What is New in Stroke Prevention Medication?

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Disclosures

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Outline

- Antiplatelets and Anticoagulant Indications and Non-Indications
- Perioperative Management of Antithrombotic Therapy
- Management of PFO
- Stroke in setting of Low Ejection Fraction
- Cancer Associated Stroke

Antiplatelet Therapy & Anticoagulation

Antiplatelet Therapy- (single/ double/+DOAC?)

WHO GETS DUAL ANTIPLATELET THERAPY?

1) Minor Stroke/TIA

- Anyone with symptoms of **minor stroke (NIHSS 0-3)/TIA,** not a major risk of bleeding:
  - A **single loading dose of clopidogrel (300 mg or 600mg) + ASA 160mg** followed by **ASA 81mg + Clopidogrel 75mg x 21d followed by monotherapy after**
- Longer duration DAPT (beyond 21days) **is not recommended**
- Patients should be counseled that ASA + clopidogrel should continue for only 21 days, followed by monotherapy
- Another reasonable short-term dual antiplatelet treatment option is low-dose ASA + **ticagrelor** (180 mg loading dose, followed by 90 mg bid) x 30 days

Antiplatelet Therapy

2) Stroke/TIA secondary to Intracranial atherosclerotic disease (ICAD)

- If symptomatic **intracranial** atherosclerotic stenosis of 70-99%, and low estimated bleeding risk, the **SAMMPRIS protocol** should be considered → DAPT x 3mths, followed by monotherapy + high-dose statin, BP treatment, and structured lifestyle modification

3) Patients with a recent extracranial or intracranial stent

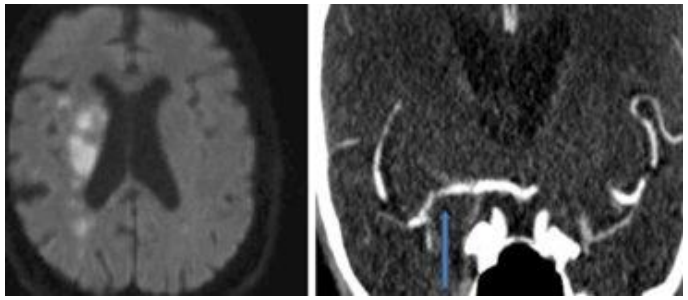
- Duration varies 3months- 1year

4) Patients with large vessel dissection

- Duration varies 3months- 1year

Antiplatelet + Low dose rivaroxaban

- For carefully selected patients with CAD or PAD meeting **COMPASS trial criteria,** rivaroxaban 2.5 mg BID + low-dose ASA is reasonable. This should not be used within first month after stroke
  - + low bleeding risk
  - + no hx of lacunar stroke or hemorrhagic stroke



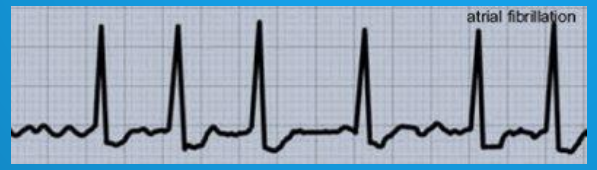
- Meet criteria for CAD or PAD
- Subjects with CAD must also meet at least 1 of the following:
  - Age ≥65 y or
  - Age <65 y with disease in 2 vascular beds or at ≥2 additional CV risk factors:
    - Current smoking
    - Diabetes mellitus
    - Renal dysfunction with eGFR <60 mL/min
    - Heart failure
    - Nonlacunar ischemic stroke ≥1 mo ago

Anticoagulation Therapy- no AF

For patients with an embolic stroke of undetermined source (ESUS), and no known atrial fibrillation, **anticoagulant therapy is not currently recommended over low-dose acetylsalicylic acid** for secondary stroke prevention [Evidence Level A].

Additional trials are ongoing to investigate this issue

Anticoagulation for Atrial Fibrillation



- **Stroke while on DOAC Therapy**
- For patients with afib who experience ischemic stroke or TIA in spite of anticoagulant therapy:
  - ID & address medication nonadherence
  - ensure correct DOAC dosing or warfarin INR control
  - avoid DOAC drug-drug interactions
  - investigate and treat other potential stroke etiology
  - promote general vascular risk factor modification
- **Continue current DOAC or switch to different anticoagulant are both reasonable**. Currently, evidence is lacking to make specific recommendations
- **Routine addition of ASA to anticoagulant is not recommended** because of ↑ bleeding risk without clear evidence of benefit unless medical indication

Anticoagulation Effectiveness for Atrial Fibrillation- KEY

- For patients prescribed DOAC, avoid inappropriate under-dosing as associated with ↑stroke risk
- For patients with **afib and chronic stable CAD (+ >1-year post-PCI or CABG)**
  - **addition of antiplatelet to DOAC therapy is not recommended** as ↑ bleeding risk without providing any significant benefit in reducing ischemic events (cardiac or cerebral)
- *Refer to current CCS guidelines for patients with recent coronary ischemic* events
- *See CSBPR Appendix Four for Selection of Anticoagulant Agents for Management of Atrial Fibrillation after stroke or TIA*

Perioperative Recommendations if on OAC

STEP 1: First risk stratify bleeding risk during the surgery

- **HIGH RISK**: major abdominal surgery (e.g., cancer resection), major thoracic surgery, major orthopedic surgery, and any cardiac, spinal, or intracranial surgery. Any patient having neuraxial anesthesia is classified as high-bleed-risk because of the risk for spinal epidural hematomas which could cause limb paralysis
- **LOW/MODERATE RISK:** most surgeries that are < 1h and there is no neuraxial anesthesia
- **MINIMAL RISK:** tooth extractions, root canal, skin biopsies, cataract surgery, and selected colonoscopies, for which anticoagulants can be continued without interruption. Permanent pacemaker and internal cardiac defibrillator implantation, as well as cardiac catheterization

STEP 2: Look at recommendations for DOAC interruption

- **Minimal risk:** no interruption
- **Low to moderate-bleed-risk** surgery or procedure (major abdominal/ thoracic/ orthopedic OR any cardiac, spinal or intracranial)
  - stop DOAC day before procedure + day of procedure (i.e., skip 2 days total), & restart day after procedure
- **High-bleed-risk** surgery or procedure, stop DOAC 2 days before procedure, day of procedure, and one day after procedure (i.e., skip 4 days total)

Note: exception of patients on dabigatran with impaired renal function (CrCl <50 mL/min) in whom an additional 1-2 days of interruption is suggested before surgery or procedure

Refer to CSBPR Clinical Considerations for additional information

Perioperative Recommendations if on OAC

- Patients with afib receiving **warfarin**:
  - **Low to moderate stroke risk** (e.g., CHADS2 score 0-4), stop warfarin x 5 days pre-procedure, & resume within 24 hours post-procedure, without heparin bridging
  - **High stroke risk** (e.g., CHADS2 score 5-6 or prior perioperative stroke), heparin bridging is suggested during warfarin interruption, typically with twice-daily LMWH x 3 days before & 3 days after
- Patients with **mechanical heart valve** stopping warfarin 5 days pre-procedure is recommended & resume within 24 hours post-procedure
- Heparin bridging is recommended for <u>select</u> patients with mitral valve bio-prosthesis and for high-risk patients with aortic valve bio--prosthesis (e.g., with additional risk factors for stroke)
- If bridging pre-op, forego post-op bridging in select patients, especially those undergoing high-bleed-risk procedures

Perioperative Recommendations if on Antiplatelet

- For patients receiving **ASA** for stroke prevention who require elective or urgent (within 7 days) CEA or CABG, continue ASA without interruption
- For patients receiving **dual antiplatelet therapy** with ASA + P2Y12 inhibitor (e.g., clopidogrel, ticagrelor) for secondary stroke prevention who require urgent CEA (within 7 days), continue ASA + P2Y12 inhibitor perioperatively
- For patients undergoing other types of surgery, continuing **ASA** could be considered before low/moderate-bleed-risk surgery or procedure. Interrupting ASA before high-bleed-risk surgery or procedure could be considered for 7-10 days
- *Refer to Table 8 suggested management for antiplatelet therapy for elective surgery*
- *Refer to Thrombosis Canada clinical guide for peri-operative management of patients on oral anticoagulant therapy at https://thrombosiscanada.ca/clinicalguides*

Patent Foramen Ovale (PFO)

Patients with a recent ischemic stroke suspected to be related to a PFO should have an evaluation by healthcare professionals with stroke and cardiovascular expertise

Common Issues:

- For patients requiring long-term anticoagulation for other reasons, the benefit of PFO closure is uncertain, and treatment decisions should be based on individual patient characteristics & risk versus benefit profile. [Evidence Level C]
- For patients with a recent ischemic stroke attributed to a PFO who do not undergo PFO closure and are aged 60 years or younger, either antiplatelet or anticoagulant therapy is recommended for secondary stroke prevention, unless there is a separate evidence-based indication for chronic anticoagulant therapy. [Evidence Level B]

Heart Failure, Decreased Left Ventricular Ejection Fraction, Cardiac Thrombus

For patients with stroke/ TIA who are in sinus rhythm and have a **LA/ LV thrombus** demonstrated by echocardiography or other imaging modality, **anticoagulant therapy is recommended for greater than 3 months**

For patients with stroke /TIA who are in sinus rhythm and have severe left ventricular dysfunction **(ejection fraction ≤35%) without evidence of left atrial or left ventricular thrombus, the net benefit of anticoagulant therapy compared with antiplatelet therapy is uncertain**, and the choice of management strategies should be individualized

Cancer Associated Ischemic Stroke

Patients with active malignancy + ischemic stroke or TIA should undergo standard etiological work-up for stroke, including vascular imaging & cardiac rhythm monitoring

Consider stroke mechanisms associated with malignancy

- non-bacterial (marantic) endocarditis,
- hypercoagulability,
- paradoxical embolism due to venous thrombosis,
- tumor-related vascular compression,
- stroke related to anti-cancer treatments

With active malignancy + ischemic stroke or TIA in whom a cancer-associated hypercoagulable state may have contributed, **consider anticoagulation over antiplatelet**.

When anticoagulation is used, LMWH is preferred. Role of DOAC is unknown but under study -- may be reasonable after consideration of patient preference

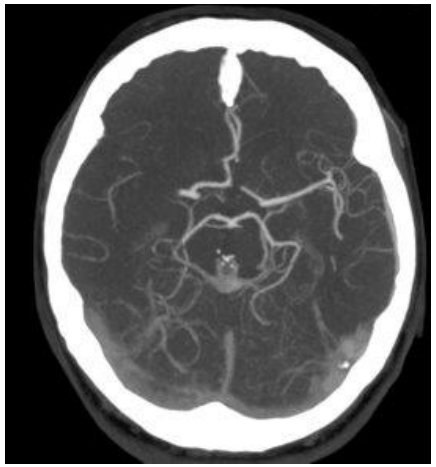
Clinical Consideration

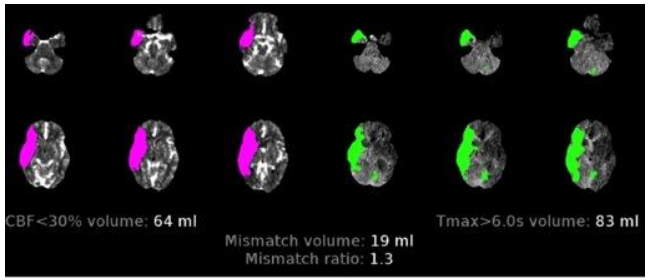
With active malignancy + ischemic stroke or TIA with concurrent VTE in whom stroke is presumed due to paradoxical embolus, follow guidelines for management of DVT and PE in cancer patients which includes LMWH and selected DOACs

Refer to www.thrombosiscanada.ca

Case: Mrs. PT

- 85yo F w Atrial Fibrillation CHADS-Vasc 5 presents after waking up L-sided weakness and neglect.
- Meds: on Apixaban etc….
- Not in thombolysis window. (i.e. >4.5h)
- Imaging
- No hyperacute therapy offered





Typical Conservation in the Stroke Unit

- Neurologist: "Do you take your apixaban regularly?"
- Patient: " Of course"
- Neurologist: "Do you ever miss any doses?"
- Patient: " No!"
- Neurologist "In the last 2 months, have you ever missed a single dose?"
- Patient. "Um…….yes."

Anticoagulation Effectiveness for Atrial Fibrillation- KEY

- **Medication adherence should be continually assessed and reinforced for patients on all oral anticoagulants at each follow-up visit**