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Foreword

Peripheral vascular disease: basic and clinical perspectives

Erich Minar & Martin Schillinger

Peripheral vascular disease (PVD) is a serious medical problem and an indicator of systemic atherosclerosis. Concerning development and manifestation of PVD, atherosclerosis and, in further consequence, atherothrombosis are the main etiopathogenic factors. Atherosclerosis is principally a systemic disease not limited to an isolated vessel segment. This is the reason for a high coincidence of PVD with manifestations of atherothrombosis in other vessel areas. In patients with primary diagnosis of PVD, the prevalence of atherosclerotic manifestations in other vessel areas is higher than in patients with a primary diagnosis of coronary or cerebrovascular disease. The diagnosis of PVD is, therefore, a marker for more generalized and severe atherosclerosis. Patients with intermittent claudication have a relatively good prognosis concerning amputation-free survival, while otherwise the prognosis concerning overall survival is poor, with coronary artery disease being by far the most common cause of death. Patients with chronic critical limb ischemia have an even worse prognosis with a 20% mortality in the first year after presentation.

Unfortunately, the importance of PVD is often underestimated, especially in comparison with coronary and cerebrovascular disease. This book will help to increase the basic knowledge concerning different aspects of this important disease. The initial chapter provides an excellent overview of the most important data concerning epidemiology, risk factors and prognosis of PVD. Our understanding about pathogenesis of atherosclerosis has

changed fundamentally during the last few decades. While atherosclerosis was formerly considered a bland lipid storage disease, substantial advances in basic and clinical studies have illuminated the role of inflammation and the underlying cellular and molecular mechanisms that contribute to atherogenesis. Genetic factors are responsible for a basic risk of a patient for development of atherosclerotic disease, and this basic risk is modified under the influence of further modifiable personal and environmental factors. The major established risk factors for PVD include smoking, hyperlipidemia, diabetes and hypertension, with 95% of individuals with prevalent PVD having at least one of these risk factors. The Reduction of Atherothrombosis for Continued Health (REACH) Registry demonstrated that atherothrombotic patients throughout the world have similar risk factor profiles. However, conventional risk factors for atherosclerosis do not account for all the atherosclerotic entities.

In the diagnostic chapter, the importance of clinical diagnosis is stressed. A careful history taking and clinical examination remain the gold standard in diagnosis of PVD and enable the identification of an at risk patient without complex apparative diagnostic methods. In most cases, it is possible by clinical examination alone to distinguish intermittent claudication from nonvascular causes that may mimic claudication (pseudoclaudication). Calculation of the ankle–brachial index is established worldwide as the initial screening test. There is a consistent series of prospective epidemiological studies indicating that an abnormal ankle–brachial index predicts cardiovascular disease. Furthermore, there is a strong correlation between ankle–brachial index, as a measure of the severity of the PVD and mortality. Morphologic evaluation is only necessary if any kind of revascularization is being planned. Duplex sonography as the primary diagnostic step for evaluation of morphology and for planning the kind of revascularization – endovascular or surgical technique – enables visualization and quantification of severity of lesions. This can be done by duplex ultrasound, computed tomographic angiography or magnetic resonance angiography, while digital subtraction angiography as the former gold standard should not be used for diagnostic purposes anymore.

The following chapters address conservative therapy as well as endovascular and surgical revascularization. Therapy in patients with PVD has two main goals: improvement of prognosis and survival of these patients, and improvement of symptoms and quality of life. The first goal can be achieved by risk factor modification and antiplatelet therapy, while revascularization and also in some cases additional pharmacologic therapy with vasoactive drugs are used for symptomatic relief. Regular exercise training is important for both therapeutic goals. Many clinical trials have demonstrated the

effectiveness and physiologic mechanisms of exercise training for claudicants. However, there are limitations and many factors such as motivation and other physical problems often play a prominent role. Owing to restrictions in training ability or poor compliance, only 30% of all patients with intermittent claudication benefit from physical training. Supervised exercise therapy is suggested to have clinically relevant benefits compared with nonsupervised regimens, which is the main prescribed exercise therapy for people with intermittent claudication.

The main reason to administer antiplatelet therapy to patients with PVD is to prevent severe vascular events, such as myocardial infarction, stroke or vascular death. There are different vasoactive drugs in use with varying – mostly poor – levels of evidence to support their use. Cilostazol – a phosphodiesterase III inhibitor with vasodilator, metabolic and antiplatelet activity – currently has the best overall evidence for treatment benefit in patients with claudication.

Clinicians and scientists are intrigued by the promise of therapeutic angiogenesis to improve vascular perfusion beyond surgical and interventional limits simply by forming new collateral blood vessels. However, it is still a long way from bench to bedside and patient benefit. Beside angiogenic molecules cell therapy was also tested to improve blood perfusion in these patients. Preliminary data are promising – especially with cell therapy – however, large randomized trials are still necessary to unequivocally show the benefit of this therapy.

Technology and techniques of endovascular revascularization as a minimally invasive therapy for treatment of patients with PVD have evolved rapidly during the last decade and there is now a growing body of experience in the treatment of even complex cases. Owing to the reduced invasiveness and lower complication rate compared with open vascular surgery it has gained increased acceptance by physicians, and especially also by patients. Endovascular approaches now represent the initial strategy for management of most of these mostly polymorbid and, therefore, high-risk patients. While endovascular therapy has already been established in the iliac and femoropopliteal segment for many years, during the last few years the tibioperoneal arteries have also become an increasingly accepted area for endovascular interventions in patients with critical limb ischemia.

Different technologies, especially stent implantation – resolving the problems of residual stenosis, elastic recoil and flow-limiting arterial dissection – enable an optimization of the primary technical result, which is especially important in patients with critical limb ischemia. However, there are still recommendations that patients with longer or more complex

lesions in the aortoiliac and especially the femoropopliteal and crural segments should be treated primarily by surgery. The main reason for preference of vascular surgery in these patients is the increased restenosis rate with the need for repeated interventions.

A potential future improvement of local drug application for the necessary time span without the disadvantages of permanent stent implantation can be expected by the development of completely bioabsorbable drug-eluting stents.

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