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Editorial

# Peripheral artery disease: A highly prevalent untreated and uncontrolled independent cardiovascular disease

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Peripheral artery disease (PAD) prevalence is high in developed countries and increasing in low-income ones, involving more than the 20% of subjects older than 80 years in high-income countries [1]. Its diagnosis is, however, yet largely undertaken and delayed, with a large risk to loose the possibility of an effective management [2]. While PAD risk factors are well-known and overlapping with those for coronary artery disease (CAD), the epidemiological association between PAD, CAD/stroke and mortality is yet conflicting. This relationship is deeply examined in the interesting paper published by Matsushita et al. in this issue of *Atherosclerosis* [3]. In this study, individuals with both PAD and coronary heart disease (CHD)/stroke had the worst 12-year survival (25.5%), followed by those with PAD but without CHD/stroke (47.7%) and those with CHD/stroke but without PAD (53.2%). Adjusted hazard ratio of mortality was 2.70 (95% CI, 2.07–3.53) for PAD with CHD/stroke, 1.81 (1.54–2.12) in CHD/stroke without PAD, and 1.68 (1.35–2.08) in PAD without CHD/stroke vs. no CHD/stroke or PAD. These data are particularly interesting because coming from the large and well-characterized cohort of the National Health and Nutrition Examination Survey (NHANES) (N. 6780 subjects aged ≥40 years) with a long follow-up of about 12 years. The groups was balanced by gender, while ethnicities were less represented. These data are impressive and require some attention, as well as critical evaluation. What is different between PAD and CHD/stroke from disease history and awareness by patients? Certainly, CHD and stroke in the most part of cases are easily recognized by the patient itself, and even better by non-specialist physicians. On the other side, PAD could develop on long-term, with symptoms that could be masked by physical training or by osteoarticular symptoms. Of note, the results were obtained using a simple, reproducible, widely available and low-cost tool such as measurement of the ankle brachial index (ABI), which consists of the ratio between the systolic blood pressure of the lower extremity and the upper extremity. ABI may be measured either with automated devices, or with a simple Doppler devices and a blood pressure sphygmomanometer, and can be used by many medical providers such as physicians, technicians or nurses. A low ABI (i.e. <0.9) represents a reliable measure indicating the presence of lower extremity artery disease and has a demonstrated independent predictive value for various types of cardiovascular events and mortality in several populations.

From a preventive point of view, the lifestyle and pharmacological approach to PAD, CAD and stroke primary and secondary prevention is very similar (improvement of lifestyle, optimization of blood pressure control mainly by the use of renin-angiotensin system modulators and calcium-channel blockers, and/or anti-aggregants), however, the effect of a specific intervention is quite different. For instance, tailored physical exercise positively in PAD patients improve neoangiogenesis, muscle perfusion, attenuate progression of lower-limb myophathy, slow atherosclerotic processes, with improvement in patients' functional capacity and health-related quality of life, reducing on the other side the risk of extreme complications such as amputation [4]. Intensive lipid-lowering treatment in PAD patients also has an impressive preventive effect: in particular, treatment with proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors on top of statins, where peripheral vascular events risk are reduced by 42% (HR 0.58 [0.38–0.88]). However, in a large US cohort including 250,103 PAD patients, lipid-lowering treatment is yet suboptimal with less than 40% treated, LDL-C remains elevated, and lipid-lowering treatment intensity is a poor surrogate for achieved LDL-C [5]. The large COMPASS trials, enrolling 7470 patients with PAD, showed that the combination of rivaroxaban (2.5 mg twice a day) plus aspirin (100 mg once a day) compared with aspirin alone reduced the risk of major adverse limb events, including major amputation, of 46% (HR 0·54 95% CI 0.35-0.82, $p = 0{\cdot}0037$) [6].

All these evidence supports a call for action in terms of early PAD

*Abbreviations:* PAD, Peripheral artery disease; CAD, Coronary artery disease; CHD, Coronary heart disease; ABI, Ankle brachial index.

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diagnosis and of patient tailored preventive intervention with all the available demonstrably safe effective therapeutic tools.

## Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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