

## EDITORIAL

## Real Life Lessons in Peripheral Artery Disease - A Priority for Public Healthcare

In this issue of the Journal, Schwaneberg et al. present a large retrospective German cohort study which assesses the trends in treatment patterns and comorbidities in patients with lower extremity peripheral artery disease (PAD).<sup>1</sup> The authors demonstrate an increasing number of peripheral vascular interventions (PVI), and fewer major amputations. Of note, these interventions were performed in sicker and older patients, with an increased disease related reimbursement cost.

Interestingly, while the estimated incident cases of PAD among the cohort slightly decreased, a significant increase of prevalent PAD cases, numbers of hospitalisations and PVI was observed. The interpretation of these results is a reduction of new cases combined with prolonged periods of chronic disease, through a higher life expectancy and repeated revascularisations. Considering the incidence estimations, the study has a limited observation time and a limited number of people insured by the company, and it remains unclear whether the decrease of incident cases could also be the consequence of fewer people being at risk at the end of the timeframe. It should be remembered that claims data from an insurance database are not truly population based. Even with this limitation in mind, the authors have demonstrated an increasing number of PVI performed to increasingly ill and older patients with rising costs. They have also demonstrated, without doubt, an increasing trend of relevant cardiovascular comorbidities in patients with PAD, such as hypertension, cardiac dysrhythmia, and renal failure.

A recent epidemiological study by Song et al.<sup>2</sup> has suggested that in 2015, PAD affected around 236 million people worldwide with a global prevalence of 5.6%. Advanced age, smoking, hypertension, diabetes, and concomitant cardiovascular diseases were confirmed to be associated with a higher risk of PAD in both high income countries (HIC) and low to middle income countries (LMIC), these latter countries representing 73% of global cases. The 236 million PAD cases in 2015 represent a relative increase of 17% from 202 million in 2010. However, this increase did not occur evenly in HIC and LMIC. Across five years, the relative increase was higher in LMIC than in HIC (22.6% vs. 4.5%). It is therefore likely that the observed increase of prevalent cases in the cohort reported by Schwaneberg et al.<sup>1</sup> in a HIC, is at the lower end of the observed prevalence of PAD worldwide, which reinforces their message.

The 2017 European Society of Cardiology (ESC) guidelines on the diagnosis and treatment of PAD, in collaboration with the European Society for Vascular Surgery (ESVS), emphasised the

need to improve the diagnosis of PAD, with most patients with PAD being asymptomatic or presenting with atypical symptoms, and highlighted the need to assess walking capacity to detect clinically masked PAD.<sup>3</sup> Furthermore, even if asymptomatic, these patients with PAD are at high risk of cardiovascular events and should benefit from preventive strategies and control of risk factors. The ESC/ESVS guidelines recommend ankle brachial index as first line test for PAD screening, duplex ultrasonography being the first imaging method.<sup>3</sup> The observed rise of PVI in the study by Schwaneberg et al.<sup>1</sup> is not unexpected considering the growing number of patients with intermittent claudication and compromised daily life activity despite supervised exercise therapy. It should, however, be emphasised that data from imaging tests should always be analysed with symptoms and haemodynamic data prior to any intervention.

In the study by Schwaneberg et al.,<sup>1</sup> among >200,000 hospitalisations, 49.4% occurred in patients with chronic limb threatening ischaemia (CLTI) with a high prevalence of diabetes. To help the clinician, a new classification system (Wifl) has been proposed as the initial assessment of all patients with ischaemic rest pain or wounds.<sup>4</sup> Wifl stands for Wound, Ischaemia (based on objective haemodynamic studies) and foot Infection (from local to systemic since the benefit of revascularisation is also dependent upon infection control). The increasing number of PVI together with a decrease in the number of major amputations as observed by Schwaneberg et al.<sup>1</sup> are encouraging and suggest appropriate revascularisation of patients with CLTI together with best medical treatment and risk factor control.

The study from Schwaneberg et al.<sup>1</sup> has some obvious shortcomings. It is a *post hoc* study of health insurance claims data of patients with PAD. It is well known that such registries collected by healthcare providers for billing purposes have a risk of upcoding comorbidities even if data are cross checked by independent physicians as it has been the case in Germany. By contrast, major factors such as smoking may be missed if they do not have any billing impact. The finding of diabetes as a decreasing comorbidity in PAD patients is counterintuitive, given the current epidemics of diabetes and metabolic syndrome that are associated with increased rates of PAD.<sup>5</sup>

But perhaps most importantly, this study lacks granularity when considering mid and long term outcomes and patient follow up. The reader would have been interested to know more about the fate of these PAD patients after PVI, particularly in the long term.<sup>6</sup> Unfortunately, stratified information about surveillance outcomes after vein bypass or endovascular treatment is lacking. A consensus document

regarding the follow up of patients after revascularisation for PAD has recently been published by the ESC working group on Aorta and Peripheral Vascular Diseases and the ESVS and would complement this registry by recommending a standardised follow up emphasising the importance of multidisciplinary management of these patients with a clinically reasonable and cost effective strategy.<sup>7</sup>

However, the efforts of Schwaneberg et al.<sup>1</sup> are to be commended because their study on more than 156,217 patients is a real life and contemporary picture of PAD not limited to highly selected patients as in most randomised studies. In the era of big data, these studies will become more frequent. The major advantages of big data relate to the sheer size of the data sets, their variety and speed of accumulation. There remains, however, a significant risk of selection bias or bias by indication when using big data for comparisons of (non-randomised) diagnostic or therapeutic strategies. A recent study by Perez et al.<sup>8</sup> reporting the results of a large scale assessment of a smart watch to identify atrial fibrillation in more than 400,000 participants is an example of a large scale pragmatic study using user owned connected devices to assess outcomes, a technology that might also be suitable to assess functional outcomes in patients with PAD.

In conclusion, Schwaneberg et al.<sup>1</sup> reconfirm, in a large scale study, that PAD is an increasing major public health challenge in European HIC countries. Other epidemiological studies have shown that this is also the case elsewhere, particularly in LMIC countries. With the demographic trend towards increased ageing and diabetes, an ever greater increase in the number of patients with PAD is expected in the future, reinforcing the need for an early diagnostic tool. The editors of the *European Journal of Vascular and Endovascular Surgery* (EJVES) strongly encourage the reporting of high quality data from other countries, allowing us to carefully evaluate the evolution of disease patterns and of the treatments that we offer to our patients.<sup>9</sup>

## REFERENCES

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