Anticoagulation in Non-valvular Atrial Fibrillation (v1.6)

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MAQI² Michigan Anticoagulation Quality Improvement Initiative

Determining Need for Anticoagulation

- The need to anticoagulate is primarily based on ischemic stroke risk
- CHA_2DS_2-VASc is the recommended ischemic stroke risk tool
- DOACs are now recommended over warfarin except in patients with mod-to severe mitral stenosis or a mechanical heart valve
- Anti-platelets alone are NOT recommended for stroke prevention.

CHA_2DS_2-VASc Scoring Tool	
Condition	Points
Congestive heart failure	1
Hypertension	1
Age > 75 years	2
Diabetes mellitus	1
Stroke/TIA or thromboembolism (prior)	2
Vascular disease (MI, PAD, or aortic plaque)	1
Age 65-74 years	1
Sex Category (Female)	1

Score	Stroke Risk	2019 AHA /ACC Recommendation
≥3	High	Anticoagulate (men and women)
2	High/Interm.	Anticoagulate (men) Consider (women)
1	Interm./Low	Consider oral anticoagulant in men
0	Low	Reasonable to omit anticoagulation

CHA_2DS_2-VASc Score	Yearly Stroke Risk (%)	
	No treatment	With anticoagulant
0	0	0
1	1.3	0.5
2	2.2	0.8
3	3.2	1.1
4	4.0	1.4
5	6.7	2.3
6	9.8	3.4

For additional information about anticoagulation in atrial fibrillation, visit www.anticoagulationtoolkit.org

Anticoagulant Selection

		Pros	Cons	Dosing (see package	Contraindications/	Assessment/
Warfarin (Coumadin®)		• Inexpensive • Can be monitored • Can be reversed • Less GI bleeding • Once daily dosing	• Many food/drug interactions • Frequent INRs and dose changes • May require bridging around procedures • More intracranial bleeds	• Initial: 5mg/day (consider 2.5mg if high bleed risk) • Subsequent dosing based on INR with target range of 2-3	• Pregnancy (except mechanical heart valves) • Concomitant use of antibiotics, antifungals, herbal products, and inhibitors/inducers of CYP2C9, 1A2, and/or 3A4.	• Baseline: INR and CBC • INR 3-5 days after initiation and approx. 7 days after dose changes • INRs can be gradually spaced out if stable
DOACs	All	• No frequent monitoring and dose changes • Few drug interactions • Few food interactions (except rivaroxaban) • No bridging needed • Less intracranial bleeding	• More expensive • No accurate direct measurement • Reversal agents expensive and may not be available • Rely heavily on renal elimination	• DOAC specific (see below)	• Mechanical heart valves • Pregnancy/nursing • Triple positive antiphospholipid syndrome • Severe hepatic impairment • Bariatric surgery • Use carefully in patients with renal impairment	• Renal function, liver function, and CBC before initiation and at least yearly • Assess pt at week 1, 3, and 3 months from initiation
DOACs	Apixaban (Eliquis®)	• Less major bleeding and lower all-cause mortality compared to warfarin • Only DOAC to not have higher risk of GI bleed compared to warfarin	• Twice/daily dosing	• 5mg BID • 2.5mg BID if two of: age≥80, wt≤60kg, SCr ≥1.5 • 2.5mg BID if co-administered with strong dual inhibitors of CYP3A4 and P-gp	• Strong dual CYP3A4 and P-gp inhibitor and at least two of: age≥80, wt≤60kg, Cr≥1.5 • Strong dual inducers of CYP3A4 and P-gp	• See DOAC info above • In addition, regularly assess weight and age (may need dose adjustment)
DOACs	Dabigatran (Pradaxa®)	• Only DOAC to be superior to warfarin in ischemic stroke prevention	• Relies most on renal clearance • Twice/daily dosing • Increased dyspepsia • Must stay in original packaging • More GI bleeding than warf.	• 150mg BID (if CrCl>30mL/min) • 75mg BID (CrCl 15-30mL/min or CrCL 30-50 mL/min with dronedarone or ketoconazole)	• P-gp inducers (eg. rifampin) • P-gp inhibitors if CrCl <30mL/min	• See DOAC info above • Use Cockcroft–Gault with actual weight to calculate CrCl
DOACs	Edoxaban (Savaysa®)	• Less major bleeding compared to warfarin • once/daily dosing	• Inferior stroke prevention in patients with CrCl >95 mL/min	• 60mg daily (CrCL >50 to ≤95mL/min) • 30mg daily (CrCl 15-50 mL/min)	• CrCl >95 mL/min[3] • Rifampin • Mod/severe hepatic impairment	• See DOAC info above • Use Cockcroft–Gault with actual weight to calculate CrCl
DOACs	Rivaroxaban (Xarelto®)	• Once/daily dosing	• Should be taken with largest meal of the day • More GI bleeding compared to warfarin	• 20mg daily (CrCl >50 mL/min) • 15mg daily (CrCl ≤50mL/min)	• Combined P-gp and strong CYP3A4 inhibitors or inducers • Mod/severe hepatic impairment • Combined P-gp and moderate CYP3A4 inhibitors if CrCl <80	• See DOAC info above • Use Cockcroft–Gault with actual weight to calculate CrCl

Patient Education

Anticoagulation

- Watch for s/sx of bleeding (especially intracranial)
- Notify healthcare provider if any s/sx of bleeding but seek immediate medical care if serious bleeding
- Notify clinic before starting any new med (including OTC) or having proc.
- ASA/NSAIDs ↑ bleeding. Avoid NSAIDs and only use ASA if clear indication.
- Avoid dangerous activities that could lead to injuries (use protective gear)
- Notify dentist or physician that you are on anticoagulant prior to procedure
- Don't stop without consulting healthcare provider
- Provide written materials covering the above topics

Warfarin-specific

- Maintain stable Vitamin K intake (eg. green leafy vegetables, broccoli, brussel sprouts, green tea)
- Notify if illness or change in health status (may effect INR)
- Alcohol can increase INR
- Visit www.anticoagulationtoolkit.org for patient handouts

DOAC-specific

- Very important not to miss a dose (since short half life)
- Dabigatran must be kept in original packaging
- Rivaroxaban should be taken with largest meal of the day
- Visit www.anticoagulationtoolkit.org for patient handouts

Long-term Management

- Follow-up: at each f/u, assess for compliance, s/sx of bleeding or thromboembolism, interacting medication, and reinforce patient education.
- Bleeding
  - Nuisance: minor bleeding common (epistaxis, bleeding gums, etc.) Not reason to d/c anticoagulant. Teach how to prevent/manage.
  - Major bleeds: In most cases, resuming anticoagulation after bleeding controlled is best (~14 days after GI, within 1 mo. for intracranial)
- Periprocedural: Most pts don't need to have anticoag. interrupted for low bleed risk proc. unless pt has high bleed risk.(see table below) See warfarin and DOAC-specific peri-procedural info if interruption necessary.

High risk pt.	Eg. major bleed <3 mos, platelet abnormalities (including ASA use), hx of bleeding during prior bridging
Low risk proc.	Eg. minor dental and dermatological, cataract/glaucoma, diagnostic endoscopies
High risk proc.	Eg. major surgeries, procedures in highly vascularized organs (eg. kidneys), spinal procedures

- Follow-up:
  - INRs 3-5 days after re-starting or any changes that can effect INR (ex. med or diet change) and approx. 7 days after any dose changes
  - INRs can gradually be spaced out to monthly
  - Dose changes per a standardized protocol
- Periprocedural: If high-risk proc. or high-risk pt. (see table bottom left), stop 5 days before. Bridging should be considered if CHA_2DS_2-VASc ≥7, stroke <3 mos, or MHV. If bridging, start LMWH (UFH if CrCl<30) 3 days before proc. and stop 24 hrs before proc.(at least 4 hrs if UFH). Restart warfarin within 24 hrs of proc. at previous dose. Restart LMWH or UFH 24 hrs after low-risk proc. or 48-72 hours after high-risk proc. Stop LMWH/UFH when INR is therapeutic
- Switching to DOAC: stop warfarin and start DOAC when INR<2 (apixaban, dabigatran), ≤2.5 (edoxaban), <3 (rivaroxaban)

- Follow-up: annually assess CBC, liver function, renal function (more frequently if renal insufficiency), weight, and age. Adjust dose per package insert dosing instructions (above), if necessary.
- Periprocedural: If DOAC is to be interrupted, most pts should stop one day before low risk procedures and 2 days before high risk procedures. For dabigatran pts with CrCl<50, stop 2 days before low risk procedures and 4 days before high risk procedures. Bridging is rarely needed. DOAC can be restarted 24 hours after low risk procedure and 48-72 hours after higher risk procedure.
- Switching to another DOAC: discontinue current DOAC and start new one at next scheduled dose.
- Switching to warfarin: see DOAC package insert for instructions.

References

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- Joglar, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation Circulation. 2023;148:e00–e00. DOI: 10.1161/CIR.0000000000001193

- Drug package inserts
    - Warfarin: https://packageinserts.bms.com/pi/pi_coumadin.pdf
    - Apixaban: https://packageinserts.bms.com/pi/pi_eliquis.pdf
    - Dabigatran: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf
    - Edoxaban: http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true