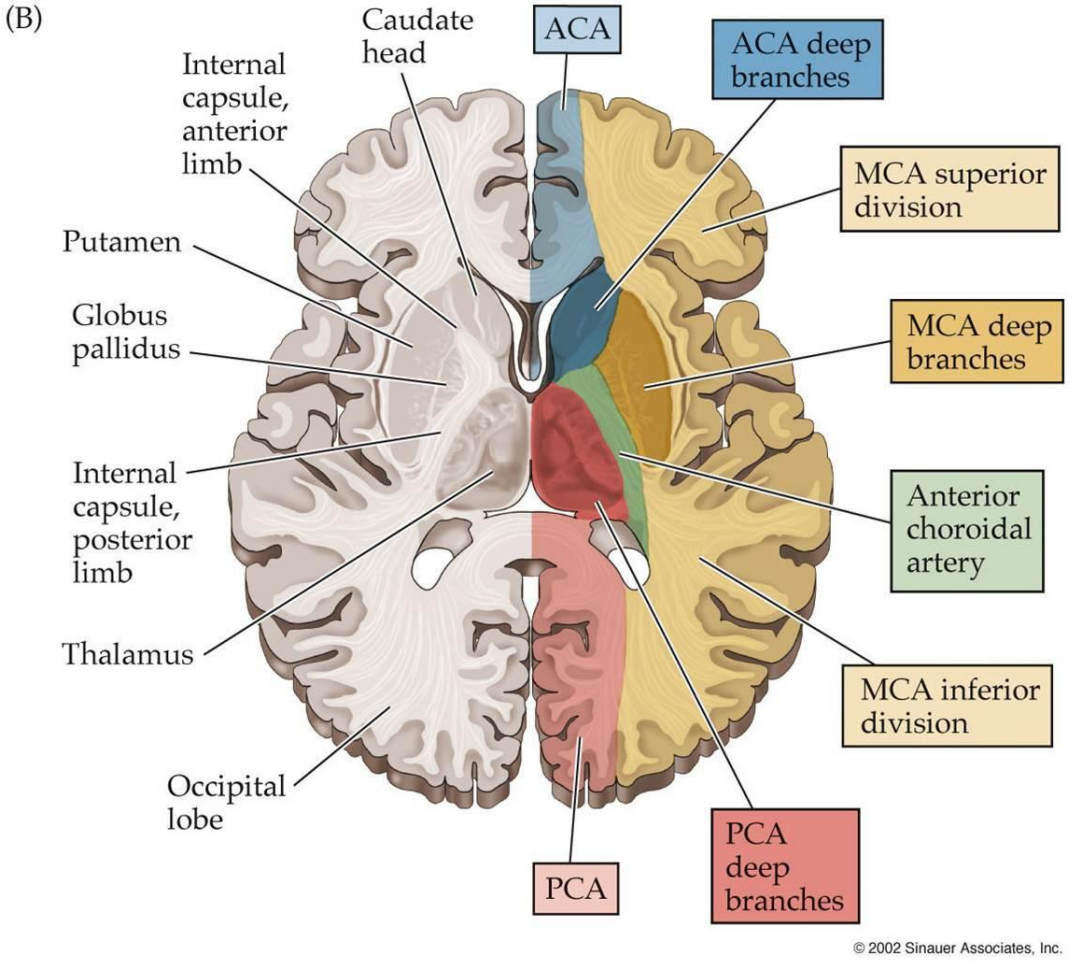
  - Posterior Circulation
    - Symptoms
      - Ataxia/vertigo, cranial nerve findings, impaired consciousness, severe dysarthria, visual loss/diplopia
      - Often Crossed Findings
        - » E.g. Left facial droop, right arm/leg weakness




#POFPS43

Biological Psychology 6e, Figure 2.12 (Part 1)

# Vascular Territories



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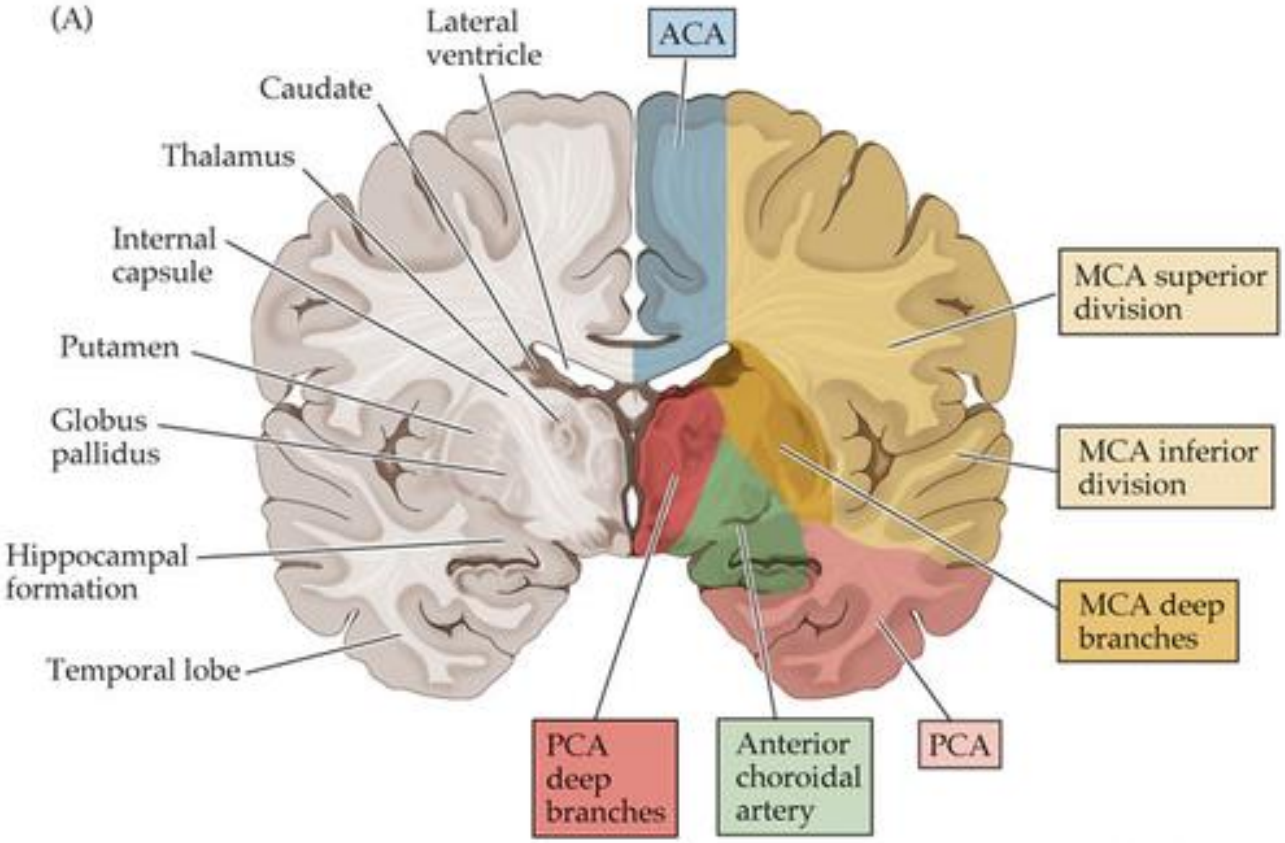
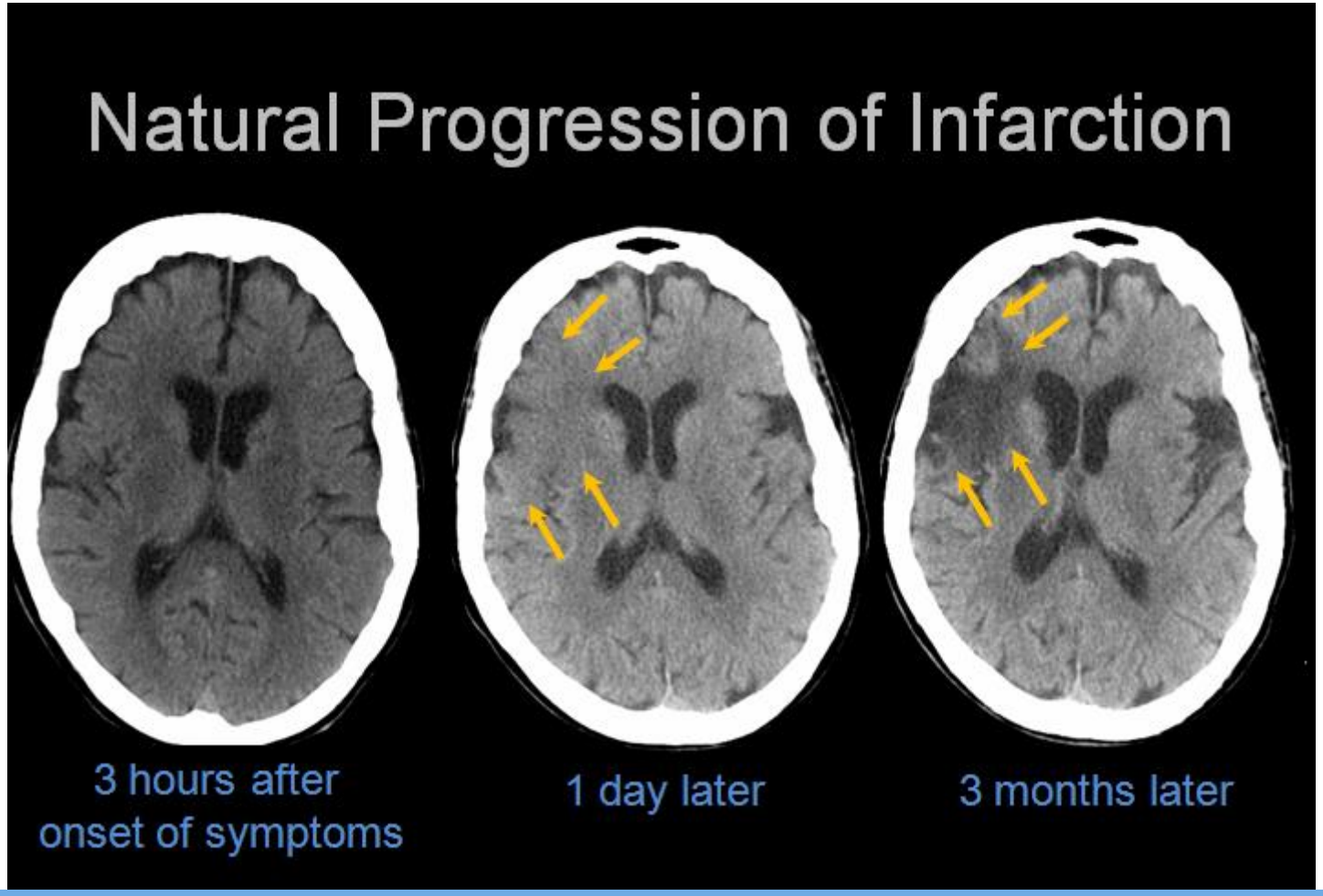


# Ischemic Stroke



# EMERGENT DIAGNOSTICS AND MANAGEMENT

# Imaging

- Patients with suspected stroke should have a NCCT done within 20 minutes of arrival (I)
- There is insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to tPA (III)
  - But tPA should not be used when there is extensive hypodensity
- Use of multimodal CT or MRI should not be used to select patients for tPA in setting of wake-up stroke or unclear time of onset (III)
- Perfusion studies should not be used in selecting patients for endovascular treatment in <6hr window (III)

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- ~~Perfusion studies should not be used in selecting patients for endovascular treatment in <6hr window (III)~~

# Labs etc.

- Finger stick glucose should be checked for all suspected stroke patients (I)
  - If Hypoglycemic <60mg/dL
    - Treat with Dextrose (I)
  - Optimal glucose management 140-180 (IIa)
- Troponin should be ordered, but not delay tPA (I)
- EKG should be obtained, but not delay tPA (I)

# Perfusion

- Hypotension & hypovolemia should be corrected to maintain organ function (I)
- BP <185/110 is recommended for use of IV tPA (I) and for patients with planned mechanical thrombectomy (IIa)
- BP<220/110 who don't get tPA should have BP lowered by 15% in first 24hrs (IIb)

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# Temperature

- Treatment of fever >38 should include search for source of infection and treatment with antipyretics (I)
- Hypothermia should be used in context of clinical trials as its efficacy is not established (IIb)

# ACUTE INTERVENTION

# IV tPA

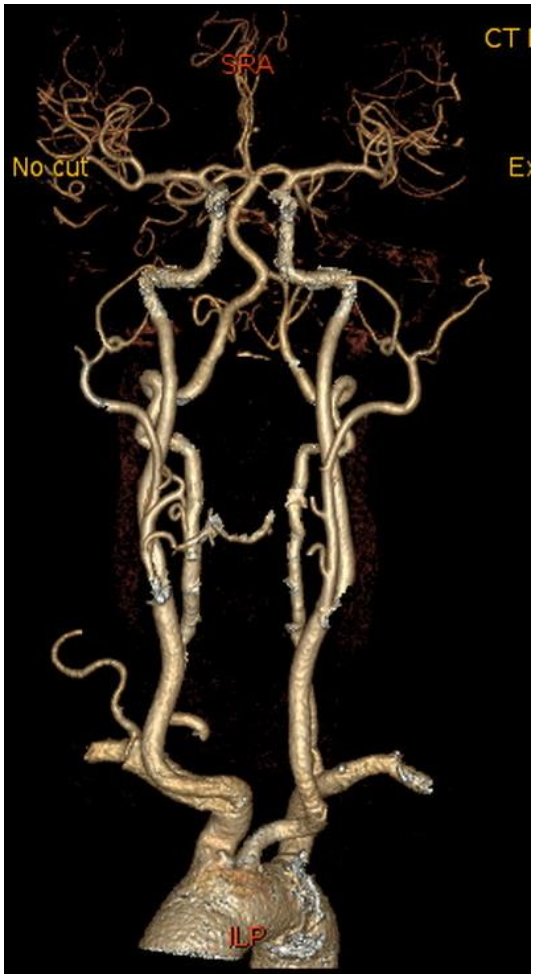
- recombinant tissue plasminogen activator
  - Plasminogen cleaves fibrin to break up clotted blood
  - Use with 3 hrs (I) or up to 3-4.5 hrs in select pts (I)
    - Should be used even in pts in whom ET is being considered (I)
  - 2-5% risk of symptomatic intracranial hemorrhage (sICH)
    - sICH is defined by a worsening of 4pts from baseline NIHSS
    - Age, time from onset, uncontrolled HTN, and DMII are the biggest contributors to risk of ICH
  - 30% likelihood of improved long term outcomes with use of IV tPA
  - For every 15 minute delay in IV tPA, outcomes are worsened by 4%

# CT Angiogram

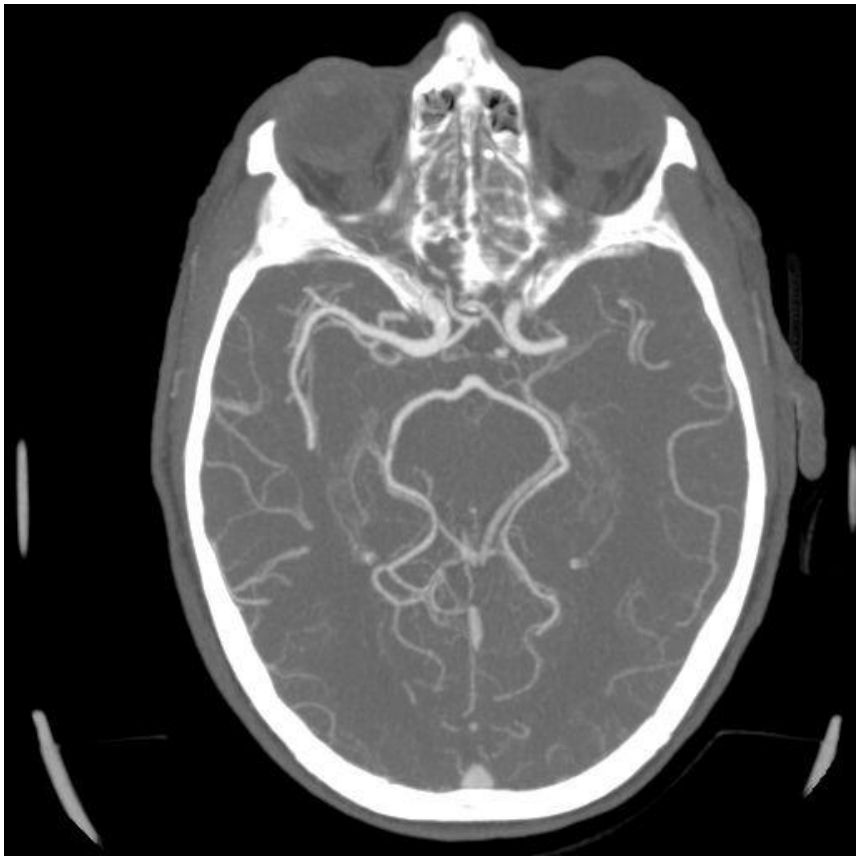
- Head and Neck imaging (IIa)
- Patient Populations
  - Suspected LVO
  - Within 6hrs of onset and not IV tPA candidate
- Cr level is not needed (IIa)
- Should never delay delivery of IV tPA

(I)

  - Processes should run in parallel and not in series
  - Can give bolus of tPA and hang drip while preparing the contrast and programming the CT scanner



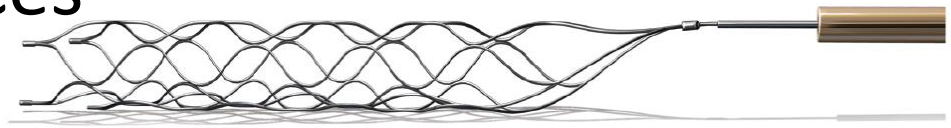
# CTA LVO



- ICA, MCA, & Basilar arteries are those in which Endovascular Therapy is an option

# Endovascular Therapy

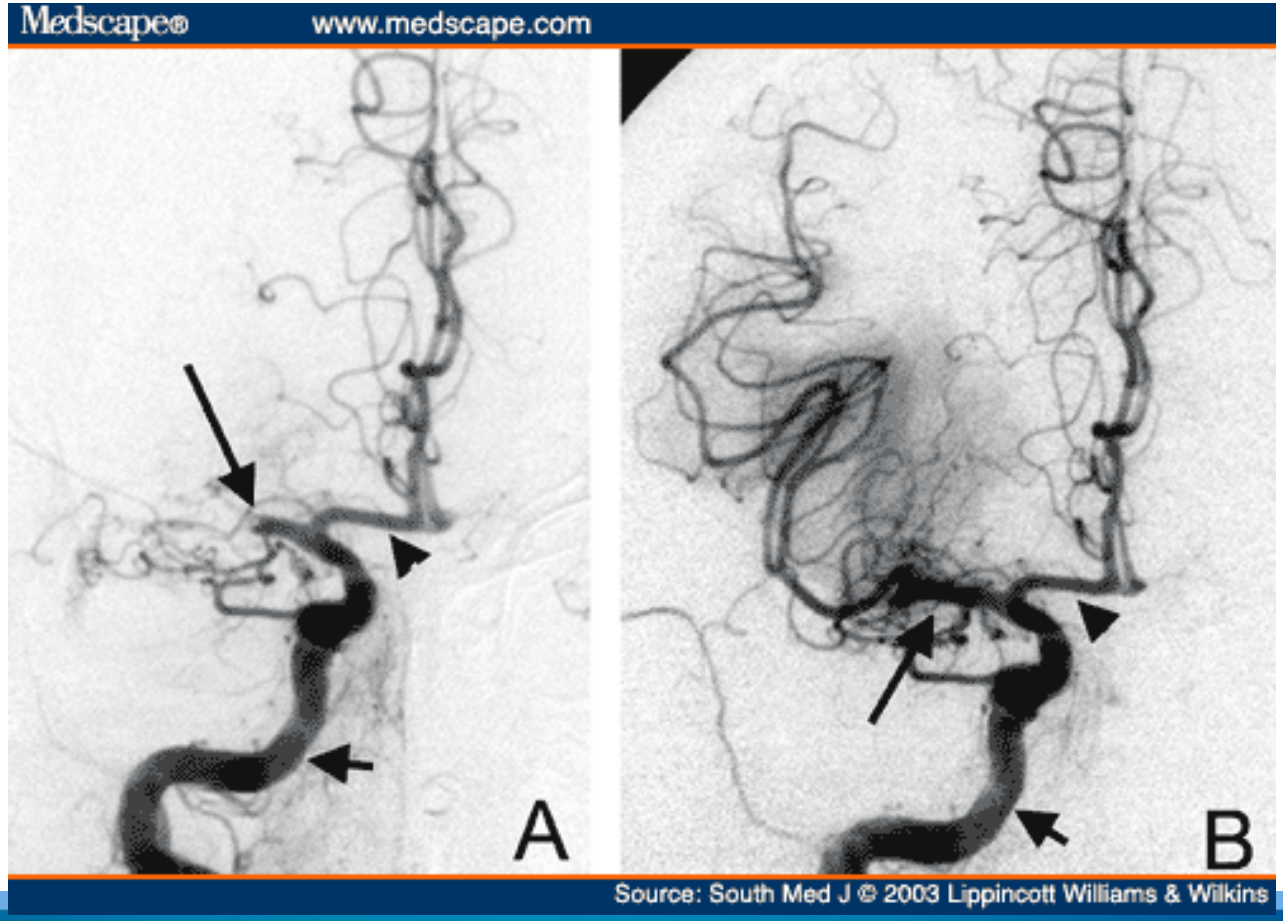
- Access typically via Groin (femoral artery)
- Clot Retrieval Devices
  - Stent Retriever (I)



    - Stent deployed across clot, wait several minutes for tines of stent to set into the clot, then pulled back
  - Suction Catheter (IIb)

    - Suction is applied at the proximal portion of the clot and a separator is moved back and forth through the clot to break it into pieces

# Endovascular Therapy



# Endovascular Therapy

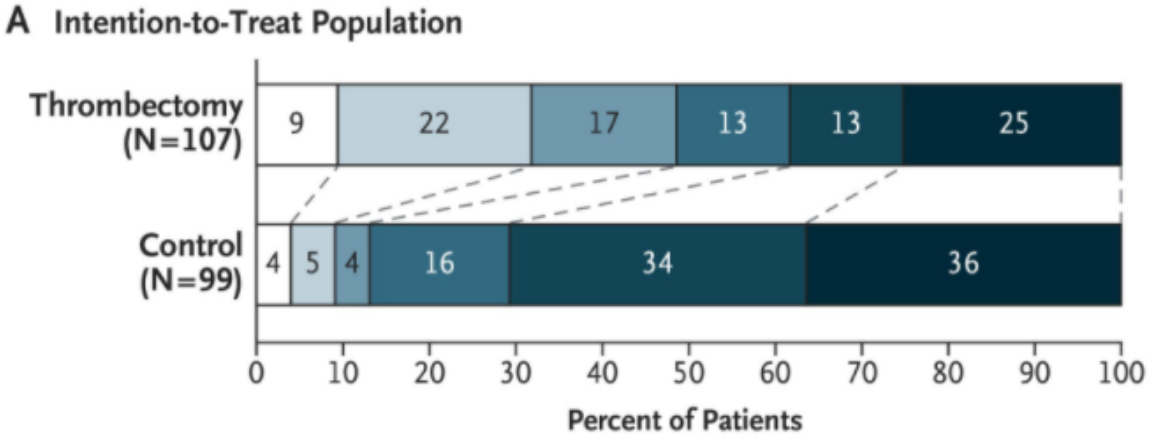
- MR CLEAN*
  - In patients with acute ischemic stroke due to a proximal intracranial arterial occlusion, intraarterial treatment (with retrievable stents in 82% of patients) within 6 hours improved functional outcome at 90 days.
  - Alteplase was given to 89% of patients before randomization.
  - MRS 0-2: 32.6% compared to 19.1% ---- OR 2.16
- ESCAPE †
  - Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times
  - 315 patients, stopped early due to benefit
  - ARR for thrombectomy 3.1
  - MRS 0-2: 53% compared to 29%
- EXTEND-IA ‡
  - EXtending the time for Thrombolysis in Emergency Neurological Deficits with Intra-Arterial therapy
  - 70 patients, stopped early due to benefit
  - Early neuro improvement: 80% compared to 37%
  - MRS 0-2: 71% compared to 40%
- SWIFT-PRIME •
  - Solitaire™ With the Intention For Thrombectomy as PRIMary treatment for acute ischemic strokE
  - 196 patients, stopped early due to benefit
  - OR for mRS shift p-value 0.0002
  - MRS 0-2: 60% compared to 35%

*N Engl J Med 2015; 372:11-20
† N Engl J Med 2015; 372:1019-1030
‡ N Engl J Med 2015; 372:1009-1018
•N Engl J Med 2015; 372:2285-2295

# DAWN

- 6-24hrs from LKW
- NIHSS >10
- Three groups
  - Age >80, <21 cc infarct
  - Age <80, <31 cc infarct
  - Age <80, NIHSS >=20, 31-51 cc of infarct

N Engl J Med 2018; 378:11-21



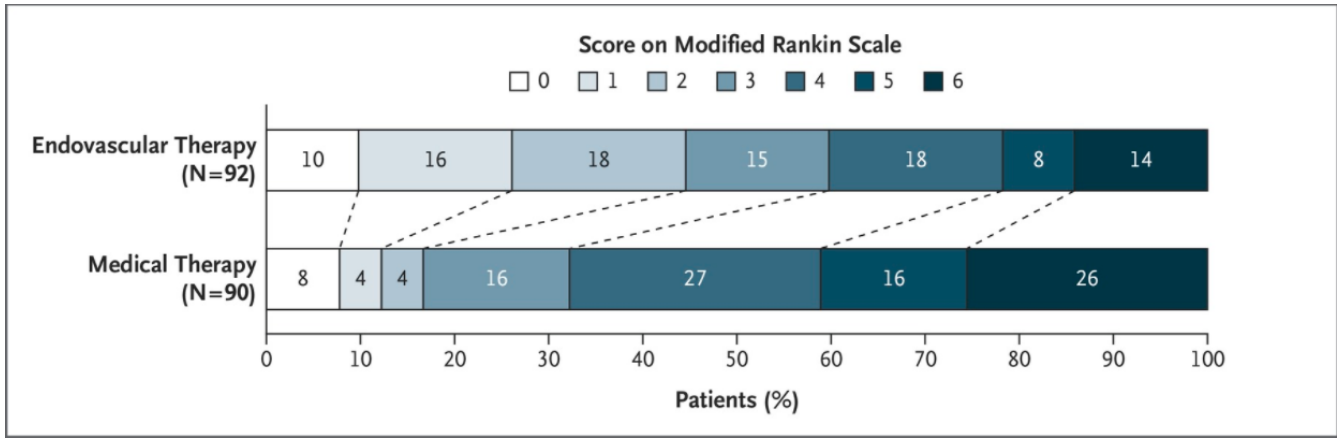

NNT=2.8

# DEFUSE

Much looser inclusion criteria than DAWN

N Engl J Med 2018; 378:708-718

- DEFUSE
  - 6-16hrs from LKW
  - NIHSS >=6
  - Core infarct <70cc with penumbra of ≥15cc




NNT=9

# LVO Summary

- Endovascular Thrombectomy is an effective way to improve functional outcomes in LVO
- Select populations may benefit in extended windows
- Use of advanced imaging (eg Perfusion) is critical in determining optimal candidacy when time >6hrs (I)
- Selection of patients for transfer from other sites is dependent on exam characteristics suggesting presence of LVO and CT findings

# STROKE EVALUATION

# Evaluation

**Diagnostic Testing**

- Brain Imaging
- Vascular Imaging
- Cardiac Evaluation
- Glucose
- Cholesterol
- Other

**Stroke Etiology**

- Small Vessel
- Large Vessel
- Cardioembolism
- Other Determined
- Undetermined

# Brain Imaging

- NCCT for everyone!  (I)
- MRI for everyone?  (III) no benefit
- MRI for some… 
  - May provide additional information for diagnosis, plan or subsequent treatment (IIb)
  - Can help you to understand and refine the differential of stroke etiology
  - Unanswered questions about utility to predict future risk, eg. Cerebral microbleeds

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  - Can help you to understand and refine the differential of stroke etiology
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# Vascular Imaging

- For patients with strokes in the carotid territory, carotid imaging should be performed (I)
  - CTA, MRA, Duplex
- Intracranial imaging for some…
  - No benefit for all (III)
  - May provide additional information to plan subsequent secondary stroke prevention (IIb)

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# Cardiac Evaluation

- Monitoring for first 24 hours for all (I)
- Prolonged cardiac monitoring may provide additional information (IIb)
  - Find more Afib with things like Loop Recorders, but studies were not powered to show difference in rates of stroke
- Echo
  - For all (III) no benefit
  - For some may provide additional benefit (IIb)
    - Any study that looked at this was poorly designed and flawed.

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# Other Testing

- Glucose
  - Screen for Diabetes with A1C (IIa)
- Lipids
  - Routine for all presumed atherosclerotic related strokes (III) no benefit
  - However, if athero related stroke, and already on a statin, check it because they might need addition of a PSCK-9 inhibitor (IIb)
- Homocysteine
  - Don't check it (III)
- Coagulopathy
  - No one knows if it's worth it (IIb)
  - Routine screening for APAS not recommended (III)
- Obstructive Sleep Apnea
  - Routine screening not recommended (III)

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# MANAGEMENT AND PREVENTION

# Secondary Prevention

- A –appropriate antithrombotics
- B – blood pressure management
- C – cholesterol management
- D – Diet/Diabetes management
- E – Exercise
- F – forget smoking (no fumar)

# Anti-Platelet Agents

- ASA
  - COX inhibitor, prevents formation of TXA2
- Clopidogrel (Plavix)
  - ADP receptor antagonist at P2Y12 receptor (prodrug)
- Ticagrelor (Brilinta)
  - ADP receptor antagonist at P2Y12 receptor (active)
- ASA/ERDP (Aggrenox)
  - ERDP is a phosphodiesterase inhibitor
- Cilostazol
  - Phosphodiesterase inhibitor

# Antithrombotics

- ASA should be administered within 24-48hrs after onset of AIS (I)
  - Not an alternative to TPA or EVT (III)
- Treatment of minor stroke with 21 days of DAPT (ASA/Plavix) started within 24hrs of stroke can be beneficial for up to 90 days after stroke (IIa)
  - CHANCE trial
- Ticagrelor is not recommended over ASA (III)
  - SOCRATES trial

# Antithrombotics

- Urgent anticoagulation for AIS is not recommended (III)
- For non-cardioembolic stroke, antiplatelets are recommended over anticoagulants (I)
- For non-cardioembolic strokes, the benefit of increasing the dose of ASA or changing to an alternative antiplatelet is not well established (IIb)
- Selection of antiplatelet agents should be individualized (I)
- Adding ASA to anticoagulation for AIS patients with AF and CAD is of uncertain benefit (IIb)
- Anticoagulation for AF in AIS should be started within 4-14 days (IIa)
- For hemorrhagic transformation, initiation or continuation of antithromboticcs can be considered on an individual basis (IIb)
- For treatment of dissection, either antiplatelet or anticoagulants for 3-6 months is reasonable (IIb)

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# Blood Pressure

- Target goal <140/90
  - <130/80 for lacunar stroke
  - Initiation of anti-HTN Tx in the hospital is safe and reasonable and may improve long term control (IIa)
- ACEi, ARB, CCB, Diuretics (JNC 8)

# Cholesterol

- If already taking a statin, continue it (IIa)
- Age <=75 with ASCVD, start high intensity statin (I)
  - atorvastatin 80 or rosuvastatin 20
- If high intensity contraindicated, use moderate intensity (I)
- Age >75, weigh risk-benefit (IIb)

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# Diabetes/Diet

- Screen for Diabetes with A1C (IIa)
- Goal A1C<7%

# Exercise

- 40 minutes 3-4 days per week of moderate to vigorous intensity exercise

# (No) Fumar

- Smokers should quit (I)
  - Counseling, nicotine replacement, oral smoking cessation medications can be used (I)
  - In hospital initiation of varenicline (Chantix) may be considered (IIb)
  - In hospital initiation of behavioral therapy may be considered (IIb)

# (No) Fumar

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# Other Random Things

- Foley catheters are bad (III)
- Supplemental oxygen should be used to maintain sats >94% (I)
- Hemodilution by volume expansion has no benefit for all (III)
  - Hypovolemia should be corrected (I)
- High Dose Albumin has no benefit (III)
- Start nutrition within 7 days (I); use of NG tubes in patients with dysarthria is reasonable if short term recovery expected, otherwise use a PEG tube (IIa)

# Summary

- The information in this presentation represents guideline recommendations, not hard and fast rules
- Medicine remains an art and diagnostic and treatment plans should always be individualized

# THANK YOU