Oral Anticoagulants in Non-valvular Atrial Fibrillation: CADTH Recommendations and Clinical Practice Guidelines

For people with atrial fibrillation, warfarin has been the mainstay of stroke prevention for many years. With several new oral anticoagulants available, many clinicians are looking for guidance on selecting therapy. In Canada, the Canadian Cardiovascular Society recommends these new drugs in preference to warfarin, whereas CADTH recommends that warfarin remain first-line therapy. Why the difference?

CADTH is not a guideline group, but rather a health technology assessment (HTA) group. HTA provides a systematic analysis of the literature on a specific health technology (a drug, device, or procedure), whereas clinical practice guidelines provide recommendations from experts on how to treat specific patients. The two approaches are quite different.

**Health Technology Assessment**
- Consistent, rigorous, systematic review methodology.
- Includes assessment of cost-effectiveness, or value for money.
- Purpose is to guide use of a specific technology. Given this new drug or technology, how should I deploy it? Where, when, and in whom should it be used for best effect or best value?
- Population perspective. Considers wise use of resources and greatest good for greatest number.

**Clinical Practice Guideline**
- Methodology varies between guideline development groups.
- Generally does not consider cost-effectiveness.
- Purpose is to guide treatment of a specific patient. Given a patient with this condition, how do I screen, diagnose, treat, and/or monitor him or her?
- Clinician perspective. Written for individual practitioners treating individual patients.

The key differences between CADTH recommendations and clinical practice guidelines (Canada, US, and Europe) on the use of oral anticoagulants in non-valvular atrial fibrillation are summarized in Table 1.
Table 1: Comparison of CADTH Recommendations and Canadian, US, and European Clinical Practice Guidelines on the Use of Oral Anticoagulants in Non-valvular Atrial Fibrillation

<table>
<thead>
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<tbody>
<tr>
<td>• Warfarin</td>
<td>NOACs preferred for most</td>
<td>NOACs preferred for most</td>
<td>NOACs preferred for most</td>
<td>Warfarin (Evidence: A) and NOACs (Evidence: B) are both options</td>
<td>Options: warfarin (if INR ≥ 70% TTR) or NOAC</td>
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<tr>
<td>• NOACs if unable to achieve adequate anticoagulation with warfarin</td>
<td>Preference is less marked if stable INR and no bleeding complications</td>
<td>Preference is less marked if stable INR and no bleeding complications</td>
<td>Warfarin (Evidence: A)</td>
<td>NOACs preferred in most patients if used as studied in trials</td>
<td></td>
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<tr>
<td>Role of Antiplatelets</td>
<td>ASA preferred over ASA ± clopidogrel</td>
<td>ASA if: CHADS2 = 0 → and if either female or vascular disease alone</td>
<td>ASA if: CHADS2 = 0 → if vascular disease alone</td>
<td>ASA one of the options if: CHA2DS2-VASc = 1</td>
<td>If patient refuses OAC (and CHA2DS2-VASc ≥ 1): ASA + clopidogrel (preferred)</td>
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<td>Methods</td>
<td>Systematic review &amp; NMA</td>
<td>GRADE system used to evaluate evidence and strength of recommendations</td>
<td>Not described</td>
<td>Transparent, comprehensive literature search. Levels of evidence given for each recommendation</td>
<td>Generic recommendations for writing any ESC guideline are described on the society's website. They suggest a formal literature review, a system for ranking levels of evidence, and grading each recommendation</td>
</tr>
<tr>
<td>Values and Preferences</td>
<td>Safety, efficacy and clinical benefit, cost-effectiveness, and consideration of patient-specific clinical preferences if selecting NOACs</td>
<td>Described in detail</td>
<td>Available in supplementary materials</td>
<td>Not described</td>
<td>Not described</td>
</tr>
<tr>
<td>Authorship</td>
<td>CDEC 13 authors</td>
<td>21 authors (primary panel): 14 had affiliations with pharmaceutical industry</td>
<td>18 had affiliations with NOAC manufacturers</td>
<td>16 authors (primary panel): 5 had relationships with pharmaceutical industry</td>
<td>All 8 authors declare multiple relationships with industry. All but 1 author report funding from multiple NOAC manufacturers</td>
</tr>
<tr>
<td></td>
<td>No conflicts of interest were declared</td>
<td>13 reported funding from NOAC manufacturers</td>
<td>16 reported funding from NOAC manufacturers</td>
<td>2 had financial relationships with multiple NOAC manufacturers</td>
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</table>

*Evidence Level A: Multiple populations evaluated; data derived from multiple randomized clinical trials or meta-analyses.

*Evidence Level B: Limited populations evaluated; data derived from a single randomized trial or non-randomized studies.

Note: CHADS2 and CHA2DS2-VASc are clinical scoring tools that correlate with stroke risk.
CADTH’s Key Findings

• Warfarin is the recommended first-line therapy for preventing stroke in patients with atrial fibrillation.
  • Warfarin is proven to be a safe, effective, and cost-effective first choice for therapy.
  • Many patients taking warfarin do well on the medication. For these patients, there is no evidence to support switching therapies.

• New oral anticoagulants are a second-line option for some patients with non-valvular atrial fibrillation who are not doing well on warfarin.
  • Although the newer drugs are as effective at preventing stroke as warfarin, they are more expensive and little is known about their long-term safety.
  • If a new oral anticoagulant is prescribed, patients must be monitored.
    • Regular assessments of adherence to treatment, kidney function, drug interactions, and bleeding risk are necessary.
    • If bleeding occurs, there is no antidote or proven management strategy.
  • For people who are able to use an anticoagulant, anticoagulant drugs should be used in preference to antiplatelet drugs.

References


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