Anticoagulation in Non-valvular Atrial Fibrillation

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
- Bleed risk and patient preference should also be considered
- Aspirin is NOT recommended for stroke prevention in patients with high stroke risk

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
Total score=	

Score	Stroke Risk	AHA /ACC Recommendation
≥2	High	Anticoagulate
1	Intermediate	Consider oral anticoagulant or ASA
0	Low	No antithrombotic

Score	Yearly Stroke Risk (%)		
	No tx	With Aspirin	With anticoagulant
0	0	0	0
1	1.3	1.0	0.5
2	2.2	Not rec.	0.8
3	3.2	Not rec.	1.1
4	4.0	Not rec.	1.4
5	6.7	Not rec.	2.3
6	9.8	Not rec.	3.4

For additional information about anticoagulation in Atrial Fibrillation, visit www.anticoagulationtoolkit.org

Anticoagulant Selection

		Pros	Cons	Dosing (see package inserts for full info)	Contraindications/ Precautions	Assessment/ Monitoring
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 • Not easily reversed (except dabigatran) • Rely heavily on renal elimination	• DOAC specific (see below)	• Mechanical heart valves • Pregnancy/nursing • BMI>40, or weight >120kg • Bariatric surgery • Significant renal dysfunction (CrCl<30 mL/min3)	• Renal function, liver function, and CBC before initiation and at least yearly • Assess pt at week 1, 3, and 3 months from initiation
	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 • Severe hepatic impairment	• See DOAC info above • In addition, regularly assess weight and age (may need dose adjustment)
	Dabigatran (Pradaxa®)	• Has an effective reversal agent but may not be readily available at all facilities • 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
	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/min3 • Rifampin • Mod/severe hepatic impairment	• See DOAC info above • Use Cockcroft–Gault with actual weight to calculate CrCl
	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 15-50mL/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	Warfarin-specific	DOAC-specific
• 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	• 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	• 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. DO NOT bridge unless CHA_2DS_2-VASc ≥7 or stroke <3 mos. 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, timing of last dose is based on procedure bleed risk, pt CrCl, and specific DOAC (see MAQI toolkit p. 56). Consider holding DOAC longer if patient on P-gp and CYP3A4 inhibitor. Bridging is rarely needed. DOAC can be restarted day 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

- January CT, Wall S, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. Circulation. 2014;130:e199-e267.
- Holbrook A, Schulman S, Witt D, et al. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. CHEST 2012; 141(2)(Suppl):e152S–e184S
- Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010 Feb;137(2):263-72.
- Doherty J, Gluckman TJ, Hucker WJ, et al. 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation. Journal of the American College of Cardiology Jan 2017, 23217.
- 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
    - Rivaroxaban: https://www.xareltohcp.com/shared/product/xarelto/prescribing-information.pdf

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