The Canadian Cardiovascular Society’s
ATRIAL FIBRILLATION GUIDELINES

Canadian Cardiovascular Society

This document is linked to an updated summary of all standing CCS AF recommendations, from 2010 to the present 2016 Focused Update; the supplement is available at www.ccs.ca.

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

Please visit www.ccs.ca for more information or additional resources.

**Co-Chairs:**

Laurent Macle and Atul Verma

**CCS Atrial Fibrillation Guidelines Primary Panel**

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HISTORY AND PHYSICAL EXAM
- Establish pattern (new onset, paroxysmal, persistent or permanent)
- Establish severity (including impact on quality of life)
- Identify etiology
- Identify reversible causes (hyperthyroidism, ventricular pacing, supra-ventricular tachycardia, exercise, etc)
- Identify risk factors whose treatment could reduce recurrent AF or improve overall prognosis (i.e. hypertension, sleep apnea, left ventricular dysfunction, etc)
- Take social history to identify potential triggers (i.e. alcohol, intensive aerobic training, etc)
- Elicit family history to identify potentially heritable causes of AF (particularly lone AF)
- Determine thromboembolic risks
- Determine bleeding risk to guide appropriate antiplatelet or antithrombotic therapy
- Review prior pharmacological therapy for AF, both for efficacy and adverse effects
- Measure blood pressure and heart rate
- Determine patient height and weight
- Comprehensive precordial cardiac examination and assessment of jugular venous pressure, carotid and peripheral pulses to detect evidence of structural heart disease

12-LEAD ELECTROCARDIOGRAM
- Document presence of AF
- Assess for structural heart disease (myocardial infarction, ventricular hypertrophy atrial enlargement, congenital heart disease) or electrical heart disease (ventricular pre-excitation, Brugada syndrome)
- Identify risk factors for complications of therapy for AF (conduction disturbance, sinus node dysfunction or abnormal repolarization)
- Document baseline PR, QT and QRS intervals

ECHOCARDIOGRAM
- Document ventricular size, wall thickness and function
- Evaluate left atrial size (if possible, left atrial volume)
- Estimate ventricular filling pressures and pulmonary arterial pressure
- Exclude significant valvular or congenital heart disease (particularly atrial septal defects)

OTHER
- Complete blood count
- Coagulation profile
- Renal function
- Thyroid and liver function
- Fasting lipid profile
- Fasting glucose
# Additional Investigations for Selected Patients

<table>
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<tr>
<th>Investigation</th>
<th>Potential Role</th>
</tr>
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<tbody>
<tr>
<td>Chest radiography</td>
<td>Exclude concomitant lung disease, heart failure, baseline in patients receiving amiodarone</td>
</tr>
<tr>
<td>Ambulatory electrocardiography (Holter monitor, event monitor, loop monitor)</td>
<td>Document AF, exclude alternative diagnosis (atrial tachycardia, atrial flutter, AVNRT/AVRT, ventricular tachycardia), symptom-rhythm correlation, assess ventricular rate control</td>
</tr>
<tr>
<td>Treadmill exercise test</td>
<td>Investigation of patients with established symptom-rhythm correlation of coronary artery disease, assessment of rate control</td>
</tr>
<tr>
<td>Trans-esophageal echocardiography</td>
<td>Rule out left atrial appendage thrombus, facilitate cardioversion in patients not receiving oral anti-coagulation, more precise characterization of structural heart disease (mitral valve disease, atrial septal defects, cor triatriatum, etc)</td>
</tr>
<tr>
<td>Electrophysiologic study</td>
<td>Patients with documented regular supra-ventricular tachycardia (i.e. atrial tachycardia, AVNRT/AVRT, atrial flutter) that is amenable to catheter ablation</td>
</tr>
<tr>
<td>Serum calcium and magnesium</td>
<td>In cases of suspected deficiency (i.e. diuretic use, gastro-intestinal losses) which could influence therapy (i.e. sotalol)</td>
</tr>
<tr>
<td>Sleep Study (ambulatory oximetry or poly-somnography)</td>
<td>In patients with symptoms of obstructive sleep apnea or in select patients with advanced symptomatic heart failure</td>
</tr>
<tr>
<td>Ambulatory blood pressure monitoring</td>
<td>In cases of borderline hypertension or to assess blood pressure control</td>
</tr>
<tr>
<td>Generic testing</td>
<td>In rare cases of apparent familial AF (particularly with onset at a young age) with additional features of conduction disease, Brugada syndrome or cardiomyopathy</td>
</tr>
</tbody>
</table>
Established Patterns and Severity of Atrial Fibrillation

Patterns of Atrial Fibrillation

- Newly Diagnosed AF
  - Paroxysmal: Self-terminating <7d
  - Persistent: Sustained ≥7d
  - Permanent: Decision to continue in AF

SAF Score*

<table>
<thead>
<tr>
<th>SAF Score</th>
<th>Impact on QOL**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 0</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>1</td>
<td>Minimal effect on QOL</td>
</tr>
<tr>
<td>2</td>
<td>Minor effect on QOL</td>
</tr>
<tr>
<td>3</td>
<td>Moderate effect on QOL</td>
</tr>
<tr>
<td>4</td>
<td>Severe effect on QOL</td>
</tr>
</tbody>
</table>


** QOL = quality of life
Overview of AF Management

Major Goals of AF/AFL Arrhythmia Management

- Identify and treat underlying structural heart disease and other predisposing conditions
- Relieve symptoms
- Improve functional capacity/quality of life
- Reduce morbidity/mortality associated with AF/AFL
  - Prevent tachycardia-induced cardiomyopathy
  - Reduce/prevent emergency room visits or hospitalizations secondary to AF/AFL
- Prevent stroke or systemic thromboembolism
Algorithm for Rate vs Rhythm Control for Patients with Symptomatic AF

- Rate and Rhythm Management

Symptomatic AF

Attempt Rate Control
- Beta-blocker
- Calcium channel blocker

Symptoms Resolve

Yes → Continue Rate Control

No → Modify Rate Control - Consider Rhythm Control

Special circumstances in which to consider early rhythm control:
- Highly symptomatic
- Multiple recurrences
- Extreme impairment in QOL
- Arrhythmia-induced cardiomyopathy

Paroxysmal AF

- Low burden recurrence
  - Pill in pocket anti-arrhythmic therapy
- High burden recurrence
  - Maintenance anti-arrhythmic therapy
  - Catheter ablation

Persistent AF

- Consider cardioversion
  - Symptoms improve, but AF recurs
  - Symptoms improve, and patient maintains sinus rhythm
  - Observe. If AF recurs, determine if symptomatic
  - Symptoms don’t change in sinus rhythm and AF recurs

Symptoms don’t change in sinus rhythm and AF recurs
Digoxin and Mortality - Recommendations

- We suggest that digoxin can be considered as a therapeutic option to achieve rate-control in patients with AF and symptoms caused by rapid ventricular rates whose response to beta-blockers and/or calcium channel blockers is inadequate, or in whom such rate-controlling drugs are contraindicated or not tolerated (Conditional Recommendation, Moderate Quality Evidence).

**Values and preferences:** Digoxin is considered as a second-line agent in that, although some published cohort, retrospective, and subgroup studies show no harm, there are others that suggesting possible harm.

**Practical tip:** When digoxin is used, dosing should be adjusted according to renal function and potential drug interactions. With analyses that suggested higher drug concentrations are associated with adverse outcomes, maximum trough digoxin serum concentration of 1.2 ng/mL would be prudent. When digoxin is being used to treat patients with concomitant left ventricular systolic dysfunction, its use should be dictated by the recommendations of the CCS Heart Failure Clinical Guidelines.
Overview of Rate Management

Rate Control Drug Choices

Heart Failure
- Beta-Blockers ± Digoxin

CAD
- Beta-Blockers* CCB△ Combination Rx

No Heart Failure or CAD
- Beta-Blockers* CCB△ Digoxin* Combination Rx

Drugs are listed in alphabetical order
* Beta-Blockers preferred in CAD
△ Non-dihydropyridine calcium channel blockers (diltiazem, verapamil)
≠ We suggest that digoxin not be used as initial therapy for active patients and be reserved for rate control in patients who are sedentary or who have left ventricular systolic dysfunction
## Managing Rate Control - Recommended Drugs

### β-Blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>50 - 150 mg p.o. daily</td>
<td>bradycardia, hypotension, fatigue, depression, bronchospasm</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>2.5 - 10 mg p.o. daily</td>
<td>as per atenolol</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>25 mg - 200 mg p.o. bid</td>
<td>as per atenolol</td>
</tr>
<tr>
<td>Nadolol</td>
<td>20 - 160 mg p.o daily - bid</td>
<td>as per atenolol</td>
</tr>
<tr>
<td>Propranolol</td>
<td>80 - 200 mg p.o. tid</td>
<td>as per atenolol</td>
</tr>
</tbody>
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### Calcium Channel Blockers and Digoxin

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verapamil</td>
<td>120 - 480 mg p.o. daily 120 - 240 mg p.o. bid</td>
<td>bradycardia, hypotension, constipation</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>120 - 480 mg p.o. daily 120 - 240 mg p.o. bid</td>
<td>bradycardia, hypotension, ankle swelling</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.0625 mg - 0.25 mg p.o. daily</td>
<td>bradycardia, nausea, vomiting, visual disturbance</td>
</tr>
</tbody>
</table>
Overview of Rhythm Management

Rhythm Control Choices
Normal Systolic Function
No Hx of CHF

- Dronedarone+
- Flecainide‡
- Propafenone‡
- Sotalol#

→ Catheter Ablation

→ Amiodarone

Rhythm Control Choices
Hx of CHF or Left Ventricular
Systolic Dysfunction

- EF > 35%
  - Amiodarone
  - Sotalol*
  - Catheter Ablation

- EF ≤ 35%
  - Amiodarone

Drugs are listed in alphabetical order
+ Dronedarone should be used with caution in combination with digoxin
‡ Class I agents should be AVOIDED in CAD and should be COMBINED with AV-nodal blocking agents
# Sotalol should be used with caution in those at risk for torsades de pointes VT (e.g. female, age > 65 yr, taking diuretics)

* Sotalol should be used with caution with EF 35-40% and those at risk for torsades de pointes VT (e.g. female, age > 65 yr, taking diuretics)
### Managing of Rhythm Control - Recommended Drugs

<table>
<thead>
<tr>
<th>Drug/Dose</th>
<th>Efficacy</th>
<th>Toxicity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flecaïnine 50-150 mg BID</td>
<td>30-50%</td>
<td>Ventricular tachycardia, Bradycardia, Rapid ventricular response to AF or atrial flutter (1:1 conduction)</td>
<td>Contraindicated in patients with CAD or LV dysfunction Should be combined with an AV nodal blocking agent</td>
</tr>
<tr>
<td>Propafenone 150-300 mg TID</td>
<td>30-50%</td>
<td>Ventricular tachycardia, Bradycardia, Rapid ventricular response to AF or atrial flutter (1:1 conduction) Abnormal taste</td>
<td>Contraindicated in patients with CAD or LV dysfunction Should be combined with an AV nodal blocking agent</td>
</tr>
<tr>
<td>Amiodarone 100-200 mg OD (after 10g loading)</td>
<td>60-70%</td>
<td>Photosensitivity, Bradycardia, GI upset, Thyroid dysfunction, Hepatic toxicity, Neuropathy, Tremor, Pulmonary toxicity, Torsades de pointes (rare)</td>
<td>Low risk of proarrhythmia Limited by systemic side effects Most side effects are dose &amp; duration related</td>
</tr>
<tr>
<td>Dronedarone 400 mg BID</td>
<td>40%</td>
<td>GI upset, Bradycardia, Hepatic toxicity</td>
<td>Should not be used for rate control or for rhythm control in patients with a history of CHF or LV EF &lt; 40% Should be used with caution when added to digoxin Liver enzyme monitoring required New agent – limited experience outside clinical trials</td>
</tr>
<tr>
<td>Sotalol 80-160 mg BID</td>
<td>30-50%</td>
<td>Torsades de pointes, Bradycardia, Beta-blocker side effects</td>
<td>Should be avoided in patients at high risk of torsades de pointes VT – especially women &gt;65 years taking diuretics or those with renal insufficiency QT interval should be monitored 1 week after starting Use cautiously when EF&lt;40%</td>
</tr>
</tbody>
</table>
• We recommend catheter ablation of AF in patients who remain symptomatic following an adequate trial of antiarrhythmic drug therapy and in whom a rhythm control strategy remains desired \textit{(Strong Recommendation, Moderate Quality Evidence)}.  

• We suggest catheter ablation to maintain sinus rhythm as first-line therapy for relief of symptoms in highly selected patients with symptomatic, paroxysmal atrial fibrillation \textit{(Conditional Recommendation, Moderate Quality Evidence)}.  

• We recommend curative catheter ablation for symptomatic patients with typical atrial flutter as first line therapy or as a reasonable alternative to pharmacologic rhythm or rate control therapy \textit{(Strong Recommendation, Moderate Quality Evidence)}.  

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

<table>
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<tr>
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<th>Longstanding†</th>
<th>Persistent</th>
<th>Paroxysmal</th>
</tr>
</thead>
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<tr>
<td>1st line</td>
<td>--</td>
<td>--</td>
<td>+</td>
</tr>
<tr>
<td>Failed 1st drug</td>
<td>--</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Failed 2nd drug</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Failed multiple drugs</td>
<td>+ +</td>
<td>+ + +</td>
<td>++ +</td>
</tr>
</tbody>
</table>

*+ Indicates balance of benefit to risk in favour of catheter ablation.†Ongoing symptomatic AF ≥ 1 year*
The “CCS Algorithm” ("CHADS65") for OAC Therapy in AF

Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, corticosteroids, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low creatinine clearance, age ≥ 75, low body weight).

* A NOAC is preferred over warfarin for non-valvular AF

The use of NOACs is contraindicated in the presence of mechanical heart valves, rheumatic mitral stenosis, or moderate and severe nonrheumatic mitral stenosis.
<table>
<thead>
<tr>
<th>FACTOR</th>
<th>DEFINITION</th>
</tr>
</thead>
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<tr>
<td>Congestive heart failure</td>
<td>Documented moderate to severe systolic dysfunction; signs and symptoms of heart failure with reduced ejection fraction; or recent decompensated heart failure that required hospitalization irrespective of ejection fraction</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Resting blood pressure $&gt; 140$ mm Hg systolic and/or $&gt; 90$ mm Hg diastolic on at least 2 occasions or current antihypertensive pharmacological treatment</td>
</tr>
<tr>
<td>Age 65</td>
<td>Age $\geq 65$ years</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Fasting plasma glucose concentration $\geq 7.0$ mmol/L (126 mg/dL) or treatment with oral hypoglycemic agents and/or insulin</td>
</tr>
</tbody>
</table>
| Stroke / transient ischemic attack / peripheral embolism | Ischemic stroke: focal neurologic deficit of sudden onset diagnosed by a neurologist, lasting $> 24$ hours, and caused by ischemia;  
Transient ischemic attack: focal neurological deficit of sudden onset diagnosed by a neurologist, lasting $< 24$ hours;  
Peripheral embolism: thromboembolism outside the brain, heart, eyes, and lungs, or pulmonary embolism (defined by the responsible physician) |
| Vascular disease                            | Coronary artery disease, peripheral artery disease, or aortic plaque                                                                     |
## Recommendations for Dosage of Oral Anticoagulants Based on Renal Function

### Therapeutic Choices in Patients with Chronic Kidney Disease and Stroke Risk Factors (CHADS₂ ≥ 1)

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
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<tr>
<td>CrCL &gt; 50 mL/min</td>
<td>Dose adjusted for INR 2.0-3.0</td>
<td>150 mg bid*</td>
<td>20 mg daily</td>
<td>5 mg bid</td>
</tr>
<tr>
<td>CrCL 30-49 mL/min</td>
<td>Dose adjusted for INR 2.0-3.0</td>
<td>Consider 110 mg bid in preference to 150 bid</td>
<td>15 mg daily</td>
<td>5 mg bid (consider 2.5 mg bid)†</td>
</tr>
<tr>
<td>CrCL 15-29 mL/min</td>
<td>No RCT Data‡</td>
<td>No RCT Data</td>
<td>No RCT Data</td>
<td>Very limited RCT data§</td>
</tr>
<tr>
<td>CrCL &lt; 15 mL/min (or the patient is dialysis-dependent)</td>
<td>No RCT Data‖</td>
<td>No RCT Data‖</td>
<td>No RCT Data‖</td>
<td>No RCT Data‖</td>
</tr>
</tbody>
</table>

ARISTOTLE, Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; bid, twice daily; CrCl, creatinine clearance; INR, international normalized ratio; RCT, randomized clinical trial.

*Consider dabigatran 110 mg oral bid if age > 75 years.
† Consider apixaban 2.5 mg oral bid 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.
‡ Dose-adjusted warfarin has been used, but data regarding safety and efficacy are conflicting
§ The ARISTOTLE trial did include patients with a CrCl as low as 25 mL/min, but this was a very small number of patients (1.5% of patients in the trial).
‖ Dose-adjusted warfarin has been used, but data regarding safety and efficacy are conflicting and might lean toward causing harm.
‖‖ No published studies support a dose for this level of renal function; product monographs suggest the drug is contraindicated for this level of renal function.
Reversal Agents for NOACs - Recommendations

We recommend administering idarucizumab for emergency reversal of dabigatran's anticoagulant effect in patients with uncontrollable or potentially life-threatening bleeding and/or in patients requiring urgent surgery for which normal hemostasis is necessary (Strong Recommendation, Moderate Quality Evidence).

Values and Preferences: This recommendation places relatively greater value on the ability of idarucizumab to reverse coagulation parameters indicative of dabigatran's effect, its potential to decrease bleeding-related outcomes and risks of urgent surgery and its safety and tolerability profile, and less value on the absence of a control group in the RE-VERSE AD trial and the cost of the drug.

Practical tips - In the acute, life-threatening bleeding situation where standard resuscitation (such as local measures, transfusion, etc) is not anticipated to be sufficient (e.g. ICH), or in the situation where it has not stabilized the patient, idarucizumab should be administered as soon as possible. Although dilute thrombin time and ecarin clotting time were used to identify the presence of dabigatran in REVERSE-AD, these tests are not widely available. Thrombin time (TT) and activated partial thromboplastin time (aPTT) are widely available and can qualitatively identify the presence of active dabigatran in a patient, however obtaining these tests should not delay the administration of idarucizumab. In many instances of life-threatening bleeding, clinicians have to base a treatment decision on a history of dabigatran use rather than laboratory evidence. Renal function and timing of the last dose of dabigatran provide key information regarding the likely extent of remaining dabigatran effect. The timing of surgery may permit clinicians to obtain coagulation parameters like stat TT or aPTT to identify patients who no longer have dabigatran present, and who would be unlikely to benefit from idarucizumab. No dose adjustment for idarucizumab is required in patients with renal impairment. In some patients, coagulation parameters may rise between 12-24 hours after initial administration of idarucizumab, possibly reflecting redistribution of extravascular dabigatran into the intravascular space. Reversing dabigatran therapy exposes patients to the thrombotic risk of their underlying disease. OAC should be reintroduced as soon as medically appropriate.
Management of Antithrombotic Therapy - General Recommendations

General recommendations regarding antithrombotic therapy in the context of concomitant AF and CAD (asymptomatic, stable CAD, elective PCI, NSTEMI or STEMI):

- We recommend that patients who have concomitant AF and CAD receive a regimen of antithrombotic therapy that is on the basis of a balanced assessment of their risks of stroke, of a coronary event and of hemorrhage associated with use of antithrombotic agents (Strong Recommendation, High Quality Evidence).

- When OAC is indicated in the presence of CAD, we suggest a NOAC in preference to warfarin for NVAF (Conditional Recommendation, Low Quality Evidence).

Values and Preferences: The suggestion for use of a NOAC rather than warfarin places relatively greater weight on the ease of use of NOACs versus warfarin and on the data from RCTs of NOACs versus warfarin for NVAF, showing equal or greater reduction of stroke, equal or less major bleeding, less intracranial bleeding and no net increase in CAD outcomes. It places relatively less weight on the absence of long-term data on the effect of NOACs on coronary outcomes as opposed to the data for efficacy of warfarin.

Practical Tip - When CAD is present, some expert clinicians prefer a combination of a NOAC and aspirin rather than NOAC alone in preference to warfarin alone for patients perceived to be at higher risk of coronary events and low risk of major bleeding and may choose a NOAC alone as a reasonable option in those with average to lower risk of coronary events and higher risk of bleeding.

Practical Tip - In general, the recommended doses of NOACs are the usual doses studied in the RCTs of NVAF. For patients requiring combinations of antiplatelet and OAC agents for concomitant AF and CAD, we suggest that measures be employed to reduce the risk of bleeding, including careful consideration of HAS-BLED risk factors and vigorous efforts to mitigate them; specific measures during invasive procedures (radial access, small-diameter sheaths, early sheath removal from femoral site and minimized use of acute procedural anti-thrombotic therapies); consideration of routine proton pump inhibitor (PPI); avoidance of prasugrel and ticagrelor in conjunction with OAC; the use of warfarin in the lower INR range; consideration of the lower effective doses of NOACs; and delaying non-urgent catheterization until there is clarity about coagulation status and renal function. If the risk of restenosis is relatively low, the option of a BMS rather than a second generation DES should be considered.
Recommendations for Patients with an Indication for Primary Prevention or Stable CAD/Arterial Vascular Disease

For patients with AF, with an indication for primary prevention or stable CAD/arterial vascular disease (peripheral vascular disease or aortic plaque), the selection of antithrombotic therapy should be based on their risk of stroke as follows:

- If the patient has no evidence of CAD/vascular disease and is aged < 65 years with no CHADS$_2$ risk factors, we suggest no antithrombotic therapy for stroke prevention (Conditional Recommendation, Moderate Quality Evidence).

- If the patient has stable CAD/vascular disease and is aged < 65 years with no CHADS$_2$ risk factors, we suggest aspirin 81 mg daily (Conditional Recommendation, Moderate Quality Evidence).

- If the patient has stable CAD/vascular disease and is aged ≥ 65 or the CHADS$_2$ ≥ 1, we recommend OAC therapy (Strong Recommendation, High Quality Evidence).
Management of Antithrombotic Therapy

For patients with AF with an indication for primary CAD prevention or stable CAD/arterial vascular disease

- **Age < 65 and CHADS\(_2\) = 0**
  - No CAD / vascular disease
  - †No antithrombotic therapy

- **Age < 65 and CHADS\(_2\) = 0**
  - Stable CAD / vascular disease
  - ASA

- **Age ≥ 65 or CHADS\(_2\) ≥ 1**
  - Stable CAD / vascular disease
  - OAC* alone

* A NOAC is preferred over warfarin for non-valvular AF
† Primary CAD prevention with ASA may be considered in selected high-risk patients
Recommendations for Patients with AF and Recent Elective PCI

For patients with AF and recent elective PCI, the selection of antithrombotic therapy should be based on their risk of stroke as follows:

- If the patient is aged < 65 years with no CHADS$_2$ risk factors, we recommend an APT therapy regimen without OAC, as per Part 7, Recommendations 6-9 of the Supplementary Material (adapted from the CCS 2012 APT guidelines).

- If the patient is aged ≥ 65 years or the CHADS$_2$ ≥ 1, we suggest that clopidogrel 75 mg daily and OAC be given, without concomitant ASA, for 12 months post-PCI (Conditional Recommendation, Moderate Quality Evidence), to be followed by OAC alone (Strong Recommendation, High Quality Evidence).

**Practical Tip** - Some patients who are at high risk of stent thrombosis and whose risk of major bleeding is acceptable may continue OAC with clopidogrel for longer than 12 months after ACS, whereas those at particularly high risk of major bleeding may have their clopidogrel discontinued earlier than 12 months and continue to receive only OAC.
For patients with AF and recent elective PCI

Age < 65 and CHADS$_2$ = 0

ASA + Clopidogrel for 12 months

ASA alone after 12 months

Age ≥ 65 and CHADS$_2$ ≥ 1

OAC* + Clopidogrel for 12 months

OAC* alone after 12 months

* A NOAC is preferred over warfarin for non-valvular AF
For patients with AF, in association with NSTEACS or STEMI, the selection of antithrombotic therapy should be based on their risk of stroke as follows:

- **If the patient is aged < 65 years with no CHADS$_2$ risk factors**, we recommend an APT therapy regimen without OAC, as per Part 7, Recommendations 11-19 of the Supplementary Material (adapted from the CCS 2012 APT Guidelines).

- **If the patient is aged ≥ 65 or the CHADS$_2$ ≥ 1 and no PCI is undertaken**, we suggest the combination of clopidogrel 75 mg daily (rather than prasugrel or ticagrelor) and OAC be given, without concomitant ASA, for 12 months, to be followed by OAC alone (Conditional Recommendation, Low Quality Evidence).

- **If the patient is aged ≥ 65 or the CHADS$_2$ ≥ 1 and PCI is undertaken**, we suggest the combination of aspirin 81 mg daily and clopidogrel 75 mg daily and OAC (TT) for 3-6 months (duration depending on the perceived risks of coronary thrombosis and major bleeding). After 3-6 months we suggest the combination of clopidogrel and OAC to be continued until 12 months after ACS, to be followed by OAC alone (Conditional Recommendation, Low Quality Evidence).

**Values and Preferences:** The suggestion of TT for the first 3-6 months places greater weight on more reduction of coronary events (versus OAC + clopidogrel) and on more SSE prevented (versus DAPT) but less weight on the increased risk of major bleeding. The balance of stroke/systemic embolus prevented and major bleeds caused could be judged as appropriate only for patients with a higher risk of stroke (e.g. CHADS$_2$ ≥ 2).

**Practical Tip** - Some patients who are at high risk of stent thrombosis and whose risk of major bleeding is acceptable may continue the combination of OAC and clopidogrel for longer than 12 months post ACS.

**Practical Tip** - Some patients at particularly high risk of major bleeding may have their clopidogrel discontinued earlier than 12 months and continue to receive only OAC.

**Practical Tip** - Some clinicians may prefer the combination of clopidogrel and OAC beginning from the time of PCI, placing more weight on the reduced bleeding and no increase of thrombotic events compared to TT in the WOEST trial and less value on the fact that only 25% of patients in this trial had PCI for ACS. A combination of aspirin and ticagrelor, or aspirin and prasugrel, or aspirin and clopidogrel may also be used in preference to TT for some patients with CHADS$_2$=1 at the lower end of the stroke risk spectrum (e.g. isolated hypertension), reserving TT or OAC + clopidogrel for patients at higher stroke risk.
For patients with AF in association with NSTEACS or STEMI

- **Age < 65 and CHADS₂ = 0**
  - No PCI
    - ASA + Ticagrelor or Clopidogrel for 12 months
    - ASA alone after 12 months

- **Age ≥ 65 or CHADS₂ ≥ 1**
  - PCI
    - ASA + Ticagrelor or Prasugrel or Clopidogrel for 12 months
    - ASA alone after 12 months
  - No PCI
    - OAC* + Clopidogrel for 12 months
    - OAC* alone after 12 months
  - PCI
    - OAC* + Clopidogrel + ASA for 3 to 6 months
    - OAC* + Clopidogrel through to 12 months

* A NOAC is preferred over warfarin for non-valvular AF
Management of AF in the ED - Recommendations

**Immediate Risk for Stroke?**

- **Low Risk**
  1. Clear onset < 48 hours, or
  2. Therapeutic OAC ≥ 3 wks

  - Pharmacological or electrical CV at 150-200 J (immediate anticoagulation in ED before CV not required)

  - **Antithrombotic therapy**
    - Initiate OAC upon discharge from ED (or continue current OAC) if age ≥ 65 or CHADS₂ ≥ 1
    - Otherwise, initiate ASA if CAD or vascular disease
    - Early expert follow-up to review long-term OAC

- **High Risk**
  No therapeutic OAC ≥ 3 weeks and one of:
  1. Onset > 48 hours or unknown, or
  2. Stroke/TIA < 6 months or
  3. Mechanical or rheumatic valve disease

  - Rate control
  - Therapeutic OAC for 3 weeks before outpatient CV
  - Trans-esophageal echocardiography (TEE) guided CV

- **Unstable - AF causing:**
  1. Hypertension, or
  2. Cardiac ischemia or
  3. Pulmonary edema

  - Consider urgent electrical CV if rate control not effective

  - **Antithrombotic therapy**
    - Initiate immediate OAC in ED and continue for ≥ 4 weeks if any “high-risk” features present * (see box above)
    - Early follow-up to review long-term OAC
### Management of AF in the ED - Recommendations

#### Recommended IV Drugs for Rate Control

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diltiazem*</td>
<td>0.25 mg/kg IV bolus over 10 min; repeat at 0.35 mg/kg IV</td>
<td>Hypotension, bradycardia</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5-5mg IV bolus over 2 min; up to 3 doses</td>
<td>Hypotension, bradycardia</td>
</tr>
<tr>
<td>Verapamil*</td>
<td>0.075-0.15mg/kg over 2 min</td>
<td>Hypotension, bradycardia, bronchospasm</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.25 mg IV each 2 h; up to 1.5mg</td>
<td>Bradycardia, Digitalis toxicity</td>
</tr>
</tbody>
</table>

*Calcium-channel blockers should not be used in patients with heart failure or left ventricular dysfunction.

#### Recommended Drugs for Pharmacological Conversion

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Efficacy</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1 A Procainamide</td>
<td>15-17 mg/kg IV over 60 min</td>
<td>++</td>
<td>5% hypotension</td>
</tr>
<tr>
<td>Class 1C*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propafenone</td>
<td>450-600 mg PO</td>
<td>+++</td>
<td>Hypotension, 1:1 flutter, bradycardia</td>
</tr>
<tr>
<td>Flecaainide</td>
<td>300-400 mg PO</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>1-2 mg IV over 10-20 min</td>
<td>++</td>
<td>2-3% Torsades de pointes</td>
</tr>
<tr>
<td>Ibutilide</td>
<td>Pre-treat with MgSO4 1-2 gm IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Class IC drugs should be used in combination with AV nodal blocking agents (beta-blockers or calcium-channel inhibitors). Class IC agents should also be avoided in patients with structural heart disease.
Periprocedural Anticoagulation Management - Recommendations

Refer to the AF supplementary material for recommendations on the following:

- Preprocedural interruption of various antithrombotic agents: Part 11, Recommendations 4-7 of the Supplementary Material.
- Pre- and postprocedural management of heparin bridging: Part 11, Recommendations 10 and 11 of the Supplementary Material.
- Reintroduction of antithrombotic agents after an invasive procedure: Part 11, Recommendations 12 and 13 of the Supplementary Material.

- We suggest that interruption of anticoagulant therapy, particularly for VKAs, in a patient with AF/AFL is not necessary for most procedures with a low risk of bleeding, such as cardiac device implantation (pacemaker or implantable defibrillator), and most dental procedures (see table) (Conditional Recommendation, Moderate Quality Evidence).

- When a decision to interrupt warfarin therapy for an invasive procedure has been made for a patient with AF/AFL, we suggest that bridging therapy with LMWH or UFH be instituted when the INR is below therapeutic level only in patients at high risk of thromboembolic events (CHADS2, score 4, mechanical heart valve, stroke/transient ischemic attack within 3 months, rheumatic heart disease) (Conditional Recommendation, Low-Quality Evidence).

- We recommend no bridging (LMWH or UFH) for NVAF patients receiving NOACs who undergo elective surgery or invasive procedures requiring interruption of anticoagulation (Strong Recommendation, Moderate-Quality Evidence).

- Practical tip - Duration of preprocedural interruption of NOACs should be adjusted according to renal function (see Part 11, Recommendations 6 and 7 of the Supplementary Material). The Thrombosis Canada Perioperative Anticoagulant Management Algorithm is a helpful tool to aid decisions regarding periprocedural anticoagulation (http://thrombosiscanada.ca/?page_id=4502&calc=perioperativeAnticoagulantAlgorithm).
Bleeding Risks for Various Invasive / Surgical Procedures

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Intermediate Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Any surgery or procedure with neuraxial (spinal or epidural) anesthesia</td>
<td>• Other intra-abdominal surgery (e.g. laparoscopic cholecystectomy, hernia repair)</td>
<td>• Dental extractions (1 or 2 teeth), endodontic (root canal) procedure, subgingival scaling or other cleaning</td>
</tr>
<tr>
<td>• Neurosurgery (intracranial or spinal)</td>
<td>• Other general surgery (e.g. breast)</td>
<td>• Cataract surgery</td>
</tr>
<tr>
<td>• Cardiac surgery (e.g. CABG, heart valve replacement)</td>
<td>• Other intrathoracic surgery</td>
<td>• Dermatologic procedures (e.g. biopsy)</td>
</tr>
<tr>
<td>• Major intra-abdominal surgery</td>
<td>• Other orthopedic surgery</td>
<td>• Gastroscopy or colonoscopy without biopsies</td>
</tr>
<tr>
<td>• Major vascular surgery (e.g. aortic aneurysm repair, aortofemoral bypass)</td>
<td>• Other vascular surgery</td>
<td>• Coronary angiography</td>
</tr>
<tr>
<td>• Major orthopedic surgery (e.g. hip or knee replacement)</td>
<td>• Non-cataract ophthalmologic surgery</td>
<td>• Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used)</td>
</tr>
<tr>
<td>• Lung resection surgery</td>
<td>• Gastroscopy or colonoscopy with biopsies</td>
<td>• Selected procedures (e.g. thoracentesis, paracentesis, arthrocentesis)</td>
</tr>
<tr>
<td>• Urological surgery (e.g. prostatectomy, bladder tumour resection)</td>
<td>• Selected procedures (e.g. bone marrow biopsy, lymph node biopsy)</td>
<td></td>
</tr>
<tr>
<td>• Extensive cancer surgery (e.g. pancreas, liver)</td>
<td>• Complex dental procedure (e.g. multiple tooth extractions)</td>
<td></td>
</tr>
<tr>
<td>• Intestinal anastomosis surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Reconstructive plastic surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Selected procedures (e.g. kidney biopsy, prostate biopsy, cervical cone biopsy, pericardiocentesis, colonic polypectomy)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The procedural/ surgical risk categorization list may be updated based on new information, and can be found at Thrombosis Canada. ([http://thrombosiscanada.ca](http://thrombosiscanada.ca))

* Selected ophthalmic procedures may be high risk such as those with retrobulbar block
Surgical Therapy for AF - Recommendations

Surgical AF ablation procedures

- We suggest that a surgical AF ablation procedure should be considered in association with mitral valve, aortic valve or CABG surgery in patients with AF, when the likelihood of success is deemed to be high, the additional risk is low and sinus rhythm is expected to achieve substantial symptomatic benefit (Conditional Recommendation, Moderate Quality Evidence).

Values and preferences: This recommendation recognizes that individual institutional experience and patient considerations best determine for whom the surgical procedure is performed. Importantly, the symptomatic benefit of sinus rhythm needs to be balanced with the attendant risks of ablation surgery, including the need for permanent pacing. This recommendation also recognizes that LA endocardial access is not routinely required for aortic or coronary surgery; limiting ablation to newer epicardial approaches.

Surgical LAA exclusion for stroke prevention

- In patients with AF, we suggest that closure (excision or obliteration) of the LAA should be considered as part of the surgical ablation of AF associated with mitral, aortic valve or coronary artery bypass surgery if this does not increase the risk of the surgery (Conditional Recommendation, Low Quality Evidence).

Values and preferences: This recommendation places a high value on the potential for stroke reduction and a lower value on loss of atrial transport-function with LAA-closure. It places less value on the need to continue OAC even after LAA surgical excision.
We recommend that postoperative AF may be appropriately treated with either a ventricular response rate-control strategy or a rhythm-control strategy (Strong Recommendation, Moderate Quality Evidence).

**Values and preferences:** This recommendation places a high value on the randomized controlled trials investigating rate control as an alternative to rhythm control for AF, including one trial specifically addressing the cardiac postoperative period. Choice of strategy should therefore be individualized based on the degree of symptoms experienced by the patient.

We suggest that patients who have a contraindication to beta-blocker therapy and to amiodarone before or after cardiac surgery be considered for prophylactic therapy to prevent POAF with intravenous magnesium (Conditional Recommendation, Low Quality Evidence) or colchicine (Conditional Recommendation, Low Quality of Evidence) or with biatrial pacing (Conditional Recommendation, Low Quality of Evidence).

**Values and preferences:** This recommendation places a high value on preventing POAF using novel therapies that are supported by lower-quality data; with a higher value on the lower probability of adverse effects from magnesium versus colchicine. The use of biatrial pacing needs to be individualized by patient and institution, as the potential for adverse effects may outweigh benefit based on local expertise.
<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dosage*</th>
<th>Cautions</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op beta blocker</td>
<td>any in usual therapeutic dose (i.e. metoprolol 50 mg) PO q12h or q8h for at least 2 pre-op days, day of surgery, and at least 6 post-op days</td>
<td>reactive airways disease, decompensated CHF</td>
<td>sinus bradycardia AV block</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>hypotension bronchospasm</td>
</tr>
<tr>
<td>Pre-op amiodarone</td>
<td>10 mg/kg/day (rounded to nearest 100 mg) divided into two daily PO dosages for 6 pre-op days, day of surgery, and 6 post-op days</td>
<td>30%-50% reduction in the dosages of other drugs with antiarrhythmic or sinus/AV nodal effects and warfarin will be required</td>
<td>sinus bradycardia AV block</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>hypotension torsade de pointes VT (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pulmonary toxicity (rare)</td>
</tr>
<tr>
<td>Post-op amiodarone</td>
<td>900 – 1200 mg IV over 24 hrs beginning within 6 hours of surgery, then 400 mg PO tid each of the next 4 days</td>
<td>30%-50% reduction in the dosages of other drugs with antiarrhythmic or sinus/AV nodal effects and warfarin will be required</td>
<td>sinus bradycardia AV block</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>hypotension torsade de pointes VT (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pulmonary toxicity (rare)</td>
</tr>
<tr>
<td>Magnesium sulfate</td>
<td>1.5 gm IV over 4 hrs first pre-op day, immediately post-op, and next 4 post-op days. Other trials have omitted the pre-op dosage</td>
<td>renal failure</td>
<td>hypotension (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>sedation (very rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>respiratory depression (very rare)</td>
</tr>
</tbody>
</table>

*Dosages used in the randomized studies vary widely and the optimal dosages for this indication have not been established. The dosages provided are those used in the largest positive trial of that therapy and are referenced to that study.*
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