ATRIAL FIBRILLATION
POCKET GUIDE

Based on content from the CCS/CHRS 2020 Comprehensive Atrial Fibrillation Guidelines

Canadian Cardiovascular Society
Leadership. Knowledge. Community.

ATRIAL FIBRILLATION

About this Pocket Guide

This pocket guide is a quick-reference tool that features diagnostic and management recommendations based on the 2020 CCS/CHRS Comprehensive Atrial Fibrillation (AF) Guidelines.

These recommendations are intended to provide a reasonable and practical approach to the care of AF patients for primary care physicians, specialists, nurses, and allied health professionals. These recommendations are subject to change as scientific knowledge and technology advance and practice patterns evolve, and are not intended to be a substitute for clinical judgment. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

Recommendations were developed according to GRADE standards with the strength of recommendations now classified as “Strong” or “Weak” (previously “Strong” or “Conditional”).

For the complete CCS Guidelines on AF, please visit www.ccs.ca.

Co-Chairs
Jason G. Andrade and Laurent Macle.

CCS Atrial Fibrillation Guideline Panel Members
Primary Panel: Martin Aguilar, Clare Atzema, Alan Bell, John A. Cairns, Christopher C. Cheung, Jafna L. Cox, Paul Dorian, David J. Gladstone, Jeff S. Healey, Paul Khairy, Kori Leblanc, M. Sean McMurtry, L. Brent Mitchell, Girish M. Nair, Stanley Nattel, Ratika Parkash, Louise Pilote, Roopinder K. Sandhu, Jean-François Sarrazin, Mukul Sharma, Allan C. Skanes, Mario Talajic, Teresa S. M. Tsang, Atul Verma, Subodh Verma, Richard Whitlock, D. George Wyse.
Secondary Panel: David Bewick, Vidal Essebag, Peter Guerra, Milan Gupta, Brett Heilbron, George Klein, Simon Kouz, Daniel Ngui, Pierre Page, Calum Redpath and Jan Surkes.

Table of Contents

SAF Score	Symptoms Attributed to AF, Impact on QOL
Class 0	**Asymptomatic**
1	**Minimal effect:** • minimal and/or infrequent symptoms, or • single episode of AF without syncope or HF
2	**Minor effect:** • mild awareness of symptoms in patients with persistent/permanent AF, or • rare episodes (e.g., < a few per year) in patients with paroxysmal or intermittent AF
3	**Moderate effect:** • moderate awareness of symptoms on most days in patients with persistent/permanent AF, or • more common episodes (e.g., > every few months) or more severe symptoms, or both, in patients with paroxysmal or intermittent AF
4	**Severe effect:** • very unpleasant symptoms in patients with persistent/permanent AF and/or • frequent and highly symptomatic episodes in patients with paroxysmal or intermittent AF and/or • syncope thought to be due to AF and/or • congestive heart failure secondary to AF

**Dorian P, Cvitkovic SS, Kerr CR; et al. Can J Cardiol. 2006; 22(5):383-386*
QOL, Quality of life;
HF, heart failure

Clinical Patterns Atrial Fibrillation

Pattern	Definition
Paroxysmal AF	Continuous AF episode lasting longer than 30 seconds but terminating within 7 days of onset.
Persistent AF	Continuous AF episode lasting longer than 7 days but less than 1 year.
“Longstanding” persistent AF	Continuous AF >1 year in duration, in patients in whom rhythm control management is being pursued.
Permanent AF	Continuous AF for which a therapeutic decision has been made not to pursue sinus rhythm restoration.
Valvular AF	AF in the presence of any mechanical heart valve, or in the presence of moderate to severe mitral stenosis (rheumatic or nonrheumatic)

Baseline Evaluation for All Patients

Complete AF History		
Establish	• The date of first symptomatic attack and the date of first objective confirmation • The duration and frequency of episodes (e.g. the dominant pattern of AF) • The presence and nature of symptoms related to AF • Symptom severity (including impact on quality of life)	
Identify	**1. Risk factors / Comorbid conditions** **See page 5* **2. Triggers for AF episodes** • Stimulants • Alcohol • Sleep deprivation • Emotional Stress • Physical Exertion • Sleep/Nocturnal • Digestive	**3. Reversible causes / AF secondary to:** • Cardiac or non-cardiac surgery • Acute cardiac pathology • Acute pulmonary pathology • Acute infection • Thyrotoxicosis • Alcohol • Pharmacologic agents (e.g. Ibrutinib) • Supraventricular tachycardia • Ventricular pacing
Review	• Family history to identify potentially heritable causes of AF • Prior pharmacologic and non-pharmacologic interventions for AF, with a focus on efficacy, tolerance and adverse effects • AF-related healthcare utilisation (e.g. emergency department visits, hospitalisations and cardioversions)	

Baseline Evaluation for All Patients

Examination

- Measure blood pressure and heart rate
- Determine patient height, weight, body mass index (BMI) , and waist circumference
- Comprehensive cardiopulmonary examination with a focus on determination of the causes of AF (e.g. comorbid risk conditions, or secondary causes of AF)

Routine Investigations

1. 12-lead electrocardiogram

- Document presence of AF
- Document PR, QRS, and QT intervals (e.g. baseline prior to therapy initiation)
- Identify potential causes of AF (e.g. structural heart disease such as myocardial infarction, ventricular hypertrophy, atrial enlargement, congenital heart disease)
- Identify factors that increase risk of adverse outcomes (e.g. conduction distrubances, sinus node dysfunction, or repolarization abnormalities)
- Identify high risk conditions (e.g. manifest pre-excitation)

2. Echocardiogram

- Evaluate ventricular size, wall thickness, and function
- Evaluate left atrial size and left atrial volume
- Exclude significant valvular or congenital heart disease (e.g. atrial septal defect)

3. Laboratory Investigations

- Complete blood count
- Coagulation profile
- Serum electrolytes including calcium and magnesium
- Renal function
- Liver function
- Thyroid function
- Fasting lipid profile
- Fasting glucose, hemoglobin A1C

Risk Markers and Co-morbid Conditions Associated with AF

Established Risk Factors	Emerging Risk Factors	Potential Risk Factors
• Advancing age • Male sex • Hypertension • HF with reduced ejection fraction • Valvular heart disease • Overt thyroid disease • Obstructive sleep apnea • Obesity • Excessive alcohol intake • Congenital heart disease (e.g. early repair of atrial septal defect)	• Prehypertension and increased pulse pressure • Chronic obstructive pulmonary disease • HF with preserved ejection fraction • Subclinical hyperthyroidism • Coronary artery disease • Morphometric (increased height, increased birth weight)	• Familial/genetic factors • Tobacco use • Left atrial dilatation • LV hypertrophy • Inflammation • Diabetes • Pericardial fat • Subclinical atherosclerosis • Chronic kidney disease • Excessive endurance exercise • Electrocardiographic (atrial conduction delay, PR interval prolongation)

Modifiable Cardiovascular Risk Factors

Management of modifiable risk factors to reduce cardiovascular events

- In patients with established AF or at high risk of developing AF, we recommend a systematic approach to the identification of traditional modifiable cardiovascular risk factors and/or conditions associated with AF, with strict guideline-adherent management to reduce major cardiovascular events *(Strong Recommendation; High-Quality Evidence)* and to prevent recurrence of the arrhythmia and/or decrease its symptom burden *(Strong Recommendation; Low-Quality Evidence)*.

Values and preferences: This recommendation places a high value on a comprehensive, holistic and systematic approach to the management of AF. Given the contribution of modifiable risk factors to the development and progression of AF, a systematic approach to the identification of modifiable cardiovascular risk conditions offers a potential therapeutic target to improve outcomes in this population. This recommendation recognizes the association between these modifiable cardiovascular risk factors (including but not limited to hypertension, HF, diabetes mellitus, obesity, inactivity, sleep apnea, and alcohol misuse), and major adverse cardiovascular outcomes (e.g. stroke, MI, cardiovascular death) and AF outcomes (AF burden/exacerbations, AF-related emergency department visits/hospitalizations).

Practical tip: Screening for common cardiovascular risk factors and/or conditions (hypertension, obesity, inactivity, sleep apnea, diabetes, and alcohol misuse) should be performed in addition to screening for AF-specific risk conditions (HF, valvular heart disease, thyroid dysfunction).

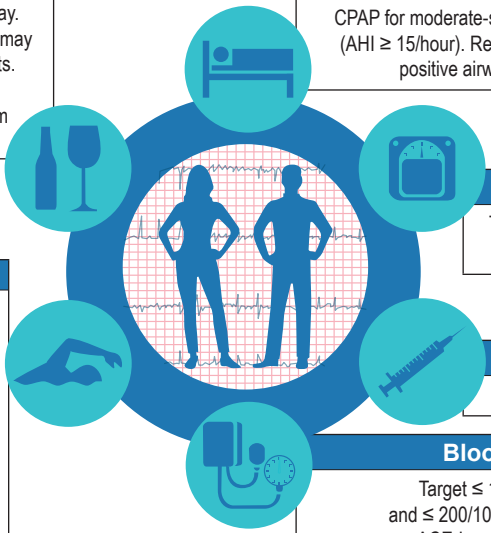
Alcohol and Tobacco

Limit to ≤ 1 standard drink[1] per day. Complete abstinence from alcohol may be preferred in selected patients.

Target complete abstinence from tobacco-related products.

Sleep Apnea

CPAP for moderate-severe obstructive sleep apnea (AHI ≥ 15/hour). Regular assessment of continuous positive airway pressure adherence.



Weight Loss

Target a weight loss of ≥10% to a BMI of less than 27 kg/m^2.

Exercise

1. Moderate intensity aerobic exercise ≥ 30 minutes a day at least 3-5 days per week (target ≥ 200 minutes weekly).
2. Resistance exercise 2-3 days per week.
3. Flexibility exercises at least 10 minutes per day at least 2 days per week in those >65 years of age.

Diabetes

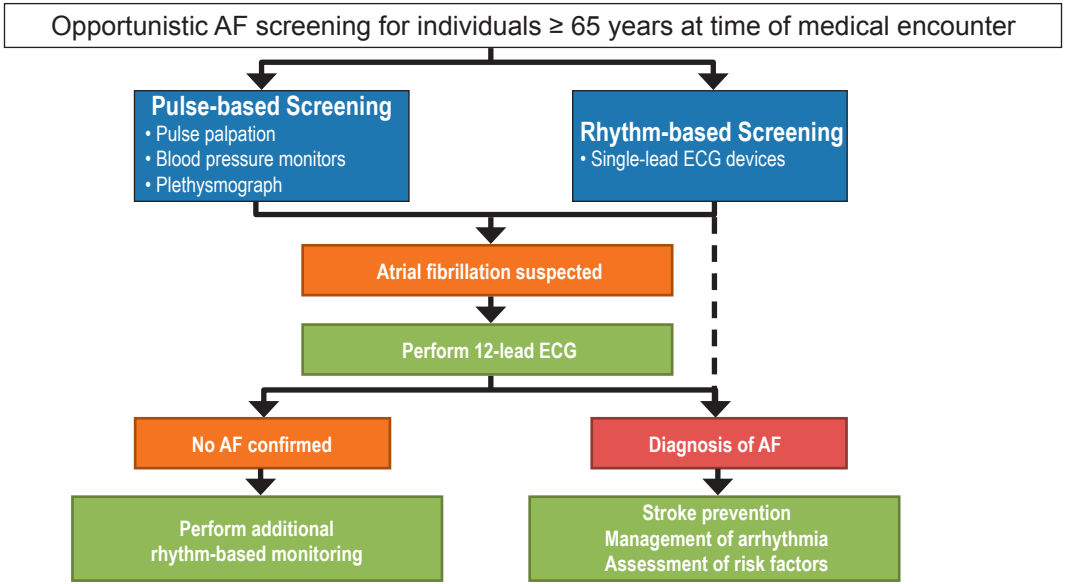
Target a HbA1c of ≤7.0%.

Blood Pressure

Target ≤ 130/80 mmHg at rest and ≤ 200/100 mmHg at peak exercise. ACE-I or ARB may be preferred.

[1]*defined as containing 14 g of alcohol; 44 ml (1.5 fluid oz.) of 80-proof liquor, 148 mL (5 fluid oz.) of wine or 355 ml (12 fluid oz.) of beer.*

Approach to Opportunistic Atrial Fibrillation (AF) Screening



Opportunistic AF Detection in the General Population

- We recommend that opportunistic screening for AF should be conducted in people ≥65 years at the time of medical encounters *(Strong Recommendation; Low-Quality Evidence)*.

Practical tip: Screening can be efficiently and cost-effectively performed using opportunistic pulse checks during routine medical encounters; consideration can also be made to use rhythm-based devices (e.g. single-lead ECG rhythm device).

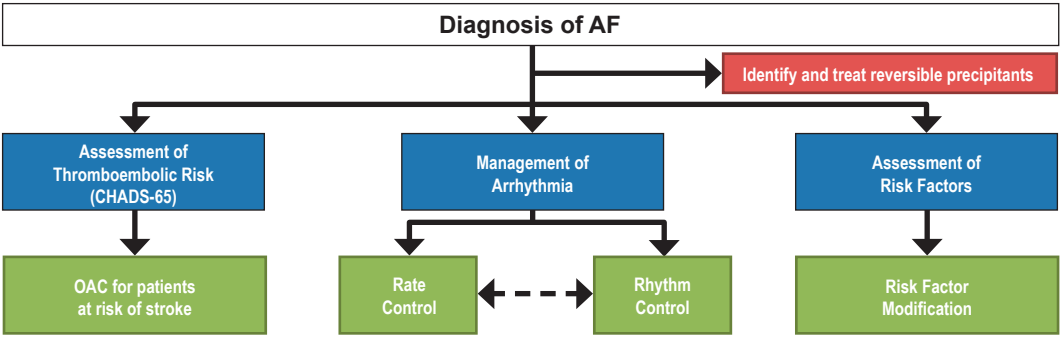
- We recommend downstream confirmatory testing when AF is suspected but not documented, or when the documentation method does not include electrocardiographic rhythm acquisition *(Strong Recommendation; Low-Quality Evidence)*.

Values and preferences: Confirmatory testing for AF is highly dependent on the type of AF. The effectiveness of the various AF screening methods depends on duration of monitoring (e.g. single 12-lead ECG vs. continuous monitoring). The use of new technologies for screening require validation before implementation.

OAC therapy for highly selected patients with subclinical AF

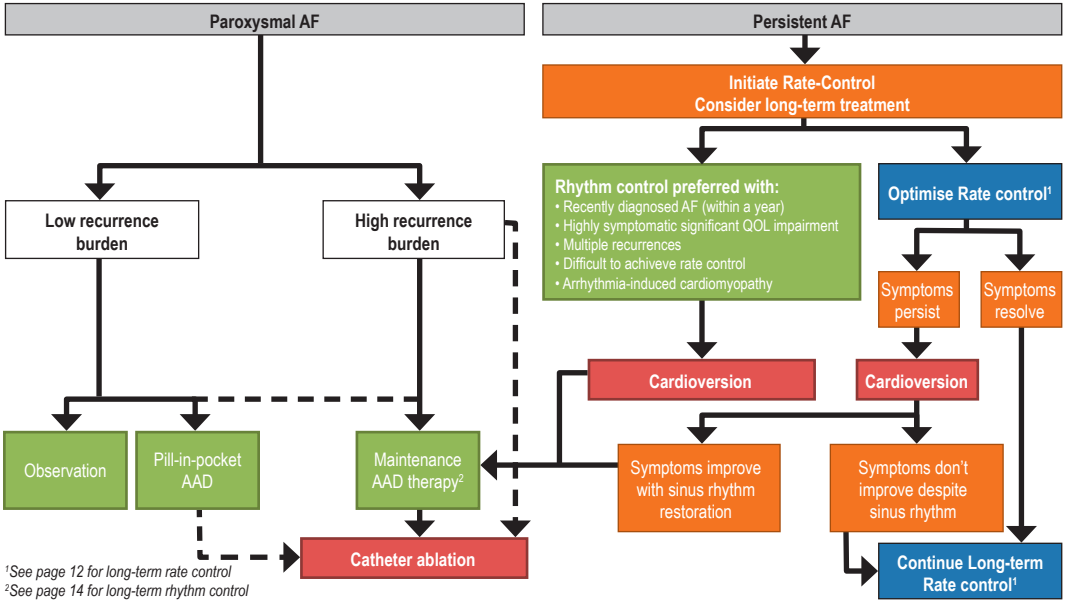
- We suggest that it is reasonable to prescribe OAC for patients with AF who are aged ≥65 years or with a $CHADS_2$ score ≥1 who have episodes of subclinical AF lasting >24 continuous hours (*Weak Recommendation; Low-Quality Evidence*).

Overview of AF Management



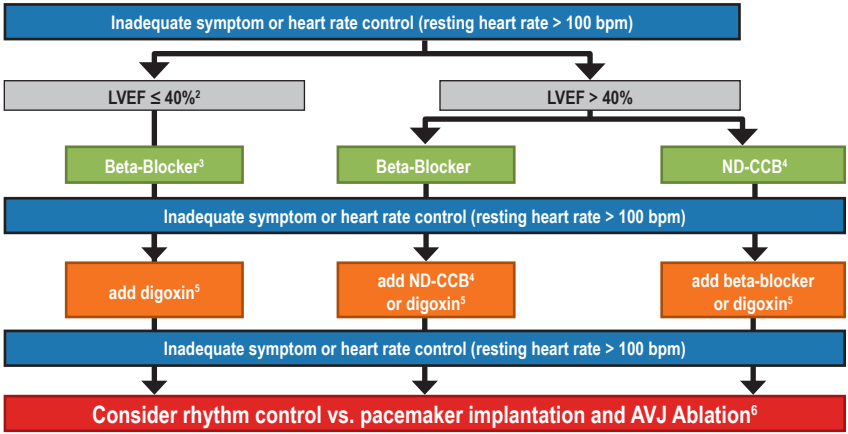
Major Goals of AF Management	Anticipated Outcome
Prevent stroke or systemic thromboembolism	Improvement in survival
Cardiovascular Risk Reduction	
Improve symptoms, functional capacity, and quality of life	Reduction in healthcare utilisation (e.g. emergency department visits or hospitalizations)
Prevent complications (e.g. LV dysfunction, falls)	

Approach to Rate and Rhythm Management of AF



[1]*See page 12 for long-term rate control*
[2]*See page 14 for long-term rhythm control*

Long-Term Rate Control[1]



[1] *Consider AF Symptom burden, possibility of adverse drug reactions and patient preference.*

[2] *Consider catheter ablation in patients with co-existing atrial fibrillation and heart failure.*

[3] *Evidence-based beta-blockers proven to reduce mortality (bisoprolol, carvedilol, metoprolol) are recommended.*

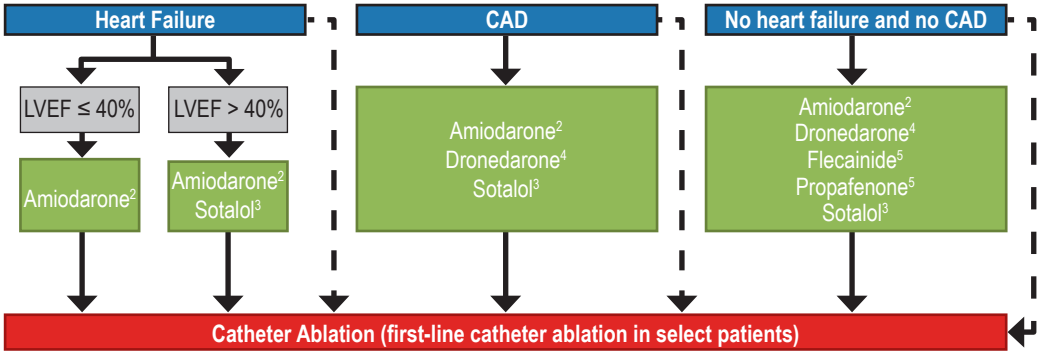
[4] *Non-dihydropyridine calcium channel blockers (diltiazem, verpamil).*

[5] *Digoxin is most beneficial in addition to first-line agents in those who fail to achieve satisfactory symptom or hear rate control, or as monotherapy in sedentary individuals with side-effects or contraindications to first-line agents. Therapeutic drug monitoring may be useful in adjusting digoxin dose.*

[6] *Consider cardiac resynchronisation therapy prior to AV junction ablation in those with reduced LVEF.*

Class	Agent	IV Therapy	Oral Therapy		Comments
			Initial	Target	
Beta-blockers	Atenolol	-	25 mg daily	100 mg daily	1. Adverse effects: bradycardia, hypotension, fatigue, and depression 2. Contraindicated with pre-excitation, or bronchospasm 3.Once daily preparations (e.g. bisoprolol) are preferred to optimize adherence 4. Agents preferred in the presence of: - LV dysfunction: bisoprolol or carvedilol - hypertension: atenolol or metoprolol - CAD: atenolol, propranolol or metoprolol 5. Carvedilol is less effective for rate control but has been associated with improved LV function in patients with LV dysfunction 6.Nadolol is effective for rate control but associated with side effects
	Bisoprolol	-	2.5 mg daily	10 mg daily	
	Carvedilol	-	6.25 mg twice daily	25 mg twice daily	
	Esmolol	500 mcg/kg IV over 1 min q4min x3 prn or 50-200 cg/kg/minute infusion	-	-	
	Metoprolol	2.5-5.0 mg IV over 2 min q5min x3 prn	12.5-25 mg twice daily	100-200 mg twice daily	
	Nadolol	-	40 mg daily	80-160 mg daily	
	Nebivolol	-	5 mg daily	40 mg daily	
	Propanolol	Initially 1–3 mg. May repeat after 2 min.	40 mg twice daily	160 mg twice daily	
ND-CCB	Diltiazem	0.25 mg/kg IV; a second bolus of 0.35mg/kg may be given in 15 min	IR 30 mg q6h-q8h or ER 120 mg daily	IR 120 mg q6h or ER 360 mg daily	1. Adverse effects: bradycardia, hypotension, constipation (verapamil), and edema (diltiazem) 2. Contraindicated in the presence of pre-excitation, CHF or LV dysfunction 3. Once daily preparations are preferred
	Verapamil	5-10mg (0.075-0.15 mg/kg) IV over 2 min	IR 80 mg tid or SR 120-240 mg daily	IR 120 mg tid or SR 360 mg daily	
Other	Digoxin	10-15 mcg/kg in divided doses Typically - 0.5 mg IV then 0.25 mg IV q6-8h for 2 doses	0.125 mg daily (loading not usually necessary as an outpatient)	0.125-0.25 mg daily	1. Adverse effects: GI upset, blurred vision, proarrhythmia 2. Rarely used as alone for rate control 3. Use with care in elderly females and those with CKD or concomitant potassium-wasting diuretic (e.g. Lasix or hydrochlorothiazide)
Class III	Amiodarone			100-200 mg daily	Rarely used for rate control due to significant side-effects and potential to convert AF to sinus rhythm (See Supplemental Table S13)

Long-Term Rhythm Control[1]



[1] *Consider AF Symptom burden, possibility of adverse drug reactions and patient preference.*
[2] *Consider alternative AADs or ablation rather than long-term amiodarone (significant risk of extra-cardiac side-effects).*
[3] *Sotalol should be used with caution in patients with high-risk features for torsade de pointes (> 65 years, women, reduced renal function, concomitant potassium-wasting diuretics). Sotalol is not recommended for patients with left ventricular hypertrophy.*
[4] *Dronedarone should be used with caution in combination with digoxin.*
[5] *Class IC agent should be combined with AV-nodal blocking agent. Use caution for patients with left ventricular hypertrophy.*

Rhythm Control – Recommended Drugs

Class	Drug	Dosage	Contraindications/Precautions		ECG Parameter for Discontinuing
Ic	Flecainide	**Starting Dose:** 50-75 mg twice daily **Maximum Dose:** 150 mg twice daily	• Advanced atrioventricular or Infranodal conduction disease • Marked sinus bradycardia • Ischemic heart disease (active ischemia or history of MI)	• Clinical heart failure or LVEF ≤40% • Brugada syndrome • LVH (ECG or echo) with repolarization abnormality (ECG)	QRS duration increases >25% from baseline or to >150 msec PR interval >200 msec
	Propafenone	**Starting Dose:** 150 mg three times daily **Maximum Dose:** 300 mg three times daily	• Advanced atrioventricular or Infranodal conduction disease • Marked sinus bradycardia • Ischemic heart disease (active ischemia or history of MI) • Clinical heart failure or LVEF ≤40%	• Brugada syndrome • Severe hepatic impairment • Myasthenia gravis • LVH (ECG or echo) with repolarization abnormality (ECG)	QRS duration increases >25% from baseline or to >150 msec PR interval >200 msec
III	Sotalol	**Starting Dose:** 40 mg twice daily **Maximum Dose:** 160 mg twice daily	• Pre-existing QTc prolongation • Marked sinus bradycardia • Advanced atrioventricular node disease • Severe renal impairment (CrCl <40 mL/min)	• Advanced age (>75 years of age) • LV dysfunction (LVEF ≤40%) • LVH (ECG or echo) with repolarization abnormality (ECG)	QTc increases >25% from baseline or to ≥500 msec
	Dronedarone	400 mg twice daily	• HF with recent decompensation • LV dysfunction (LVEF ≤40%) • Long-standing persistent or permanent AF	• Previous amiodarone-induced lung or liver injury • Pre-existing QTc prolongation	QTc increases >25% from baseline or to ≥500 msec
	Amiodarone	**Loading Dose:** 400 mg twice daily x 1 week then 400 mg once daily x 2 weeks, or 400 mg daily x 1 month **Maintenance Dose:** 100-200 mg daily	• Advanced atrioventricular or Infranodal conduction disease • Marked sinus bradycardia • Advanced pulmonary disease • Active hepatitis	• Significant chronic liver disease • Pre-existing QTc prolongation • Uncontrolled thyroid dysfunction	QTc increases >25% from baseline or to ≥500 msec

Legend: *ECG, electrocardiogram; echo, echocardiography; LVEF, left ventricular ejection fraction; msec, milliseconds; MI, myocardial infarction.*

Rhythm Management of AF in the Acute Care Setting

Medication	Dose	Time to Conversion	Relative Efficacy	Major Side Effects	Suggested Monitoring Post Administration
Class IA[1]					
Procainamide	15-18 mg/kg IV over 30-60 minutes (usual dose 1 g over 1 hour)	1 hour	++	Hypotension Bradycardia Ventricular proarrhythmia	1-hour post infusion
Class IC[2]					
Flecainide	300 mg po (>70 kg) 200 mg po (≤70 kg)	2-6 hours	++++	Hypotension Bradycardia Conversion pauses 1:1 conduction of AFL Ventricular proarrhythmia	6-hours post administration
Propafenone	600 mg po (>70 kg) 450 mg po (≤70 kg)	2-6 hours	+++		
Class III					
Ibutilide[3]	1 mg IV over 10 min (0.01 mg/kg if <60 kg) May repeat x 1	1 hour	+++	Prolonged QT Torsades de pointes Hypotension	4-hours post infusion
Vernakalant[4]	3 mg/kg IV over 10 minutes, followed by 2 mg/kg IV if no conversion	12-30 min.	++++	Bradycardia Hypotension Ventricular proarrhythmia	2-hours post infusion
Amiodarone	150 mg IV bolus then 60 mg/h x 6 hours then 30 mg/h x 18 hours	8-12 hours	++	Hypotension Bradycardia Atrioventricular block Torsades de pointes Phlebitis	

[1] Class Ia agents should be avoided in patients with hypotension, ischemic heart disease, heart failure, conduction system disease, and Brugada syndrome.
[2] Class Ic drugs (flecainide and propafenone) should be used in combination with AV nodal blocking agents (beta-blockers or calcium channel inhibitors administered ≥30 minutes prior to Class IC agent). Class Ic agents should be avoided in patients with hypotension, ischemic heart disease, significant structural heart disease, and Brugada syndrome.
[3] Consider pre-treating with 1-4 mg of IV MgSO4. Ibutilide should be avoided in patients with hypokalemia, hypomagnesemia, baseline QT prolongation, or significant structural heart disease.
[4] Vernakalant should be avoided in patients with hypotension, recent acute coronary syndrome (within 30 days), severe heart failure (NYHA III/IV), or severe aortic stenosis.

“Pill-In-The-Pocket” Antiarrhythmic Drug Therapy

Appropriate candidates

1) symptomatic patients with sustained AF episodes (e.g. ≥2 hours) that occur less frequently than monthly
2) absence of severe or disabling symptoms during an AF episode (e.g. fainting, severe chest pain, or breathlessness)
3) ability to comply with instructions, and proper medication use

PIP administration

Immediate release oral AV nodal blocker (one of diltiazem 60 mg, verapamil 80 mg, or metoprolol tartrate 25 mg) 30 minutes prior to the administration of a class Ic antiarrhythmic (300 mg of flecainide or 600 mg of propafenone if ≥70 kg; 200 mg of flecainide or 450 mg of propafenone if <70 kg).

Mandatory monitoring for initial administration

Telemetry for at least 6 hours
Blood pressure monitoring every 30 minutes
12-lead ECG monitoring every 2 hours

Determinants of initial treatment failure

1) AF persistence >6 hours after “pill-in-the-pocket” administration or electrical cardioversion required for termination
2) Adverse events including:
   - symptomatic hypotension (systolic BP ≤90 mmHg)
   - symptomatic conversion pauses (>5 seconds)
   - symptomatic bradycardia after sinus rhythm restoration
   - pro-arrhythmia (conversion to AFL/tachycardia, or episodes of ventricular tachycardia)
   - severe symptoms (dyspnea, presyncope, syncope)
   - > 50% increase in QRS interval duration from baseline.

Contraindication to PIP

1) significant structural heart disease (e.g. LVEF <50%, active ischemic heart disease, severe left ventricular hypertrophy)
2) abnormal conduction parameters (e.g. QRS duration >120 msec, PR interval >200 msec; or evidence of pre-excitation)
3) sinus node dysfunction or advanced AV block
4) hypotension (systolic BP <100mmHg)
5) prior intolerance to any of the “pill-in-the-pocket” medications

Instructions for subsequent out-of-hospital use

1) Patients should take the AV nodal agent 30 minutes after arrhythmia onset, then the Class Ic antiarrhythmic drug 30 minutes following the AV nodal agent. Following antiarrhythmic drug administration patients should rest in a supine or seated position for the next 4 hours, or until the episode resolves.

2) Patients should present to the emergency department in the event that:

   a) the AF episode did not terminate within 6-8 hours

   b) they felt unwell after taking the medication at home (e.g. a subjective worsening of the arrhythmia following antiarrhythmic drug ingestion

   c) more than one episode occurred in a 24-hour period (patients should not take a second PIP dose within 24 hours)

   d) if the AF episode was associated with severe symptoms (e.g. significant dyspnea, chest pain, pre-syncope, or symptoms of stroke), even in the absence of PIP use.

AF, atrial fibrillation; AV, atrioventricular; AFL, atrial flutter; BP, blood pressure; ECG, electrocardiogram; LVEF, left ventricular ejection fraction; msec, milliseconds; PIP, “pill-in-the-pocket”.

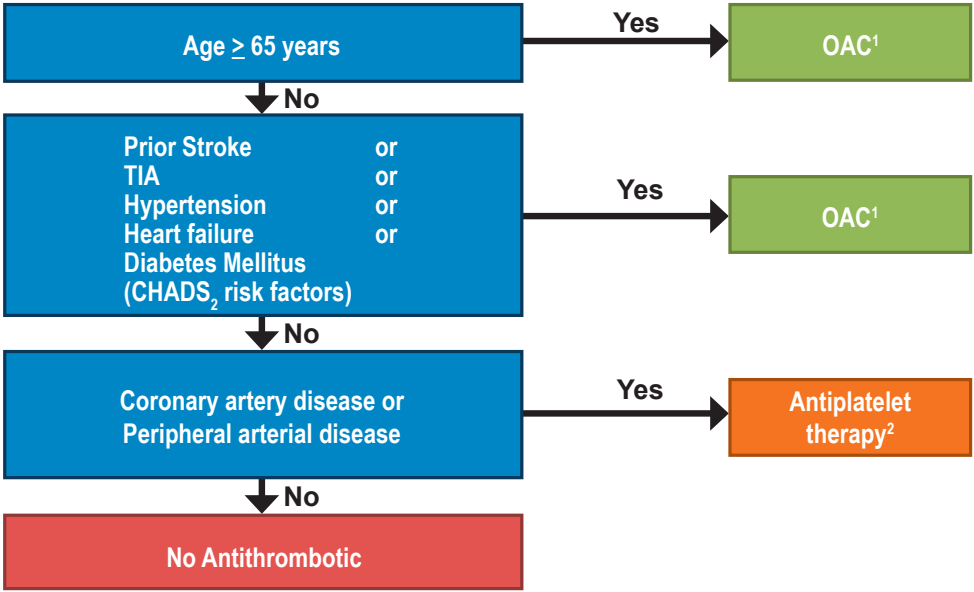
- We recommend catheter ablation of AF in patients who remain symptomatic after an adequate trial of antiarrhythmic drug therapy and in whom a rhythm control strategy remains desired *(Strong Recommendation, High-Quality Evidence)*.
- We suggest catheter ablation to maintain sinus rhythm as first-line therapy for relief of symptoms in select patients with symptomatic AF (*Weak Recommendation; Moderate-Quality Evidence*).
- We recommend catheter ablation of typical right AFL as a reasonable alternative to pharmacologic rhythm or rate control therapy (*Strong Recommendation; Moderate-Quality Evidence*).
- We suggest that catheter ablation of AF should be performed by electrophysiologists with a high degree of expertise and high annual procedural volumes (*Weak Recommendation; Low-Quality Evidence*).

Risk/Benefit Ratio* for Ablation in Patients with Symptomatic AF

	Longstanding¶	Persistent	Paroxysmal
1st line	--	--	+
Failed 1st drug	--	+	+ +
Failed 2nd drug	+	+ +	+ + +
Failed multiple drugs	+ +	+ + +	+ + +

** irrespective of the presence or absence of HF or ventricular dysfunction*
+ indicates balance of benefit to risk in favour of catheter ablation
¶ ongoing symptomatic AF ≥ 1 year

The "CCS Algorithm" (CHADS-65) for OAC Therapy in AF



[1] A DOAC is preferred over warfarin for non-valvular AF

[2] Therapeutic options include ASA 81 mg daily alone, clopidogrel 75 mg daily alone, or ASA 81 mg daily in combination with either clopidogrel 75 mg daily, ticagrelor 60 mg bid, or rivaroxaban 2.5 mg bid (depending on clinical circumstance).

Most patients should receive DOAC

- We recommend most patients should receive a DOAC (apixaban, dabigatran, edoxaban, or rivaroxaban) in preference to warfarin when OAC therapy is indicated for patients with NVAF (*Strong Recommendation; High-Quality Evidence*).

Values and preferences: This recommendation places a relatively high value on the results of several large RCTs showing that the DOACs are either noninferior or superior to warfarin in preventing AF-related stroke; that they have no more or less major bleeding compared with warfarin; that they are associated with less ICH compared with warfarin; and on the greater ease of use of DOACs compared with dose-adjusted warfarin.

- We suggest that no antithrombotic therapy be prescribed for stroke prevention for most patients with NVAF who are aged <65 years with no $CHADS_2$ risk factors *(Weak Recommendation; Moderate-Quality Evidence)*.

Values and preferences: For patients with NVAF aged <65 years with no $CHADS_2$ risk factors the current evidence does not support antiplatelet monotherapy for stroke prevention.

- We suggest that no oral anticoagulation for stroke prevention for most patients with NVAF aged <65 years with no $CHADS_2$ risk factors and stable coronary or arterial vascular disease (*Weak Recommendation; Moderate-Quality Evidence*).

Practical tip: The risk of stroke associated with AF is not sufficiently elevated to justify routine OAC therapy for those patients with stable coronary or arterial vascular disease aged younger than 65 years with AF and no CHADS2 risk factors. Treatment should be directed at the underlying coronary/peripheral arterial disease as outlined in the CCS/CAIC guidelines. Therapeutic options include ASA 81 mg daily alone; or ASA 81 mg daily in combination with either clopidogrel 75 mg daily, ticagrelor 60 mg BID, or rivaroxaban 2.5 mg BID.

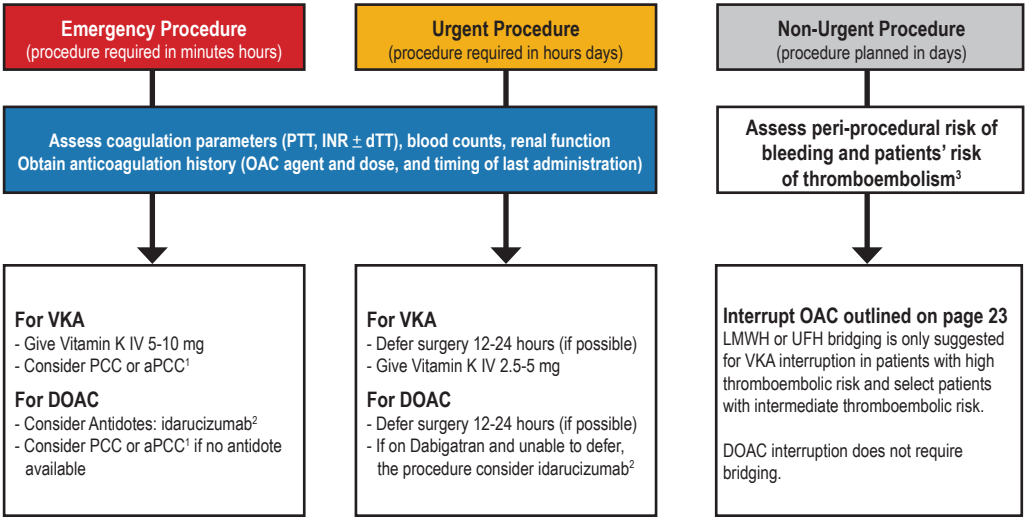
Dosage of Oral Anticoagulants Based on Renal Function

CrCl	Warfarin	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
CrCl >50 mL/min	Dose adjusted for INR 2.0-3.0	5 mg BID†	150 mg BID*	60 mg daily∞	20 mg daily
CrCl 30-49 mL/min	Dose adjusted for INR 2.0-3.0	5 mg BID†	Consider 110 mg BID	30 mg daily	15 mg daily
CrCl 15-29 mL/min	No RCT Data **	Very limited RCT Data§	No RCT Data¶	Very limited RCT Data¶	No RCT Data
CrCl <15 mL/min (or on dialysis)	No RCT Data‡	Very limited RCT Data¶	No RCT Data¶	No RCT Data¶	Very limited RCT Data¶

* Dabigatran 110 mg po BID is recommended if age ≥80 years, or ≥75 years with other bleeding risk factors including CrCl 30-50mL/min.
† Apixaban 2.5 mg po BID is recommended if 2 of the 3 following criteria are present: 1) age ≥80 years, 2) body weight ≤60 kg, or 3) serum creatinine ≥133 μmol/L.
∞ Consider Edoxaban 30mg daily if weight ≤60 kg or concomitant potent P-Gp inhibitor therapy EXCEPT amiodarone or verapamil.
** Dose adjusted warfarin has been used, but data regarding safety and efficacy is conflicting.
‡ Dose adjusted warfarin has been used, but observational data regarding safety and efficacy is conflicting and suggests harm.
§ The ARISTOTLE trial included a small number of patients with a CrCl as low as 25 mL/min.
¶ Product monographs suggest the drug is contraindicated for this level of renal function.

Legend: BID, twice daily; CrCl, creatinine clearance, INR, international normalized ratio; RCT, randomized clinical trial.

Patient on OAC Requiring Surgery/Procedure



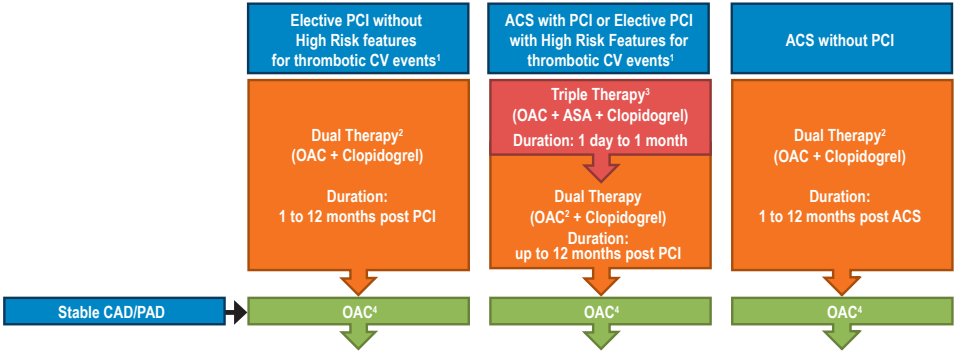
[1] Inform patients/families regarding small thrombotic risk of PCC (e.g. stroke, myocardial infarction, venous thromboembolism), but consequences of uncontrolled bleeding likely exceed the risk
[2] Idarucizumab is unlikely to improve outcomes in patients taking dabigatran with a dilute thrombin time TT <30 ng/ml, normal thrombin time, or a drug level <50ng/ML
[3] Patients considered to be high risk of thromboembolism include those with valvular AF (mechanica heart valves or moderate-severe mitral valve stenosis), non-valvular AF with a CHADS, score of 5-6, and those with recent TIA/Stroke (within 3 months).

Interruption of OAC for Non-Urgent Procedures

OAC		Day -5	Day -4	Day -3	Day -2	Day -1	Procedure	Day +1	Day +2	Day +3	Day +4
Warfarin Usually no need to interrupt VKA for procedures with low bleeding risk	VKA	No VKA	No VKA	No VKA	No VKA	INR[2]	None	VKA[5,6]	VKA[5,6]	VKA	VKA
	Heparin Bridging[1]	No LMWH	No LMWH	LMWH	LMWH	INR[2,3]	None	LMWH[6,7]	LMWH[6,7]	LMWH	LMWH
DOAC[4]	Low/Moderate bleeding risk	DOAC	DOAC	DOAC	DOAC	None	None	DOAC[6,7]	DOAC[6,7]	DOAC	DOAC
	High bleeding risk	DOAC	DOAC	DOAC	None	None	None	None	DOAC[6,7]	DOAC	DOAC
Dabigatran + CrCl <50 mL/min	Low/Moderate bleeding risk	DOAC	DOAC	DOAC	None	None	None	DOAC[6,7]	DOAC[6,7]	DOAC	DOAC
	High bleeding risk	DOAC	None	None	None	None	None	None	DOAC[6,7]	DOAC	DOAC

[1] Patients in need of bridging during interrupted VKA therapy include those with valvular AF (mechanical heart valves or moderate-severe mitral valve stenosis), non-valvular AF with a $CHADS_2$ score of 5-6, and those with a recent stroke or transient ischemic attack.
[2] INR should be performed the day prior to the procedure. If >1.5 then consider administrering vitamin K PO/IV.
[3] Give morning LMWH for bid dosed regimens (or 1/2 daily LMWH dose for once daily dosed regimens).
[4] This schedule applies to factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) and dabigatran (but only when dabigatran is used in patients with a CrCl ≥50 mL/min).
[5] VKA therapy resumption following an invasive procedure may occur almost immediately givent it will take several days for the INR to become therapeutic.
[6] Consider withholding anticoagulation therapy for the first 72 hours following cardiac surgery
[7] DOAC/LMWH resumption following an invasive procedure should only occur once hemostasis has been achieved.

AF Patients with Coronary or Peripheral Arterial Disease and an Indication for OAC (Age ≥ 65 or $CHADS_2$ ≥ 1)



1. PCI is considered high-risk based on clinical and angiographic features such as: diabetes mellitus, current smoker, chronic renal dysfunction (eGFR < 60 mL/min), prior ACS, multi-vessel disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, prior stent thrombosis, chronic total occlusion intervention, or bioabsorbable vascular scaffold.
2. The OAC component evaluated as part of dual pathway therapy regimens include: warfarin daily, apixaban 5 mg BID (reduced to 2.5 mg if they met two or more of the following dose-reduction criteria: age > 80 years of age, weight < 60 kg, or Cr > 133 µmol per liter), dabigatran 110 mg or 150 mg PO BID, edoxaban 60 mg PO daily (30 mg in patients with CrCl 15–50 mL/min, bodyweight ≤ 60 kg, or concomitant use of specified potent P-glycoprotein inhibitors), rivaroxaban 15 mg PO daily (10 mg in patients with CrCl 30-50 mL/min). A DOAC is preferred over warfarin, however if warfarin is to be used the lower end of the recommended INR target range is preferred. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA naïve).
3. The OAC component evaluated as part of triple therapy regimens include: warfarin daily, rivaroxaban 2.5 mg PO BID, or apixaban 5 mg BID (reduced to 2.5 mg if they met two or more of the following dose-reduction criteria: age > 80 years of age, weight < 60 kg, or Cr > 133 µmol per liter). A DOAC is preferred over warfarin, however if warfarin is to be used the recommended INR target is 2.0-2.5. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA naïve). Thereafter, ASA may be discontinued as early as the day following PCI or I can be continued longer. The timing of when to discontinue ASA will depend on individual patient's ischemic and bleeding risk.
4. The dose of OAC beyond one year after PCI should be standard stroke prevention doses. A combination of an OAC and single antiplatelet therapy may be used only in highly-selected patients with high-risk features for ischemic coronary outcomes, and who are also at low risk of bleeding

Antithrombotic therapy based on a balanced assessment of a patient's risk of stroke

- We recommend that AF patients with coronary or arterial vascular disease (peripheral vascular disease or aortic plaque) receive an antithrombotic therapy regimen on the basis of a balanced assessment of their risk of AF-related stroke, ischemic coronary event, and clinically relevant bleeding associated with the use of antithrombotic agents (*Strong Recommendation; High-Quality Evidence*).

Practical tip: For patients who require combinations of antiplatelet and OAC agents for concomitant AF and coronary/arterial vascular disease, measures should be used to reduce the risk of bleeding, including careful consideration of modifiable bleeding risk factors with vigorous efforts to mitigate them; consideration of proton pump inhibitor (PPI) use; avoidance of prasugrel and ticagrelor in conjunction with OACs; the use of the lower target INR range (eg, 2.0-2.5) when a VKA is used as part of combination therapy; specific measures during PCI to reduce bleeding outcomes (radial access or ultrasound-guided femoral access, use of small diameter sheaths if appropriate, early sheath removal if feasible, and minimized use of acute periprocedural antithrombotic therapies); delaying non-urgent procedures until dual or triple therapy is no longer required; use of walking aids for those with gait or balance disorders; avoidance of concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or other drugs that might increase bleeding risk; and, strict BP control.

Most patients with an indication for OAC in the presence of CAD should receive a DOAC

- We recommend a DOAC in preference to a VKA when an OAC is indicated for AF patients with coronary or arterial vascular disease (*Strong Recommendation; High-Quality Evidence*).

Values and preferences: This recommendation places a relatively high value on the results of several large RCTs that showed that the DOACs are either noninferior or superior to VKAs in preventing AF-related stroke, that they cause no more or less major bleeding compared with VKAs, that they are associated with less ICH compared with VKAs, that they are associated with greater ease of use compared with dose-adjusted VKAs, and that DOACs are not associated with an increase in ischemic coronary outcomes.

Antithrombotic Therapy in Patients with AF and CAD or Vascular Disease

Stable vascular disease and AF in patients at high risk of stroke/systemic thromboembolism

- We recommend OAC alone for patients with AF aged 65 years or older or with a $CHADS_2$ score greater than or equal to 1 and stable coronary or arterial vascular disease (*Strong Recommendation; Moderate-Quality Evidence*).

Values and preferences: The use of combination antithrombotic therapy (eg, OAC with a single antiplatelet agent) is not routinely justified for patients with AF and stable coronary or arterial vascular disease because of the observed increased risk of bleeding and all-cause mortality observed with combination therapy, without a significant reduction in ischemic coronary and cerebrovascular thrombotic events.

Practical tips:

- A combination of an OAC and single antiplatelet therapy may be considered only in highly selected patients with high-risk features for ischemic coronary outcomes, and who are also at low risk of bleeding.
- Stable coronary artery disease is defined by the absence of acute coronary syndrome for the preceding 12 months.

AF patients at higher risk of stroke in association with medically managed type I myocardial infarction

- For patients with AF aged ≥ 65 years or with a $CHADS_2$ score ≥ 1, we suggest that dual pathway therapy (OAC with P2Y12) be given without concomitant ASA up to 12 months after medically-managed type I ACS *(Weak Recommendation, Low-Quality Evidence)*.

Values and preferences: For patients with AF and type 1 MI who do not undergo revascularization, the CCS AF Guidelines Committee places relatively greater emphasis on the reduction in ischemic coronary and cerebrovascular thrombotic events, rather than the increase in bleeding observed with combination therapy.

Patient Factors
- Age (> 65 years)
- Low body weight (< 60 kg)
- Hypertension
- History of bleeding (esp. within 1y)
- Excess alcohol consumption
- Labile INR (TTR <60%)

Patient Factors
- Diabetes mellitus
- Current smoker
- CKD (eGFR < 60 mL/min)
- Prior acute coronary syndrome
- Prior stent thrombosis

Clinical Presentation
- Acute coronary syndrome

Factors that Increase Risk of Bleeding

Factors that Increase Risk of Ischemic Coronary Events

Concomitant use of:
- Antiplatelet use
- NSAIDs
- prednisone

Laboratory
- Anemia (hemoglobin <110g/L)
- Abnormal liver function
- CKD (eGFR < 60 mL/min)

Angiographic factors
- Multi-vessel disease
- Multiple (≥ 3) stents implanted
- Stenting of a bifurcation lesion
- Total stent length > 60 mm
- Left main or proximal LAD stenting
- Chronic occlusion intervention
- Bioabsorbable vascular scaffold

AF Patients Undergoing PCI

AF patients at higher risk of stroke undergoing PCI without high-risk features

- For patients with AF aged ≥ 65 years or with a $CHADS_2$ score ≥ 1, we suggest dual pathway therapy (OAC with P2Y12) (*Strong Recommendation; High-Quality Evidence*) for at least 1 month and up to 12 months after PCI after *(Weak Recommendation, Moderate-Quality Evidence)*.

AF patients at higher risk of stroke undergoing PCI for ACS or elective PCI with high-risk features

- For patients with AF aged ≥ 65 years or with a CHADS2 score ≥ 1, we recommend an initial regimen of triple therapy (OAC with P2Y12 and ASA 81 mg/d) (*Strong Recommendation; Low Quality Evidence*). After ASA discontinuation, which may occur as early as the day after PCI, we recommend that dual pathway therapy (OAC with P2Y12) be continued for up to 12 months after PCI (*Strong Recommendation; High-Quality Evidence*).

Practical tips:

- A PCI is considered high-risk for ischemic coronary outcomes based on the clinical presentation (e.g. ACS), patient characteristics (co-morbid diabetes mellitus treated with oral hypoglycemics or insulin, chronic kidney disease [eGFR < 60 mL/min], current tobacco use, prior ACS, or prior stent thrombosis), as well as PCI-related factors (multivessel PCI, multiple [≥ 3] stents implanted, total stent length > 60 mm, complex bifurcation lesion, chronic total occlusion intervention, and stent type [e.g. bioabsorbable vascular scaffold]).
- The OAC component evaluated as part of **dual pathway** therapy regimens include: warfarin daily, apixaban 5 mg BID (reduced to 2.5 mg if they met 2 or more of the following dose-reduction criteria: age older than 80 years, weight < 60 kg, or creatinine > 133 mmol/L), dabigatran 110 mg or 150 mg orally (PO) BID, edoxaban 60 mg PO daily (30 mg in patients with CrCl 15-50 mL/min, body weight 60 kg, or concomitant use of specified potent Pglycoprotein inhibitors), rivaroxaban 15 mg PO daily (10 mg in patients with CrCl 30-50 mL/min).
- The OAC component evaluated as part of a **triple therapy** regimens include: warfarin daily, rivaroxaban 2.5 mg PO BID, or apixaban 5 mg BID (reduced to 2.5 mg if they meet 2 or more of the following dose-reduction criteria: age older than 80 years, weight <60 kg, or creatinine > 133 mmol/L). All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA-naive). Thereafter, ASA may be discontinued as early as the day after PCI or it can be continued up to 30 days. The timing of when to discontinue ASA will depend on individual patient's ischemic and bleeding risk.
- For some patients <65 years of age with $CHADS_2$ score of 1 at the lower end of the stroke risk spectrum (e.g., isolated hypertension), DAPT (e.g., aspirin and ticagrelor) may be considered in preference to triple therapy (an OAC with P2Y12 and ASA).
- A DOAC is preferred over warfarin, however, if warfarin is used the lower end of the recommended INR target range is preferred. Clopidogrel is the preferred P2Y12 inhibitor. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA-naive).

Anticoagulation in the Context of Cardioversion

1. Valvular AF (any duration), or
2. NVAF Duration <12 hours and recent stroke/TIA, or
3. NVAF Duration 12-48 hours and $CHADS_2 \geq 2$, or
4. NVAF Duration >48 hours

Therapeutic OAC for ≥3 weeks before cardioversion

Alternate: TEE to exclude LA thrombus

1. Hemodynamically unstable acute AF[1], or
2. NVAF Duration <12 hours and no recent stroke/TIA, or
3. NVAF Duration 12-48 hours and $CHADS_2$ 0 or 1

Initiate OAC as soon as possible (preferably prior to cardioversion)

CARDIOVERSION[2]

ANTICOAGULATION FOR 4 WEEKS POST CARDIOVERSION

LONG-TERM ANTICOAGULATION BASED ON THE "CCS ALGORITHM" (CHADS-65)

[1] Hemodynamically unstable acute AF is defined as AF causing hypotension, cardiac ischemia, or pulmonary edema

[2] Pharmacological or electrical cardioversion

Anticoagulation in the Context of Cardioversion

Anticoagulation for at least 3 weeks before elective cardioversion

- We recommend that in addition to appropriate rate-control, most hemodynamically stable patients with AF for whom elective electrical or pharmacological cardioversion is planned should receive therapeutic anticoagulation for at least 3 weeks before cardioversion *(Strong Recommendation, Moderate-Quality Evidence)*.

Circumstances where cardioversion may be performed without a preceding period of anticoagulation

- We suggest that pharmacological or electrical cardioversion of symptomatic AF without at least 3 weeks of prior therapeutic anticoagulation (or TEE) be reserved for patients with the following characteristics *(Weak Recommendation, Low-Quality Evidence)*:
  - i) patients with non-valvular AF who present with a clear AF onset within 12 hours in the absence of recent stroke or TIA;
  - ii) patients with non-valvular AF and a $CHADS_2$ score <2 who present after 12 hours but within 48 hours of AF onset.

The use of transesophageal echocardiography as an alternative to anticoagulation prior to cardioversion

- We suggest that transesophageal echocardiography (TEE) may be used to exclude cardiac thrombus, as an alternative to at least 3 weeks of therapeutic anticoagulation before cardioversion (*Weak Recommendation; Moderate-Quality Evidence*).

Immediate initiation of anticoagulation prior to unplanned cardioversion

- When a decision has been reached that a patient will be undergoing unplanned pharmacological or electrical cardioversion of AF, we suggest that therapeutic anticoagulation therapy be initiated immediately (preferably before cardioversion) with either: 1) a DOAC, or 2) heparin followed by adjusted dose VKA (*Weak Recommendation; Low-Quality Evidence*).

Anticoagulation for at least 4 weeks post cardioversion

- We suggest that, in the absence of a strong contraindication, all patients who undergo cardioversion of AF receive at least 4 weeks of therapeutic anticoagulation (adjusted-dose VKA or a DOAC) after cardioversion (*Weak Recommendation; Low-Quality Evidence*). Thereafter, we recommend that the need for ongoing antithrombotic therapy should be on the basis of the risk of stroke as determined by the CCS Algorithm (CHADS-65) (*Strong Recommendation; Moderate-Quality Evidence*).

Values and preferences: This recommendation places relatively greater emphasis on the benefits of stroke prevention and less emphasis on risk of bleeding with a short course of anticoagulation therapy.

Practical tip: When OAC is to be used for only a short period (< 2 months) the use of a DOAC is preferred to adjusted-dose VKA.

Notes

ATRIAL FIBRILLATION

Canadian Cardiovascular Society

Leadership. Knowledge. Community.

Please visit us at
www.ccs.ca

@CCS_SCC

Printing of this pocket guide made possible through funding provided by Bayer, BMS/Pfizer Alliance, and Servier.

Pocket Guide Print / Version Number: AF-2021-03-P2