

# Antithrombotic Therapy for Secondary Stroke Prevention: What? When? For how long?

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# Presenter Disclosure

- Presenter's Name: Mathew Hodgson
- I have no current or past relationships with commercial entities
- Speaking Fees for current program:
  - I have received no speaker's fee for this learning activity

# Commercial Support Disclosure

- This program has received no financial or in-kind support from any commercial or other organization

# Outline

- Classification/Etiology
- Presentation/Workup
- Antiplatelet Monotherapy
- Dual Antiplatelets
- Anticoagulation
- Anticoagulation + Antiplatelet
- Antithrombotic failure?

# Surprise Quiz

1. If a patient is on an antiplatelet for secondary stroke prevention, and they need anticoagulation for a DVT/PE, do you continue the antiplatelet?
2. Is anticoagulation more/less/equally effective as antiplatelet therapy for secondary stroke prevention outside the context of strong indications for anticoagulation (e.g. AF, LVT, mech valves, etc)?
3. If a patient has Afib and they are on anticoagulation, does adding an antiplatelet reduce their risk of stroke?

# DEFINITIONS

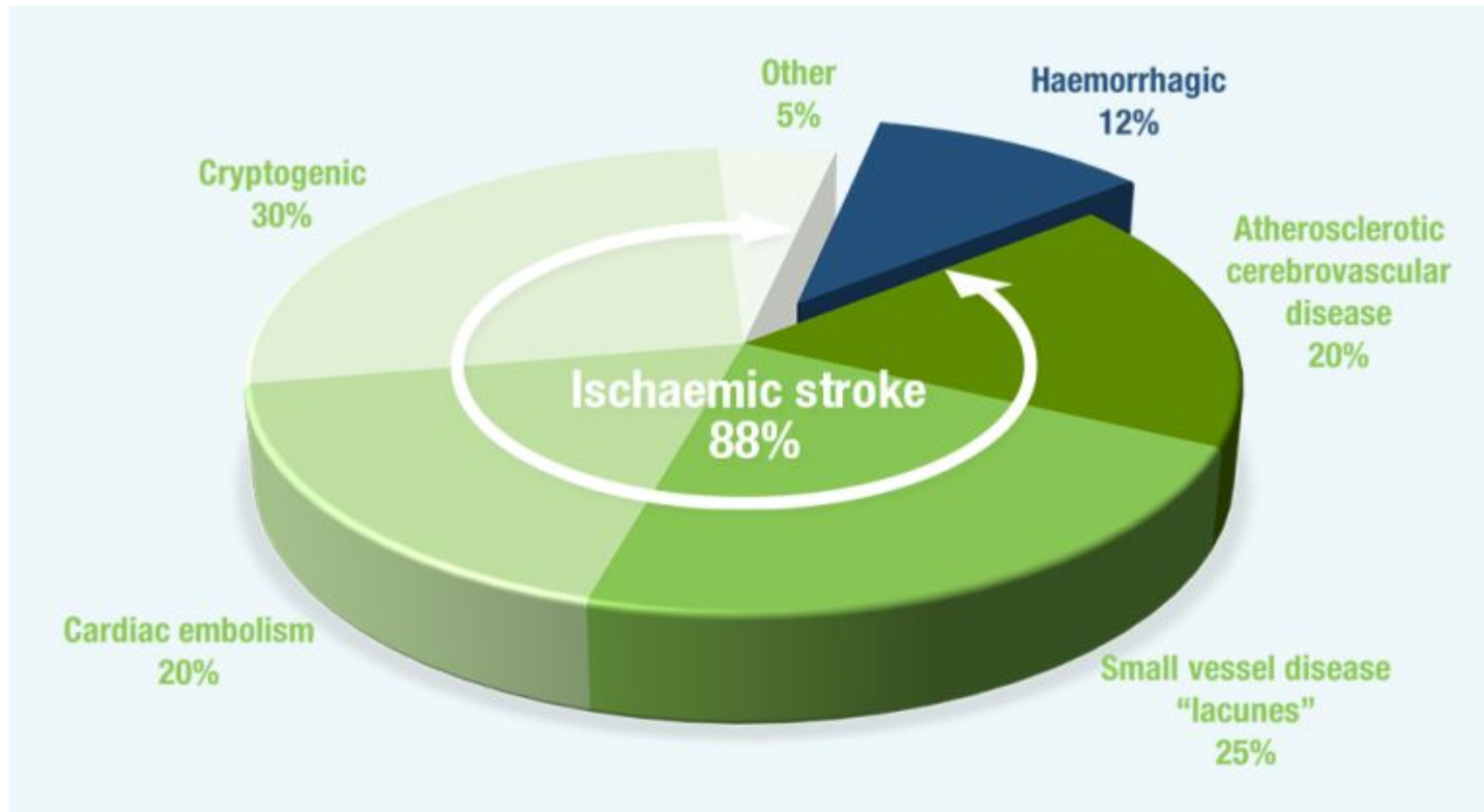
CSBPR 2018:

**Acute Stroke:** An episode of symptomatic neurological dysfunction caused by focal brain, retinal or spinal cord ischemia or hemorrhage with evidence of acute infarction or hemorrhage on imaging (MR, CT, retinal photomicrographs), and regardless of symptomatic duration.

CSBPR 2018:

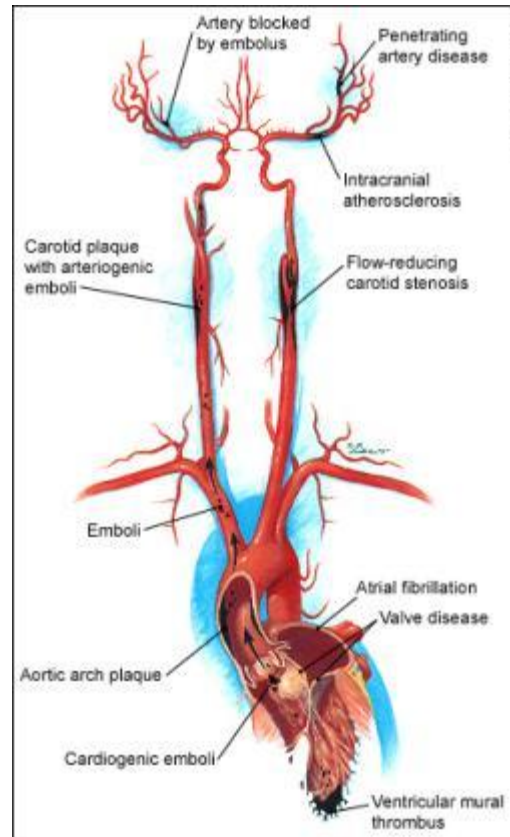
**Transient Ischemic Attack (TIA):** A brief episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, with clinical symptoms and without imaging evidence of acute infarction.

# CLASSIFICATION





# ETIOLOGY



**FIVE cardinal signs and symptoms (patient may have one or more present):**

- Severe headache (“worst of my life”)
- Sudden weakness (plegia/paralysis)
- Sudden changes in speech (aphasia, dysphasia)
- Sudden change in vision (blurred, diplopia, loss)
- Sudden dizziness/nausea/emesis (ataxia)

# Stroke Workup

- Vessel imaging (CTA/MRA/carotid ultrasound)
- TTE/TEE
- EKG/24 hour Holter
- Bloodwork (Hgb A1c, Lipid panel, TSH, C-RP, coagulation studies, homocysteine, COVID swab, etc)
- Vital signs
- Determine most likely underlying cause based on the workup and location/distribution of the infarction in order to select appropriate antithrombotic therapy

# Risk factor modification!

- Should be addressed in every patient, regardless of mechanism of stroke. Antithrombotic therapy is often just a part of the whole picture.
  - Hypertension
  - Dyslipidemia
  - Diabetes
  - Diet, sodium intake, exercise, weight, etoh intake, smoking

# Antiplatelet Monotherapy (AKA “the default”)

- ASA 160-325mg x1 then 80/81mg PO daily or 325mg PR daily
  - IST, CAST
- Clopidogrel 300-600mg x 1 then 75mg PO daily
  - CAPRIE
- Ticagrelor 180mg x 1 then 90mg BID
  - SOCRATES

# Antiplatelet Monotherapy: When and for how long?

- Urgent administration of TPA and/or EVT is of utmost importance – do not delay these therapies based on antiplatelet decision
- Start antiplatelet 24 hours post TPA/EVT once ~18hour repeat CT rules out hemorrhage
- Start antiplatelet immediately if TPA is not an option (e.g. contraindications to TPA or subacute stroke)
- Ideally start within 48 hours of symptom onset
- Antiplatelet is typically lifelong therapy, though there are some exceptions (e.g. traumatic dissection)

# Dual antiplatelets

- High risk TIA (ABCD2  $\geq 4$ )/Minor stroke (NIHSS  $\leq 3$ )
  - NIHSS 0-42, wherein 0 means no deficits. A score of 20+ is typically severely debilitating
- Extracranial or intracranial stent
- Intracranial atherosclerosis

# DAPT for TIA/Minor Stroke

- ASA 160-325mg x 1 then 81mg daily + Clopidogrel 300-600mg x 1 then 75mg daily x 21-30 days
  - CHANCE, POINT
- ASA 160-325mg x 1 then 81mg daily + Ticagrelor 180mg x1 then 90mg BID x 30 days
  - THALES



# Dual antiplatelets: When and for how long?

- TIA/Minor stroke (NIHSS  $\leq 3$ )
  - Initiate within 24 hours of symptom onset (ideally within 12 hours)
  - Reasonable to delay P2Y12 inhibitor if extracranial stenosis amenable to endarterectomy – Neurosurgery consult
  - One antithrombotic life-long (usually ASA). Clopidogrel 21-30 days, or ticagrelor x 30 days.
- Extracranial or intracranial stent
  - Start pre or periprocedurally if feasible. Duration determined by neurosurgery/IR – typically 6-12 weeks
- Symptomatic intracranial atherosclerosis
  - Initiate within 30 days of stroke, usually within 7 days. ASA 325mg daily + clopidogrel 75mg daily x 90 days, then ASA lifelong.
  - SAMMPRIS

# Anticoagulation

- **nvAFib – DOAC** or Warfarin
- vAFib – LMWH/UFH -> Warfarin
- LV Thrombus – LMWH/UFH -> Warfarin
- Mechanical valves – LMWH/UFH -> Warfarin
- APLAS – LMWH/UFH -> Warfarin
- CVST – LMWH/UFH -> Warfarin or Dabigatran (RESPECT-CVT)
- CAT – LMWH or Apixaban/Rivaroxaban/Edoxaban

# Anticoagulation: When and for how long?

- It depends on the indication and the risk of hemorrhagic transformation (i.e. the larger the infarct and the sooner you start, the higher the risk). Start patients on ASA while waiting to start AC
- nvAFib/vAFib – Start 0-14 days post stroke, Lifelong therapy
- Mech valves/APLAS – Start 0-14 days post stroke, Lifelong therapy
- LV Thrombus/CAT – Start 0-14 days post stroke, Typically minimum 3 months of therapy
- CVST – Start immediately – even if hemorrhage on initial CT, Typically minimum 3 months of therapy

# Anticoagulation + Antiplatelet

- Not routinely combined – no benefit of adding antiplatelet to anticoagulation for nvAF
  - AFIRE, WARIS II, subgroup analyses of ARISTOTLE/RELY/ROCKET AF
- Some instances where this approach would be used:
  - Afib + stent (carotid or intracranial)
    - Apixaban + clopidogrel preferred (AUGUSTUS)
  - Mechanical heart valve (warfarin + ASA)
  - Concomitant ACS
  - Stable CAD + PAD (this includes carotid stenosis!)
    - COMPASS regimen: ASA 100mg daily + rivaroxaban 2.5mg BID

# Anticoagulation + Antiplatelet: When and for how long?

- As before, gauge clot vs bleed risk, typically within 14 days
- Afib + stent – start DAPT->stent (0-14d post stroke) -> stop ASA POD #2 + start anticoagulation -> continue anticoagulation + P2Y12 inhibitor x 6 weeks, then stop P2Y12 inhibitor and continue on anticoagulation monotherapy lifelong
- Mechanical valve – UFH/LMWH->warfarin + ASA lifelong – start 0-14d post stroke
- Concomitant ACS – Resume antithrombotics 0-14d post stroke and continue regimen per cardiac requirements
- Stable CAD + PAD (COMPASS regimen) – start 30 days post-stroke, lifelong therapy

# Treatment Failure?

- Can you blame the antithrombotic?
  - Adherence (INR/Anti-Xa/TT)
  - Wrong dose/frequency
  - Drug interactions
  - Suspected mechanism of stroke
- Optimize risk factors
- Is there evidence to switch?

# Answers

1. If a patient is on an antiplatelet for secondary stroke prevention, and they need anticoagulation for a DVT/PT, do you continue the antiplatelet? **No – stop the antiplatelet until/if anticoagulation is finished, then resume antiplatelet. Anticoagulation is as effective as antiplatelet for stroke prevention (NAVIGATE ESUS, RESPECT ESUS, WARSS, WARIS II)**
2. Is anticoagulation better than antiplatelet therapy for secondary stroke prevention outside the context of strong indications for anticoagulation (e.g. AF, LVT, mech valves, etc)? **No – antiplatelet therapy and anticoagulation therapy is ~equivalent for stroke prevention, however anticoagulation has a higher bleeding risk. (NAVIGATE ESUS, RESPECT ESUS, WARSS)**
3. If a patient has Afib and they are on anticoagulation, does adding an antiplatelet reduce their risk of stroke? **No – adding antiplatelet therapy on top of anticoagulation does not reduce the risk of ischemic stroke, but it does increase the bleed risk. (AFIRE, subgroup analysis from ARISTOTLE/RELY/ROCKET AF)**

# Resources

- Canada Heart & Stroke Best Practice Recommendations
- AHA/ASA Acute Stroke/Secondary Stroke Prevention Guidelines
- Thrombosis Canada
- CCS Guidelines
- AHA/ACC Guidelines