TARGET AUDIENCE: All Canadian health care professionals.

OBJECTIVE:

To review the use of antiplatelet agents and oral anticoagulants for the secondary prevention of ischemic cardiac disease in patients presenting with ST elevation myocardial infarction (STEMI).

ABBREVIATIONS:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACS</td>
<td>acute coronary syndrome</td>
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<tr>
<td>ADP</td>
<td>adenosine diphosphate</td>
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<tr>
<td>ASA</td>
<td>acetyl salicylic acid</td>
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<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
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<td>DAPT</td>
<td>dual antiplatelet therapy</td>
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<td>MI</td>
<td>myocardial infarction</td>
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<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
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<td>PPCI</td>
<td>primary percutaneous coronary</td>
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<tr>
<td>STEMI</td>
<td>ST elevation myocardial infarction</td>
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<tr>
<td>TIA</td>
<td>transient ischemic attack</td>
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BACKGROUND:

New approaches to antithrombotic therapies have become available to treat patients with STEMI. This document summarizes the possible treatment combinations according to the method of revascularization (i.e. coronary artery bypass graft (CABG) versus percutaneous coronary intervention (PCI) versus medical therapy).

MECHANISM OF ACTION:

Acetyl salicylic acid (ASA) is an antiplatelet agent acting via the inhibition of thromboxane production. Clopidogrel (Plavix™), ticagrelor (Brilinta™) and prasugrel (Effient™) act by blocking platelet adenosine diphosphate (ADP) receptors of subtype P2Y12. Ticagrelor is a reversible blocker whereas prasugrel and clopidogrel are irreversible. Rivaroxaban (Xarelto™) is an anticoagulant acting via direct inhibition of the coagulation factor Xa.

INDICATION:

See treatment algorithm below for details.
The initial decisions should be based on whether the patient was treated with primary percutaneous coronary intervention (PPCI), thrombolytic therapy or no-reperfusion therapy.
AGENTS AND DOSING:

a) ASA: 81 mg daily indefinitely in all patients unless allergic or intolerant, in which case it should be replaced by clopidogrel.

b) Clopidogrel: 75 mg daily. A maintenance dose of 150 mg daily can be considered for the first 6 days in patients treated with PCI.

c) Ticagrelor: 90 mg twice daily.

d) Prasugrel: 10 mg daily. A dose of 5 mg daily can be considered in patients > 75 years of age or with a body weight < 60 kg. Prasugrel is currently not recommended for patients with prior stroke or transient ischemic attack (TIA).

e) Rivaroxaban is not approved by Health Canada for the secondary prevention of ischemic cardiac disease post-ACS.

LABORATORY MONITORING:

No laboratory monitoring is required for patients taking ASA, clopidogrel, ticagrelor or prasugrel. However, periodic monitoring of renal function should be performed for patients taking new oral anticoagulants (see NOAC: Monitoring guide).

ADVERSE EFFECTS:

Ticagrelor has been associated with ventricular pauses, bradycardia and short-term mild to moderate dyspnea at the start of treatment. Dyspnea has not been associated with adverse outcomes.

PERI-PROCEDURAL MANAGEMENT:

Non-CABG

The peri-procedural use of antiplatelet agents may increase the risk of bleeding and transfusion requirements associated with surgery and other invasive procedures. However, discontinuation of dual antiplatelet therapy (DAPT) within 12 months of drug-eluting stent implantation or within 6 weeks of bare-metal stent implantation is associated with a large increased risk of major adverse cardiovascular events and stent thrombosis. For this reason, procedures associated with significant bleeding risk should be delayed beyond these time frames if possible, and, if not possible, done with the patient remaining on therapy. If prasugrel can be stopped safely, it should be discontinued 7 days prior to surgery. For ticagrelor and clopidogrel, stopping 5-7 days prior to a procedure should be sufficient.
CABG
In stable patients with ACS without critical coronary anatomy who are clinically stabilized, clopidogrel and ticagrelor should be withheld for 5 days and prasugrel for 7 days before CABG. In patients with ACS, dual antiplatelet therapy should be restarted at maintenance dose within 48-72 hours post-operatively when deemed safe by the cardiac surgical team.

SPECIAL CONSIDERATIONS:
The P2Y12 receptor inhibitors (clopidogrel, ticagrelor or prasugrel) initially selected at hospital discharge should not be switched to another P2Y12 inhibitor unless there is a compelling clinical reason to do so. Such reasons may include but are not limited to stent thrombosis, allergy/intolerance and bleeding.

The P2Y12 receptor inhibitors (clopidogrel, ticagrelor or prasugrel) can be continued for more than 12 months in patients with a high thrombosis risk and a low bleeding risk. In such patients, consultation with a specialist is always preferable before discontinuing the medication.

Triple therapy with rivaroxaban, clopidogrel and ASA is more effective than the dual combination of clopidogrel and ASA on the composite outcome of cardiovascular death, myocardial infarction and stroke. However, this triple therapy has been associated with a 4-fold increase in the risk of major bleeding and with a 3-fold increase in the risk of intracranial hemorrhage. For this reason, the combination is not recommended over DAPT with ticagrelor or prasugrel plus ASA.

PEDIATRICS:
In general, the etiology of myocardial infarction (MI) in children is different from that of adults. There are no studies confirming safety and efficacy of antithrombotic therapy in children. However, there are case reports using different therapies (anticoagulant, antiplatelet and thrombolytic) in acute MI in children. Consultation with a pediatric hematologist is recommended.

REFERENCES:


Please note that the information contained herein is not to be interpreted as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare providers, and as such you should never delay seeking medical advice, disregard medical advice or discontinue medical treatment because of the information contained herein.