

# ACUTE STROKE MANAGEMENT 2019 GUIDELINES :

## TPA:

### INDICATIONS:

- Symptoms suggestive of acute ischemic stroke with onset < 4.5 hours
- Wake up stroke > 4.5 hours from LKW with DWI positive FLAIR negative MRI (*New*)

### EXCLUSION CRITERIA:

- History of prior intracranial hemorrhage (ICH, SAH or SDH)
- Known intracranial neoplasm
- Known intracranial *aneurysm* (*although recent studies showed safety with aneurysm < 10mm*)
- Known intracranial AVM
- History of prior stroke or trauma within past 3 months
- Known platelet count < 100,000
- Heparin use within 48h with elevated aPTT
- LMWH in therapeutic dose within 24h
- Warfarin use with INR > 1.7 or PT > 15
- NOAGs use within 48 hours with elevated factor Xa assay, PT or aPTT
- Suspected stroke due to infective endocarditis
- Known or suspected aortic arch dissection
- Intracranial neoplasms

### RELATIVE EXCLUSION CRITERIA:

- BP > 185/110 -> It has to be lowered first
- Seizure at onset with post-ictal weakness -> deferred to evaluating clinician
- Pregnancy -> safety/harm not established
- History of recent GI bleeding within past 21 days
- History of recent MI within past 3 months
- Known heavy burden microbleeds on prior imaging ( > 10)

### EXCLUSION CRITERIA FOR 3-4.5 HOUR WINDOW:

- Age > 80
- NOAG use even if labs are normal
- Warfarin use even if INR < 1.7
- NIHSS > 25

### EXCLUSION CRITERIA FOR WAKE-UP STROKE WITH ONSET > 4.5 HOUR WITH MRI MISMATCH:

- Same as 3 - 4.5 hours criteria:
  - Age > 80
  - NOAG or Warfarin use even with normal labs
  - NIHSS > 25
- DW lesion > third MCA territory
- Planned thrombectomy

## SPECIFIC SITUATIONS:

- Menstruation: tPA should be given, it may increase menstrual bleeding though
- Pregnancy with moderate or severe stroke: tPA should be given (there is risk of abortion or miscarriage)
- Patient is on dual antiplatelets: tPA should be given
- Extracranial dissection: tPA should be given
- Intracranial dissection: safety not established
- Brain aneurysm < 10 mm: tPA should be given
- Brain aneurysm > 10 mm: safety not established
- Brain AVM: safety not established
- Brain microbleeds < 10 spots: tPA should be given
- Brain microbleeds > 10 spots: tPA may carry a high risk of bleeding
- Recent MI < 3 months: tPA should be given
- Known intracardiac thrombus with moderate or severe stroke: tPA should be given
- Known intracardiac thrombus with mild stroke: safety not established
- Systemic malignancy with life expectancy > 6 months: tPA should be given
- Not sure if it is a Stroke mimic: tPA should be given rather than waiting for further workup

#### DO'S AND DON'T DO'S IN ACUTE STROKE ACTIVATION:

##### DO:

- Get CTA along with initial CT in thrombectomy candidates, as long as it is not going to markedly delay tPA.
- Admit patient to ICU or stroke unit after tPA

##### DON'T:

- Don't withhold tPA because of hypodensity seen on CT, as long as deficits are more than expected with the hypodensity
- Don't withhold tPA for patients who received prophylactic dose LMWH within past 24h
- Don't withhold tPA for patients with history of small number of microbleeds (< 10)
- Don't get an MRI to screen for microbleeds prior to tPA
- Don't withhold tPA for stroke patients with known sickle cell disease
- Don't give tPA to wake-up stroke outside the time window with penumbra, unless in clinical trial.
- Don't give abciximab to patients currently receiving tPA
- Don't delay tPA to monitor for further improvement
- Don't delay tPA to watch for improvement

#### QUESTIONS:

**Q1:** Should we reverse warfarin or heparin to give tPA ? No, don't reverse

**Q2:** What are the time goal for stroke treatment?

- Brain imaging within 20 minutes of arrival
- All patients DTN (door to needle) < 45 minutes
- At least 50% of patients DTN < 30 minutes

**Q3:** what if ED physician is not sure and don't have an available neurologist?

- Tele-neurology can be used, if not available then telephone consultation with neurologist on call.

**Q4:** What if I can't get consent for tPA? Patient is aphasic or confused and no family available?

- Treat with tPA as long as patient is eligible and at risk for having a disabling stroke

**Q5:** What is the role of ASPECTS in mechanical thrombectomy decision?

- Only for patients presenting within 6 hours, they must have ASPECTS > or = 6. Patients presenting after 6 hours, will need either CTP or MRI for decision making regardless of ASPECTS.

**Summary of tPA Indications:**

	Onset < 3 hours	Onset within 3 – 4.5 hours (ECASS)	Onset > 4.5 hours (Wake-Up)
<b>Indications</b>	Clinical signs of acute ischemic stroke	Clinical signs of acute ischemic stroke	Clinical signs of acute ischemic stroke Abnormal signal in DWI with no abnormal signal in FLAIR
<b>Exclusions</b>	<ul style="list-style-type: none"> <li>○ <b>Mild</b> non disabling stroke (or NIHSS 0-5)</li> <li>○ History of prior <b>intracranial hemorrhage</b> (ICH, SAH or SDH)</li> <li>○ History of prior <b>intracranial neoplasm, AVM or aneurysm</b></li> <li>○ History of prior <b>stroke or trauma</b> within past 3 months</li> <li>○ Known <b>platelet count</b> &lt; 100,000</li> <li>○ <b>Heparin</b> use within 48h with elevated aPTT</li> <li>○ <b>LMWH</b> in therapeutic dose within 24h</li> <li>○ <b>Warfarin</b> use with INR &gt; 1.7 or PT &gt; 15</li> <li>○ <b>NOAGs</b> within 48 hours with increased Xa, PT or aPTT</li> <li>○ Suspected stroke due to <b>infective endocarditis</b></li> <li>○ <b>Intracranial neoplasms</b></li> </ul>	Same as <3 hour onset plus: <ul style="list-style-type: none"> <li>○ <b>Age &gt; 80</b> (<i>relative contraindication, can be given if benefits outweigh risk of bleeding</i>)</li> <li>○ <b>NOAG</b> use even if labs are normal</li> <li>○ <b>Warfarin</b> use even if INR &lt; 1.7</li> <li>○ <b>NIHSS &gt; 25</b></li> </ul>	Same as 3-4.5 hour onset plus: <ul style="list-style-type: none"> <li>○ <b>DW lesion &gt; third MCA territory</b></li> <li>○ <b>Planned thrombectomy</b></li> <li>○ Hemorrhage in MRI</li> </ul>

**Target BP:**

tPA patients	Thrombectomy patients	Not tPA/thrombectomy patients
<b>Before tPA:</b> < 185/110	<b>Before procedure:</b> < 185/110	<b>Small vessel disease stroke:</b> no need for permissive hypertension
<b>After tPA:</b> < 180/105 for 24 hours	<b>After procedure:</b> < 180/105 (DAWN & ESCAPE used SBP < 140)	<b>Embolic stroke:</b> < 220/110 for 24 hours

**Management of tPA Complications:**

Management of intracranial bleeding after tPA:	Management of angioedema after tPA:
<ul style="list-style-type: none"> <li>▪ Get CBC, PT, aPTT, fibrinogen level and type/cross match</li> <li>▪ Cryoprecipitate 10 units over 30 minutes</li> <li>▪ Tranexamic acid 1gm over 10 minutes or aminocaproic acid 4 gm over 1 hour</li> </ul>	<ul style="list-style-type: none"> <li>▪ If only lips and anterior tongue involved -&gt; intubation may not be necessary</li> <li>▪ If palate or pharynx are involved -&gt; may require intubation</li> <li>▪ Solumedrol 125 mg IV</li> <li>▪ Diphenhydramine 50 mg IV</li> <li>▪ Ranitidine 50 mg IV</li> <li>▪ If not controlled -&gt; use epinephrine SC (0.3 ml) or nebulizer (0.5 ml)</li> <li>▪ Icatibant (selective bradykinin antagonist) may be used.</li> </ul>

## THROMBECTOMY:

### INDICATIONS:

- **Acute ischemic stroke with onset < 6 hours with all the following:**
  - ICA or M1 occlusion
  - mRS < 2
  - NIHSS  $\geq$  6
  - ASPECTS  $\geq$  6
- **Acute ischemic stroke with onset 6-24 hours with LVO:**

Only for ICA/MCA occlusion, needs CTP to screen for salvageable penumbra using one of the following criteria:

  - **DAWN Criteria: (used clinical-imaging mismatch in patients presenting 6-24h)**
    - Pre-stroke mRS < 2
    - Anticipated life expectancy > 6 months
    - NIHSS  $\geq$  10
    - Intracranial ICA or proximal MCA occlusion
    - < 1/3 MCA core infarction (determined by MRI-DWI or CTP-rCBF)
    - Clinical imaging mismatch:
      - < 80-year: **Core < 30** with NIHSS  $\geq$  10 or **Core 30-50** with NIHSS  $\geq$  20
      - > 80-year: **Core < 20** with NIHSS  $\geq$  10
    - Excluded: cervical ICA occlusion, PCA/ACA occlusion, dissection, tortuous vessels.
  - **DEFUSE 3 Criteria: (used perfusion-core mismatch in patients presenting 6-16h)**
    - Age < 90
    - ICA or proximal MCA occlusion
    - Imaging mismatch: **If Core < 70 ml and mismatch ratio > 1.8 with at least 15 ml of viable penumbra.**
    - No pre-existing terminal or debilitating illness

### DO'S AND DON'T DO'S IN ACUTE STROKE ACTIVATION:

#### DO:

- Get CTA along with initial CT in thrombectomy candidate patients, as long as it is not going to markedly delay tPA.

#### DON'T:

- Don't wait for creatinine before CTA in patients with no known prior kidney disease

### QUESTIONS:

**Q1:** Is thrombectomy safe for patients > 80 years old?

- HERMES meta-analysis did show that thrombectomy is equally effective in patients above and below 80 years old.

**Q2:** What about other patients, mRS > 1 or ASPECTS < 6 or NIHSS < 6 who present within 6 hours ?

- No studies done on these patients. It may be reasonable to do thrombectomy for selected patients, decision will be deferred to on call neurologist.

**Q3:** What about M2 and M3?

- Strong data showed benefits from thrombectomy for ICA and M1 occlusion. Although no data for M2/M3 but it still can be done if there is marked disability.

**Q4:** What about vertebral, basilar, PCA and ACA?

- Although no studies are available to assess risk versus benefits, thrombectomy may be reasonable.

**Q5:** Clot aspiration versus stent retrieval, any difference?

- COMPASS study did show that aspiration is not-inferior to stent retrieval for thrombectomy, either one can be used.

**Q6:** patient came between 6-24h, what is the maximum core infarction for thrombectomy?

- Depends, either 50 ml if you use Dawn criteria (clinical-imaging mismatch) or 70 ml if you use Diffuse3 criteria (core-penumbra mismatch ratio > 1.8).

**Q7:** So if Core infarction < 50, then how much penumbra needed for thrombectomy:

- Depends: penumbra used only for DIFFUSE3 criteria with mismatch ratio >1.8 and minimum penumbra 15 ml.
- If you use clinical-imaging mismatch then penumbra doesn't matter as long a NIHSS is way worse than expected for the core infarction (NIHSS > 10 or 20, see above).

**Summary of thrombectomy indications:**

	0–6 hours	6–16 hours	16–24 hours
Thrombectomy Indicated	<p><b>All LVO patients with:</b></p> <ul style="list-style-type: none"> <li>▪ ICA or M1 occlusion</li> <li>▪ mRS &lt; 2</li> <li>▪ ASPECTS &gt;= 6</li> <li>▪ NIHSS &gt;= 6</li> </ul>	<p><b>Same as 0–6 hours plus meeting one of the following criteria:</b></p> <p>DIFFUSE3:</p> <ul style="list-style-type: none"> <li>▪ Imaging mismatch: Core &lt; 70 ml and mismatch ratio &gt; 1.8 with at least 15 ml of viable penumbra</li> </ul> <p>DAWN:</p> <ul style="list-style-type: none"> <li>▪ NIHSS &gt;= 10</li> <li>▪ &lt; 1/3 MCA core infarction</li> <li>▪ Clinical imaging mismatch</li> </ul>	<p><b>Same as 0 – 6 hours plus meeting criteria for DIFFUSE.</b></p> <p>DAWN:</p> <ul style="list-style-type: none"> <li>▪ NIHSS &gt;= 10</li> <li>▪ &lt; 1/3 MCA core infarction</li> <li>▪ Clinical imaging mismatch</li> </ul>
Thrombectomy Reasonable	<p><b>In the following situations:</b></p> <ul style="list-style-type: none"> <li>▪ M2, M3, vertebral, basilar, PCA or ACA occlusion</li> <li>▪ mRS &gt; 1</li> <li>▪ ASPECTS &lt; 6</li> <li>▪ NIHSS &lt; 6</li> </ul>		

## OTHER ACUTE CARE MEASURES

### MANAGEMENT OF BRAIN EDEMA:

- **Osmotic therapy or brief hyperventilation (PCO<sub>2</sub> 30-34):** reasonable in patients with clinical deterioration from brain swelling
- Don't use hypothermia or corticosteroids for management of brain edema. Steroids increase risk of infection.
- **Craniectomy:**
  - Threshold: is not established, but it is reasonable to use impaired consciousness from brain swelling as a selection criteria
  - Indications:
    - **In patients < 60-years-old with MCA infarction**, decompressive craniectomy is reasonable
    - **In patients > 60-year-old with MCA infarction**, decompressive craniectomy may be considered. It lowers mortality but doesn't markedly improve outcome. Only 6% of patients above 60 who underwent craniectomy achieved moderate disability compared with 5% in non-surgical group (DESTINY trial).
    - In patients with cerebellar infarction, outcome after decompressive craniectomy can be good

### DO'S AND DON'T DO'S IN ACUTE STROKE ACTIVATION:

#### DO:

- Get EKG and troponins for all stroke patients
- Target BP after tPA or thrombectomy: <180/105
- Target BP if not candidate for tPA or thrombectomy: < 220/110
- Target SaO<sub>2</sub>: > 94 in all stroke patients
- Treat hypotension and hypovolemia
- Treat hyperglycemia with target glucose 140-180 mg/dl
- Use pneumatic compression stockings to prevent DVT. (benefits of prophylactic heparin is not established)

#### DON'T:

- Don't use hyperbaric oxygen for air embolism
- Don't use indwelling catheter routinely due to risk of UTI
- Don't do intense very early ambulation of stroke patients within first 24 hours, it reduces the odds of favorable outcome

## SECONDARY PREVENTIVE TREATMENT:

### ANTI-THROMBOTIC THERAPY (ANTIPLATELETS OR ANTICOAGULANTS):

#### Non-cardioembolic stroke:

- Aspirin is the first line preventive agents
- Dual antiplatelets (aspirin & clopidogrel):
  - Reasonable to use in mild stroke or TIA for 3 weeks (POINT and CHANCE shown more benefits than single agent with no increased risk of bleeding if used for 3 weeks)
  - Reasonable to use in patients with severe intracranial atherosclerosis > 70% for 90 days (SAMMPRIS trial)
- Recurrent stroke: -> evidence is controversial whether to switch to another agent or not (SPS3 found no benefit from switching to long-term dual antiplatelets, data analysis from aspirin failure patients in CHANCE and SOCRATES did show benefits from switching to an alternative therapy)

#### Side Note

- It would make sense to switch to dual antiplatelet therapy if patient had recurrent stroke on aspirin.
- **Switching to clopidogrel?** Many people have a loss of function variant of CYP2C9 (30% of European descent), which make clopidogrel is not as effective for use as single agent. Current studies are evaluating prasugrel and ticagrelor instead of clopidogrel for stroke prevention (not affected by CYP2C9 function).
- **Increasing the dose of aspirin?** It has shown non-beneficial. Theoretically doesn't help, aspirin inhibits thromboxane in both platelets (inhibiting platelet aggregation, irreversible) and in endothelial cells (promoting platelet aggregation by inhibiting prostacyclin, reversible), so then net effect is inhibition of platelet function due to irreversible effect on platelets compared with reversible effect on endothelial cells. Since a small dose aspirin is enough to inhibit platelets thromboxane, increasing the dose will just add inhibition of endothelial cells which promotes platelet aggregation.
- **Consider anticoagulation?** Reasonable. We used to wait for a hard proof evidence of cardioembolic stroke prior to starting warfarin, mainly to justify the bleeding risk of warfarin. Now, the bleeding risk from NOAGs is comparable with antiplatelet which makes it reasonable to switch to anticoagulation if cardioembolic stroke is suspected on brain imaging. An example would be a stroke bilateral ischemia in absence of aortic plaque.  
Cardioembolic stroke: everything has changed – BMJ 03/2018 – Dr. David Spencer

#### Cardioembolic stroke:

- **Recommended to use anticoagulation:** Atrial fibrillation, atrial flutter, MI with mural thrombus, mechanical cardiac valve or PFO with evidence of DVT
- **Reasonable to use anticoagulation:** Dilated cardiomyopathy EF < 35%, restrictive cardiomyopathy, acute STEMI without mural thrombus but with anterior or apical dyskinesia with EF < 40
- **Anticoagulation + Antiplatelets, reserved only for:**
  - Patients with atrial fibrillation with recent unstable coronary artery syndrome or coronary stenting (recommended)
  - Mechanical valve with stroke despite adequate anticoagulation (reasonable)
  - Bioprosthetic valve with stroke despite adequate antiplatelets (reasonable)
- **When to start:**
  - In most patients, it is reasonable to start anticoagulation between 4-14 days of onset.
  - In patients with hemorrhagic transformation, if mild-moderate stroke with NIHSS < 9, restarting anticoagulation or antiplatelets within 14 days of onset was not associated with progression of HT. Individual assessment is warranted.

### Side Note

- **Patients at fall risk:** usually benefits from anticoagulation will outweigh the risk of bleeding. Per Man-Son-Hing et al, it would take 295 falls to equal the risk of not taking anticoagulation in patients with atrial fibrillation.
  - **When anticoagulation seem contraindicated:** in cases of recurrent intracerebral bleeding due to amyloid angiopathy or severe recurrent GI bleeding, occlusion of left atrial appendage should be considered.
- Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls – Dr. Man-Son

### Hypercoagulable state stroke:

- **Recommended to use anticoagulation:** in patients with anti-phospholipid syndrome
- **Reasonable to use anticoagulation:** in patients with other inherited thrombophilia
- **Which anticoagulant to use:** warfarin is the anticoagulant that has been studied in thrombophilia

### Summary of antithrombotic indications:

TREATMENT	INDICATIONS
ANTIPLATELETS	<ul style="list-style-type: none"><li>▪ First line preventive stroke therapy till work up is completed</li><li>▪ Non-cardioembolic stroke, presumed to be due to small vessel disease or large artery atherosclerosis</li></ul>
ANTICOAGULANTS	<ul style="list-style-type: none"><li>▪ Atrial fibrillation or flutter (recommended)<ul style="list-style-type: none"><li>○ Anticoagulation should be restarted between 4-14 days after stroke onset in most patients. Patients with unstable angina or coronary artery stents, adding antiplatelets to anticoagulants may be warranted.</li></ul></li><li>▪ Acute anterior STEMI without mural thrombus but with anterior or apical dyskinesia with EF &lt; 40% (reasonable)</li><li>▪ MI with mural thrombus (recommended)</li><li>▪ Dilated cardiomyopathy with EF &lt; 35% (reasonable)</li><li>▪ Restrictive cardiomyopathy (reasonable)</li><li>▪ Mechanical cardiac valve (recommended)</li><li>▪ PFO with evidence of DVT (recommended)</li><li>▪ Inherited thrombophilia state (reasonable)</li><li>▪ Antiphospholipid syndrome (recommended)</li></ul>
ANTIPLATELETS + ANTICOAGULANTS	<ul style="list-style-type: none"><li>▪ Patients with atrial fibrillation with recent unstable coronary artery syndrome or coronary stenting (recommended)</li><li>▪ Mechanical valve with stroke despite adequate anticoagulation (reasonable)</li><li>▪ Bioprosthetic valve with stroke despite adequate antiplatelets (reasonable)</li></ul>
ANTIPLATELETS OR ANTICOAGULANTS	<ul style="list-style-type: none"><li>▪ For patients with extracranial carotid or vertebral dissection, treatment with either antiplatelet or anticoagulant is reasonable.</li></ul>



## HYPERLIPIDEMIA TREATMENT:

- Patients below 75-year-old, high intensity statins should be instated with target  $\geq$  50% reduction of LDL-C
- Patients above 75-year-old, moderate or high intensity statins should be used
- Patients with high LDL-C ( $> 70$  mg/dl) on maximum statin therapy, it is reasonable to add ezetimibe
- Women in childbearing age should be counseled to use contraception prior to using statins. Statins should be stopped 1-2 months prior to planned pregnancy.

Hypertension treatment:

### Side Note

- It may be helpful to inform the patient that every 10mmHg reduction in systolic blood pressure was associated with 33% reduction in stroke risk (*Neal et al, Lancet 2000*).
- There may be protective effect of some antihypertensive medications (ACAE, ARB) even in patients with no concurrent hypertension, RR of 22% (*HOPE trial*)

## CAROTID ARTERY STENOSIS:

- **CAS/CEA is recommended for:**
  - Symptomatic ICA stenosis  $> 50\%$  by angio, MRA or CTA or  $> 70\%$  by duplex and anticipated periprocedural risk of stroke  $< 6\%$ .
  - Asymptomatic ICA stenosis  $> 70\%$  by duplex (or  $> 60\%$  by angio)
- **Medical management is recommended for:**
  - Symptomatic ICA stenosis after disabling stroke (mRS  $> 3$ )
  - Asymptomatic ICA stenosis 50-70%
- **CEA compared with CAS for ICA stenosis:**
  - CAS is generally preferred except in:
    - CEA is preferred in patients  $> 70$ -year-old (associated with improved outcome)
    - CEA is preferred in patients with unfavorable vascular anatomy for stenting.
  - CAS is particularly preferred in patients with increased risk for surgery, radiation induced stenosis or restenosis after prior CEA.
  - It is reasonable to perform procedure within 2 weeks of stroke onset if no contraindications
- Patients with minor non-disabling stroke (mRS 0-2), CEA or CAS should be done between 48h and 7 days of stroke onset.
- **OTHER ARTERIAL STNEOSIS:**
  - Severe intracranial stenosis with recurrent stroke despite adequate medical treatment (may be considered, SAMMPRIS trial)
  - Vertebral stenosis with recurrent stroke despite adequate medical treatment (may be considered)

### Side Note

Medical management of ICA stenosis:

- For symptomatic ICA stenosis  $> 50\%$ , medical management alone is not enough. NASCET trial showed 20-30% risk of recurrent stroke over 18 months period in medical treatment group.

- For non-intervention candidates (<50% stenosis), dual antiplatelets was not superior to single agent antiplatelet.
  - CHARISMA, MATCH and PROGRESS trials showed that dual antiplatelet therapy was not superior to single antiplatelet agent in preventing stroke in ICA stenosis patients.
  - As usual, aspirin is preferred to clopidogrel due to genetic variability (CYP2C19 genetic variant is as common as 30% of European descents, preventing metabolism of clopidogrel to its active ingredient)

## PFO CLOSURE:

- 2019 guidelines didn't comment on value or indications of PFO closure

### Side Note

Patient selection for PFO closure: *Typically a younger patient with cryptogenic embolic stroke as detailed here.*

- **Stroke:** cortical infarcts, multiple vascular territories or strokes in same territories but of different ages. Negative workup, including at least 30-day monitoring for Afib.
- **PFO:** high risk PFO includes ASA, large shunt, large PFO > 2mm, increased atrial septal mobility
- **Patient:** RoPE score helps in patient selection, RoPE > 7 is usually associated with more favorable outcome.
  - **RoPE score:** 1 for each (no HTN, no DM, no hx of TIA/Stroke, non-smoker, cortical infarct) and age (5 points for 18-29, 4 for 30-39, 3 for 40-49, 2 for 50-59, 1 for 60-69 and 0 for > 70)
  - FDA mandates that patients be evaluated by both cardiologists and neurologists prior to the procedure.

**Brief history of PFO closure approval:**

- Amplatzer septal occlude was FDA approved in 2016 after RESPECT trial results showed superiority of PFO closure compared with medical therapy in cryptogenic stroke patients < 60-year-old.
- Cardioform septal occlude was FDA approved in 2018 after the REDUCE trial showed superiority of PFO closure compared with medical therapy in cryptogenic stroke patients < 60-year-old.
- CLOSE showed favorable results in patients with ASA or large Rt-Lt shunt (>30 bubbles in 3 cardiac cycles)
- DEFENSE-PFO showed favorable results in patients with ASA, PFO > 2mm or IAS hypermobility.

## DISSECTION:

- Extracranial carotid or vertebral dissection: either antiplatelets or anticoagulants for 3-6 months
- Intracranial carotid or vertebral dissection: antiplatelet for 3-6 months
- Recurrent stroke in setting of extracranial dissection: the value of extracranial stenting is not well established

## SUMMARY OF STROKE PREVENTION GUIDELINES

SITUATION	MANAGEMENT	EVIDENCE
Initial therapy	<ul style="list-style-type: none"> <li>▪ Aspirin or aspirin/dipyridamole</li> <li>▪ Clopidogrel is a reasonable alternative</li> <li>▪ Dual antiplatelets (aspirin &amp; clopidogrel) may be considered in small stroke or TIA for 21 days then monotherapy</li> <li>▪ Long-term dual antiplatelet regimens are not recommended (increase risk of hemorrhage)</li> </ul>	
Recurrent stroke/TIA while on aspirin	<ul style="list-style-type: none"> <li>▪ Alternative antiplatelet may be considered although there is no enough studies available yet</li> <li>▪ No evidence to support increasing dose of aspirin</li> </ul>	
Symptomatic intracranial athero	<ul style="list-style-type: none"> <li>▪ Dual antiplatelets for 90 days then monotherapy for stenosis &gt; 70%</li> <li>▪ Keep SBP &lt; 140 mmHg</li> <li>▪ Use high dose statins</li> <li>▪ Wingspan stent is not recommended as initial management of intracranial stenosis</li> </ul>	
Aortic arch atheroma	<ul style="list-style-type: none"> <li>▪ Antiplatelets</li> </ul>	
Symptomatic extracranial ICA stenosis	<ul style="list-style-type: none"> <li>▪ CEA or CAS if &gt; 70% stenosis by duplex or &gt; 50% by angio</li> </ul>	
Asymptomatic extracranial ICA stenosis	<ul style="list-style-type: none"> <li>▪</li> </ul>	
Dissection of extracranial ICA/vertebral	<ul style="list-style-type: none"> <li>▪ Either antiplatelets or anticoagulation for 3-6 months</li> <li>▪ Endovascular treatment may be considered in patients with recurrent stroke/TIA despite medical management</li> </ul>	
Atrial fibrillation	<ul style="list-style-type: none"> <li>▪ Warfarin, apixaban or dabigatran are indicated for stroke prevention</li> <li>▪ Rivaroxaban is reasonable alternative</li> <li>▪ Combination of anticoagulation and antiplatelets for stroke prevention is not recommended. Can be used if indicated from cardiac prospective (acute coronary syndrome or stent placement)</li> <li>▪ Aspirin is recommended for patients who can't tolerate anticoagulation</li> <li>▪ After acute stroke, it is reasonable to initiate anticoagulation within 14 days of stroke onset unless there is high risk for hemorrhagic conversion, delaying beyond 14 days is reasonable.</li> </ul>	

	<ul style="list-style-type: none"> <li>▪ Bridging with LMWH is reasonable when temporary interruption of anticoagulation is needed.</li> <li>▪ Usefulness of Watchman device is not certain</li> </ul>
MI with apical dyskinesia	<ul style="list-style-type: none"> <li>▪ TIA or stroke in setting of acute anterior STEMI without mural thrombus but with anterior or apical dyskinesia with EF &lt; 40% may be treated with warfarin for 3 months.</li> </ul>
MI with mural thrombus	<ul style="list-style-type: none"> <li>▪ TIA or stroke in setting of acute MI with left ventricular mural thrombus should be treated with warfarin for 3 months.</li> <li>▪ In patients who can't tolerate warfarin, apixaban, rivaroxaban, dabigatran or LMWH may be used.</li> </ul>
Cardiomyopathy	<ul style="list-style-type: none"> <li>▪ TIA or stroke in setting of dilated cardiomyopathy (EF &lt; 35%), restrictive cardiomyopathy or LVAD should be treated with warfarin.</li> </ul>
Rheumatic valvular heart disease	<ul style="list-style-type: none"> <li>▪ Anticoagulation may be considered if no other cause for stroke</li> </ul>
Mitral valve prolapse	<ul style="list-style-type: none"> <li>▪ Antiplatelets</li> </ul>
Mitral annular calcification	<ul style="list-style-type: none"> <li>▪ Antiplatelets</li> </ul>
Mechanical mitral valve	<ul style="list-style-type: none"> <li>▪ Anticoagulation with target 2-3 plus aspirin (add aspirin if low risk of bleeding)</li> <li>▪ Addition of antiplatelet is recommended in patients with history of stroke prior to valve replacement</li> <li>▪ Intensifying therapy with increasing INR or increasing aspirin to 325mg is reasonable in case of stroke despite adequate anticoagulation.</li> </ul>
Mechanical aortic valve	<ul style="list-style-type: none"> <li>▪ Anticoagulation with target 2.5-3.5 plus aspirin (add aspirin if low risk of bleeding)</li> <li>▪ Addition of antiplatelet is recommended in patients with history of stroke prior to valve replacement</li> <li>▪ Intensifying therapy with increasing INR or increasing aspirin to 325mg is reasonable in case of stroke despite adequate anticoagulation.</li> </ul>
Bioprosthetic valve	<ul style="list-style-type: none"> <li>▪ Antiplatelets (after the initial 6 month anticoagulation following valve placement).</li> <li>▪ Adding warfarin with target INR 2-3 may be considered in case of stroke despite adequate antiplatelets</li> </ul>
PFO without DVT	<ul style="list-style-type: none"> <li>▪ Antiplatelets</li> <li>▪ No data to support PFO closure.</li> </ul>

PFO with DVT	<ul style="list-style-type: none"> <li>Anticoagulation, IVC filter if anticoagulation is contraindicated</li> <li>PFO closure may be considered if patient at risk of developing another DVT</li> </ul>
Inherited thrombophilia (protein C deficiency, protein S deficiency, antithrombin III deficiency, factor V Leiden, prothrombin G20210A mutation & MTHFR C677T mutation)	<ul style="list-style-type: none"> <li>Rarely involved in ischemic stroke in adults</li> <li>Anticoagulation may be considered depending on abnormality</li> <li>Long-term anticoagulation may be reasonable in case of cerebral venous thrombosis or recurrent ischemic stroke with evidence of thrombophilia</li> </ul>
Antiphospholipid Ab but not APL syndrome	<ul style="list-style-type: none"> <li>Antiplatelets</li> </ul>
Antiphospholipid syndrome	<ul style="list-style-type: none"> <li>Anticoagulation</li> </ul>
Sickle cell disease	<ul style="list-style-type: none"> <li>Chronic blood transfusion to keep HBS &lt; 30%</li> </ul>
Pregnancy and anticoagulation	<ul style="list-style-type: none"> <li>Pregnancy with risk factor that require anticoagulation, use LMWH twice daily throughout pregnancy guided by Xa level drawn 4 hours after injection or LMWH for until the 13<sup>th</sup> week then warfarin till close delivery when LMWH is resumed.</li> </ul>
Pregnancy and antiplatelets	<ul style="list-style-type: none"> <li>Pregnancy with low risk factor that requires antiplatelets, either use LMWH or no treatment during first trimester</li> </ul>
Breastfeeding and anticoagulation	<ul style="list-style-type: none"> <li>Pregnancy with risk factor that require anticoagulation, use warfarin, LMWH or UFH</li> </ul>
Breastfeeding and antiplatelets	<ul style="list-style-type: none"> <li>Pregnancy with low risk factor that requires antiplatelets, low dose aspirin may be considered</li> </ul>
Resuming anticoagulation after ICH	<ul style="list-style-type: none"> <li>Low risk for stroke (AF without prior stroke) and high risk of ICH recurrence (elderly with lobar ICH) or poor neurological function, antiplatelet may be considered instead of anticoagulation.</li> <li>Optimal timing before restarting anticoagulation in patients with ICH, SAH or SDH who need restarting anticoagulation is uncertain but at least &gt; 1 week.</li> </ul>

