PERIPHERAL ARTERIAL DISEASE

TARGET AUDIENCE: All Canadian health care providers, mainly in the outpatient setting.

OBJECTIVE:

To assist in the selection and dosage of antiplatelet agents for patients with peripheral arterial disease, in view of the risk of vascular events and the risk of bleeding.

ABBREVIATIONS:

ABI	ankle-brachial index
ASA	acetyl salicylic acid
CV	cardiovascular
GI	gastrointestinal
PAD	peripheral arterial disease

BACKGROUND AND MECHANISM OF ACTION:

Antiplatelet agents, mainly acetyl salicylic acid (ASA), are well-recognized to prevent vascular events. In peripheral arterial disease (PAD), these agents prevent mostly cardiac events and, to a lesser extent, stroke and peripheral ischemic complications. The mechanism of action of antiplatelet agents is by inhibiting platelet aggregation with no significant effect on the hemodynamic processes such as claudication.

INDICATIONS AND AGENTS:

Asymptomatic PAD, meaning a reduced ankle-brachial index (ABI) without symptoms, although leading to a well-documented risk of cardiovascular (CV) mortality, has not been clearly shown to benefit from ASA. Two prospective studies have demonstrated this lack of effect (randomized patients with almost normal ABIs). This absence of a well-documented beneficial effect is akin to the role of ASA in primary prevention where the reduced risk of CV events is counterbalanced by an augmented risk of bleeding. Nevertheless, ASA can be considered in patients with asymptomatic PAD who have a high risk of CV events but without risk factors for bleeding.

Symptomatic PAD, manifested by claudication, peripheral emboli or a previous vascular intervention, does benefit from antiplatelet therapy, mainly ASA or clopidogrel. The dose of ASA varies in most studies between 80 and 160 mg. The effect is due mainly to the reduced risk of myocardial infarction (see STEMI & NSTEMI guides) and the magnitude of this relative risk ratio is about 25%. For patients allergic or intolerant to ASA, the use of clopidogrel is recommended. The CAPRIE study has shown that clopidogrel is superior to ASA in reducing CV events by 8.7%, an effect particularly evident in the PAD subgroup. In the CHARISMA study, the addition of

clopidogrel 75 mg to ASA 75-162 mg, compared with ASA alone, has shown a modest CV benefit of the combination in symptomatic patients, but at the cost of an almost comparable risk of moderate bleeding.

Patients who have been submitted to endovascular interventions, with or without stenting, as well as those surgically-treated should also receive ASA. Adding clopidogrel or warfarin has not been proven useful, but studies addressing these issues are somewhat small. It is not clear whether complicated distal bypasses and stents might benefit from temporary dual antiplatelet therapy or from the combination of warfarin and ASA.

Patients with abdominal aortic aneurysm should also receive ASA because of the associated coronary artery disease.

The addition of warfarin is generally associated with an increased risk of bleeding without any efficacy benefit. However, a combination of ASA and warfarin therapy may be appropriate in special circumstances such as in PAD and atrial fibrillation or in venous thromboembolism (see DVT treatment and PE guides). The use of prasugrel and ticagrelor has not been addressed in patients with PAD but there is no reason to believe they are harmful when prescribed for coronary artery disease.

DOSING:

The standard dose of ASA is 81 mg and the standard dose of clopidogrel is 75 mg.

MONITORING:

No monitoring is required.

ADVERSE EFFECTS:

The main adverse effect of ASA, seen more at higher doses, is bleeding, mainly gastrointestinal (GI) but also intracranial. The risk-benefit ratio is acceptable as long as patients are at least at moderate CV risk, which is the case for symptomatic PAD patients. The main adverse effect of clopidogrel is also bleeding but the rate of GI bleeding is less than with ASA.

PERI-PROCEDURAL MANAGEMENT:

Most procedures do not necessitate stopping ASA but it is preferable to discontinue clopidogrel about a week before any procedure associated with a high risk of bleeding (see the peri-procedural management section of each of the ASA and clopidogrel guides).

PEDIATRICS:

Peripheral arterial disease is rare in neonates and children.

REFERENCES:

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