Statins in patients at high risk of cardiovascular disease presenting with peripheral artery disease

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This editorial refers to "Statin therapy improves cardiovascular outcome of patients with peripheral artery disease" by M. Scillinger et al. on page 742

Atherosclerosis is a disease involving medium-size arteries, particularly the carotid, coronary, and femoral vessels. The detection of atherosclerosis in one of these arterial areas should prompt the clinician to intervene to protect the patient's whole arterial tree. Indeed, all patients with atherosclerosis are at high risk of ischaemic episodes, whether or not they have suffered an ischaemic event (previously referred to as secondary or primary prevention patients). One of the new concepts highlighted by the 2003 European Guidelines for the Prevention of Cardiovascular Diseases is the definition of high cardiovascular risk typologies, that is, patients with a history of ischaemic manifestations in coronary, cerebral, or femoral vessels, patients with type 2 diabetes, and other patients with multifactorial high cardiovascular risk.

High cardiovascular risk requires intensive and global therapeutic interventions. The 2003 European Guidelines for Cardiovascular Prevention underline the efficacy of 9 therapeutic targets shown to reduce cardiovascular events in high-risk patients. First among them are three lifestyle targets: smoking cessation, switch to a healthy Mediterranean-style diet, and regular physical activity. Secondly are six biomedical targets: blood pressure (systolic < 130 mm Hg and diastolic 80 mm Hg), cholesterol (total cholesterol < 175 mg/dL and LDL-cholesterol < 100 mg/dL), glycaemia (HbA1c < 6.1%), and body weight (BMI < 25 kg/m²). In addition, cardiovascular risk has been shown to be reduced by the use of three medications that inhibit, respectively, platelet aggregation (aspirin or clopidogrel), cholesterol metabolism (mainly statins, as fibrates have been shown to be efficacious only in patients with plurimetabolic syndrome or type 2 diabetes), and the angiotensin pathway (angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers). Each of these three drug-mediated medical interventions reduce cardiovascular risk by at least 25% — regardless of haemostatic status, the lipid profile, or blood pressure values — and have additive effects. Consequently, the cardiovascular risk in high-risk patients using all three drugs might be reduced to about 40% (75% × 75% × 75%). Taking these data into account, the list of therapeutic interventions would be 12 evidence-based targets.

All published randomised trials that have compared a statin to placebo in high cardiovascular risk patients have demonstrated an important reduction, both statistically and clinically, of the 5-year cardiovascular complication rate (fatal or nonfatal). In these studies, the reductions in relative and absolute risk ranged, respectively, from −25% to −35% and from −2% to −8% (NNT 12–50). In this line, the observational study by Schillinger et al. published in this issue showed a lower cardiovascular risk in patients with peripheral artery disease (PAD) using a statin. At the time of femoral angiography, about half of these symptomatic PAD patients were receiving statin treatment, a figure close to the one reported in the Euro-Aspire II study. The effects of the statin molecule and its dosage were not studied. Over a mean 21-month follow-up, patients on statin at baseline presented 52% less cardiovascular mortality. This difference might be partly explained by several biases, as confounders are never totally accounted for in nonrandomised studies. Interestingly, patients with an elevated baseline high-sensitive C-reactive protein (hs-CRP > median) showed...
the largest reduction in cardiovascular risk. This finding confirms the prognostic yield of hs-CRP in patients with symptomatic atherosclerosis, and is consistent with the results of a post hoc analysis of the CARE trial in postmyocardial infarction (MI) patients with high serum levels of inflammatory markers (hs-CRP and SAA). However, in this latter large trial, post-MI patients without high levels of inflammation markers also benefited from statin treatment. The study by Schillinger et al. did not confirm this conclusion but was not designed or powered (size and time limitations) to address the impact of statin in PAD patients without high levels of inflammation markers. A large randomised trial is needed to answer this question. Meanwhile, irrespective of serum lipid and hs-CRP levels, the general practitioner and specialist should prescribe a statin to all PAD patients to reduce their risk of cardiovascular ischaemic attacks, and aim at reaching the eleven other therapeutic targets to optimise the management of high cardiovascular risk.

References