CORRESPONDENCE

The Diagnosis and Treatment of Peripheral Arterial Vascular Disease

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Conflict of interest statement
The authors declare that no conflict of interest exists.

Emphasis on Dual Antithrombotic Therapy

In the prospective randomized double blind and placebo controlled MIRROR study, peri- and postinterventional dual antithrombotic therapy using acetylsalicylic acid (ASA) and clopidogrel was compared with treatment consisting of ASA and placebo, in patients with infrainguinal peripheral arterial vascular disease treated by endovascular intervention (percutaneous transluminal angioplasty (PTA) or stent. Patients who received dual antithrombotic therapy peri-interventionally as well as for six months after the intervention had a significantly lower repeat intervention rate at the treated vascular section after 6 months (1). The groups were not different regarding complications; in particular, no higher rate in bleeding complications was seen in the clopidogrel arm.

After the study medication was stopped after 6 months as planned, no difference in intervention rates was seen between the groups at 12 months (2).

Even though the number of cases was small (n=80), the trial provided initial evidence in support of dual antithrombotic peri-interventional and postinterventional therapy after interventional treatment of peripheral arterial vascular disease. In our opinion, dual antithrombotic therapy seems worth recommending for 6 months after intervention for peripheral arterial vascular disease (PTA or stent). It remains to be seen if a longer duration of dual therapy—for example, for 12 months—would make sense (as is usual in interventions involving the coronary arteries) or whether new antithrombotic substances may yield a further positive effect.

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Prescriptions Are the Remit of the Doctor

For responsible doctors and pharmacists, medication therapy safety has always had an important role in their patients' and customers' interests, which they understand well. Nowadays the subject has entered the political agenda—explicitly with patients' entitlement to a medication plan if at least three medical drugs are prescribed.

In their article on the diagnosis and treatment of peripheral arterial vascular disease, the authors reference international guidelines for secondary prevention in symptomatic patients with peripheral arterial vascular disease and regard a platelet inhibitor as indicated (1). One might easily concede that 75–100 mg of aspirin a day is acceptable. However, a meta-analysis (2) showed that in patients with peripheral arterial vascular disease receiving placebo, cardiovascular events occurred in 9.6% of patients, and in those receiving aspirin such events affected 8.2% of patients. This corresponds to an absolute risk reduction of 1.4% and a number needed to treat (NNT) of 71. This means that 70 out of 71 patients do not benefit from aspirin prophylaxis, but have to expect bleeds. It gets even more serious when the authors demand that all patients with peripheral arterial vascular disease should be given a statin, independently of their LDL concentration, if no contraindication exists. To date, this problem has not been investigated in an intervention study.

The future medication plan for PAVD patients thus includes already two medical drugs with very marginal effects (aspirin) or without proof of efficacy (statin). I wonder how an interprofessional panel would reach an expert consensus in this setting (studies of evidence level C). Cooperation between doctors and pharmacists is all well and good, as well as desirable—but if politically prescribed, so to speak, it might deteriorate into a questionable and annoying routine. The consensus should be that drug prescribing is the responsibility of doctors—on the basis of “thorough training in clinical pharmacology and pharmacotherapy” (3).

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In Reply:

Because of data from cardiological studies, combination therapies consisting of ASA and clopidogrel are often used in routine clinical practice after stent implantation in the coronary arteries. Robust evidence for their use in the peripheral arterial flow path is lacking.

The authors rightly mention the MIRROR Study (1), to date the only randomized study investigating this research question.

The primary endpoints in this study of 80 patients were, however, local concentrations of platelet-activating beta-thromboglobulin, CD40L, and the rate of clopidogrel resistance. The clinical endpoints reintervention and hemorrhage were defined as secondary endpoints. After dual platelet inhibition, reintervention in the target lesion was significantly rarer, but the absolute number of reinterventions (two versus eight in patients receiving ASA) was also very low. The limitations of this first randomized study in two centers were a small number of patients, the study design (clinically defined events as secondary endpoints), and the small absolute number of reinterventions. We still agree with Strobl and Tepe that the study is the first to show well-founded indications of dual platelet inhibition for six months after endovascular therapy in the femoropopliteal region. A larger multicenter randomized controlled study is required to confirm the results of the MIRROR Study. Until then, our recommendation—which is consistent with international guidelines (2)—holds: after infrainguinal endovascular therapy, a temporary combination of aspirin and clopidogrel can be recommended (consensus recommendation) (3).

Meyer critically questions the value of aspirin and statins in medication therapy of patients with peripheral arterial vascular disease. In actual fact, the event rate (primary endpoint: non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death) in the cited study reported by Berger et al (4) is 8.9% under ASA (alone or combined with dipyridole); in the control group it is 11% (relative risk 0.88; 95% confidence interval [0.76; 1.04]). The rate of major hemorrhage was not raised under ASA. Peripheral arterial events were not considered in this study.

We just do not understand the conclusion—that patients with symptomatic peripheral arterial vascular disease receiving ASA prophylaxis do not benefit—especially as in the cited study the number of strokes was reduced significantly in the group of patients with peripheral arterial vascular disease who were treated with ASA.

We presented a critical overview of the discussion around statin therapy and lipid measurements in patients with peripheral arterial vascular disease. Independently of indications of improved patency and survival rates in revascularized patients (5), administration of a statin is indicated in such patients at high cardiovascular risk, so as to reduce the rate of cardiovascular events (2).

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