DEPRESSION AND LOWER EXTREMITY ARTERIAL DISEASE: UNDERESTIMATED RELATIONSHIP

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Dear editor,

Lower extremity arterial disease (LEAD) is the third most common clinical manifestation of atherosclerosis after coronary artery disease (CAD) and stroke. It affects nearly one fifth of all adults older than 55 years of age, with increased prevalence in high-risk subgroups such as those with diabetes, renal insufficiency and smoking. Although the underlying atherosclerotic pathophysiology is shared with CAD and cerebrovascular disease, LEAD represents a distinct disorder characterised by high risk of cardiovascular morbidity and mortality as well as adverse limb events including amputation. Despite high prevalence and poor cardiovascular prognosis, LEAD is less systematically evaluated than other atherosclerotic conditions and less attention has been devoted to the detection and treatment of LEAD (Song et al. 2019).

Symptomatic LEAD varies from intermittent claudications, atypical leg pain, critical limb ischemia and occasionally acute limb ischemia. Daily function of patients with LEAD is often compromised by debilitating symptoms and tendency to more sedentary lifestyle.

Besides well-established risk factors for LEAD such as advanced age, smoking and diabetes, recent evidence proposed that depression should also be recognized as risk factor for LEAD. Around 20% of patients with LEAD have depression as comorbidity (Arya et al. 2018, Ramirez et al. 2018). McDermott et al. found that patients with LEAD had a higher prevalence of depression at baseline and a higher rate of developing new depression during follow-up compared to people without LEAD, suggesting that the association between LEAD and depression may be bi-directional (McDermott et al. 2016). Several biologic and behavioural risk factors have been identified to play a role in this likely bi-directional association. These factors include tobacco use, physical inactivity, medical nonadherence, endothelial and coagulation dysfunction and dysregulation of the hypothalamic-pituitary-adrenal axis, autonomic system and immune system (Ramirez et al. 2018).

Depression is also associated with poor LEAD outcomes. In large cohort of veterans with incident LEAD, Ayra et al. found that patients with co-morbid depression had a significantly higher risk of amputation (13%) and all-cause mortality (17%) than LEAD patients without depression, after adjusting for covariates. Additionally, patients that were treated with antidepressants had a significantly lowered risk for amputation in contrast to those without (Ayra et al. 2018).

Another large retrospective analysis of more than 110 000 patients hospitalized for critical limb ischemia found that rate of major amputation was higher in patients with comorbid depression (11.5% vs 9.1%, p<0.001). In multivariable analysis, comorbid depression was associated with 39% increased odds for major amputation. The authors noticed that patients with depression were younger, more likely women, tobacco users and with prior amputation. Comorbid depression was also independently associated with a longer hospitalization length (Zahner et al. 2019).

Working with broad spectrum of cardiovascular patients, especially LEAD patients, we notice the evolving trend of focusing solely on revascularisation strategy of affected limb, which is unfortunately often of limited duration. We think that evaluation of depression in these patients deserves at least same attention as in CAD patients. More comprehensive understanding of the factors that may influence LEAD development and prognosis should be considered. Recognizing depression as an important risk factor for poor outcomes in patients with LEAD is important to provide the high-quality care.

Currently, there is no consensus on depression screening tools nor existing guidelines for optimal management of patients with LEAD and depression. Only short comment about concomitant reactive depression in patients with LEAD was mentioned in recent European Society for Vascular Medicine Guidelines (2019) underlining that data from interventional studies of antidepressants or psychiatric treatment for patients with LEAD have not yet become available (Frank et al. 2019).

The aim of this letter is to raise awareness of depression in patients with LEAD and to encourage further research in this field, especially interventional psychiatric studies. Depression screening in this patient population should be considered. Better understanding of depression's physiologic implications on peripheral atherogenesis and recovery after endovascular or surgical interventions could provide more effective treatment strategy. In order to enhance individualized vascular treatment, an interdisciplinary approach that combines vascular and mental health care should be employed among depressed patients with LEAD.

Conflict of interest: None to declare.

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