Defining atherothrombotic risk in peripheral artery disease

IMPACT PARAGRAPH

Peripheral artery disease (PAD) is a common manifestation of atherosclerosis with a global prevalence of 5.6% and an even higher prevalence in high-income countries (7.4%). These numbers are estimates, as the disease remains underdiagnosed due to lack of awareness of clinical manifestations. Awareness was improved after the introduction of the ankle brachial index as diagnostic tool, but still millions of people with PAD are not being treated with the current medical treatment strategies as they have yet to be diagnosed with the disease. The patients that are diagnosed with PAD do receive the current optimal treatment strategies. They are however still at increased risk for cardiovascular events, with cardiovascular mortality being increased three-fold in PAD patients as compared to non-PAD patients. People who are diagnosed with the disease also have, apart from the increased adverse event risk, two times higher odds of having impaired physical function, with PAD being consistently associated with a reduction of the physical component of quality of life. Moreover, PAD considerably increases medical expenditure, especially in PAD requiring major amputation where the expenditure is twelve times higher as compared to people without PAD.

To decrease the number of adverse events and medical expenditure, as well as to improve quality of life, it is important to understand why certain PAD patients are at increased for vascular complications and why the current medical treatment strategies are insufficient in preventing adverse events. This thesis revealed that the lipid-lowering strategy can be intensified to further improve lipid profiles. Moreover, antiplatelet agents appear to inadequate in preventing adverse events with platelet reactivity being insufficiently decreased in patients who suffer from such events. Alternative medical strategies have been proposed, where the addition of a low dose of a direct anticoagulant drug to the standard antiplatelet therapy reduces the risk of cardiovascular events by 24%. This specific treatment strategy not only improves health outcomes, it also appeared to be cost-effective as compared to the standard antiplatelet therapy, especially in comorbid patients.

An important question however remains; who would benefit from such alternative treatment strategy? The combination of a low dose anticoagulant drug comes with a 70% increase in major bleeding events, and it is important not to expose patients to this increased bleeding risk when they are successfully treated with antiplatelet drugs only. Risk stratification could aid in creating tailored treatment strategies for PAD patients. In this thesis, biomarkers were identified, both newly found and as identified in the systematic review, that could be used for risk stratification. Along with these biomarkers, other variables such as prior ischemic events and decreased kidney function could be used in risk stratification models. Being able to stratify cardiovascular risk in PAD patients, medication strategies can be tailored and thereby the number of cardiovascular events can be reduced and quality of life can be preserved.