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EDITORIAL

Challenges in the management of patients with critical limb ischemia



The number of people living with peripheral artery disease (PAD) is increasing, driven mainly by population ageing [1]. Among patients with established atherosclerotic disease, those with PAD present the highest mortality, in particular from cardiovascular causes [2]. Patients with critical limb ischemia (CLI), the end-stage of PAD, have severe atherosclerosis and face significantly worse local and general outcomes than those with a milder PAD state [3]. Revascularization procedures are challenging due to the severe pattern of arterial disease with the presence of long calcified occlusions and below-the-knee arterial disease. In a multidisciplinary team approach, the management of this chronic and debilitating arterial disease present several specific challenges to improve amputation-free survival.

First, in the absence of revascularization, nearly one third of patients with CLI may experience major amputation at 6 months [4]. To achieve limb salvage, preserve functional autonomy and improve survival, revascularization of the affected limb should be performed when possible [5]. Considered as minimally invasive, with lower mortality rate as compared to conventional surgery, endovascular techniques have really taken off during the last decades [6]. The advancements in catheter-based techniques offer the possibility to perform distal revascularization of the plantar arch and the pedal artery. Recently, a novel revascularization approach consisting in a totally percutaneous extra-anatomic femoro-popliteal bypass has been proposed for limb salvage in patients with CLI and previous failure of conventional surgical and/or endovascular revascularization procedures (past ligation of the femoral and/or popliteal artery, previous surgical bypass thrombosis and/or important arterial calcifications) [7]. This endovascular approach remains a challenging procedure, particularly due to the higher hemorrhagic risk as compared with traditional endovascular techniques, and usually requires re-interventions to maintain secondary patency [7]. This technically demanding limb-salvage procedure is discussed in a well-defined subset of patients with no traditional endovascular or surgical revascularization options.

Second, despite successful revascularization procedure, diagnosis of CLI remains a marker of poor overall survival. In a recently published cohort data including 315 patients with CLI, peri-operative and short-term mortality were high following endovascular revascularization: 3.8% of patients died during the first month and cumulative mortality rate at one-year was 25.4% of patients [8]. Cardiovascular events are highly prevalent, followed by limb adverse events and infectious causes. More than a quarter of this patient cohort presented an adverse cardiovascular event in the year following revascularization. Coronary heart disease and decompensated heart failure appear as important contributors for the occurrence of adverse cardiovascular events. Incident cardiovascular event was associated with a 7-fold higher risk of mortality during the first year of follow-up [9]. As patients with CLI have severe atherosclerosis, improved survival is expected from the best risk factor treatment in association with revascularization. As no randomized trials have been conducted in CLI population regarding cardiovascular risk factor management, good practice recommendations are extrapolated from other conditions in secondary cardiovascular prevention. In particular, hypertension is one of the most prevalent risk factors in patients with CLI, affecting more than three quarter of patients [8]. In hypertensive patients with established cardiovascular disease, literature data underline that the relationship between blood pressure level and mortality is not linear but rather displays a J-shaped curve pattern, supporting a personalized approach to hypertension care. In recently published data in patients with CLI, blood pressure level at hospital admission predicts mortality in both the short-term and long-term, but with reverse quite linear pattern [8]. This pattern is different from the J-curve seen in patients with a milder PAD state, and approaches the systolic blood pressure curve and related mortality in acute cardiovascular condition [10]. These results cannot prove a causal effect of low blood pressure for mortality but suggest a possible prognostic marker. Further prospective studies will have the potential to explore the

issue of blood pressure goal in hypertensive patients with CLI.

Third, the proportion of elderly patients with CLI referred to vascular specialists is increasing. Octogenarian patients represent more than a half of patients undergoing endovascular revascularization procedure in our center [11]. Periprocedural complications and major limb amputations do not differ significantly between octogenarians and non-octogenarians. At 3-month and at one-year, cumulative mortality was two-fold higher in the octogenarian patients compared to their younger counterparts. Prevalence of cardiovascular risk factors were lower in this elderly population and were not associated with poorer survival. No significant difference was noted for treatment at hospital discharge including statins, renin-angiotensin system inhibitors, or anticoagulant drugs. Mortality may be thus determined by more specific comorbid conditions encountered in this aging population, in particular malnutrition, kidney and heart failure. Indeed, decompensated heart failure was prevalent, either as the main or one of the contributing causes of death [11]. The poorer outcome in this elderly population as compared with their younger counterparts, is not in line with previously published data of the multicenter, prospective (CRITISCH) registry [12]. Octogenarians with CLI were treated with first-line endovascular revascularization and showed comparable early and one-year amputation-free survival rates as compared to their younger counterparts, and limb salvage was even higher in octogenarians in this multicenter registry. There are two possible explanations for the increased mortality rate in our elderly patient cohort. First, the mean age in our elderly group was higher and almost 20 years higher than that registered in non-octogenarians patients, with prevalent malnutrition and institutionalized status. Second, near one third of our study population underwent multiple revascularization procedures, and especially in octogenarian patients for contralateral CLI or clinical recurrence of CLI. Of note, multiple revascularization procedures were not associated with increased mortality in the elderly patient group. However, further analysis should provide precise granular information on survival according to the number of endovascular procedures in patients with CLI, and particularly in the elderly population.

Patients with CLI, in particular the very elderly, is a growing population that is rarely included in clinical trials because of significant comorbidities and particularly end-stage organ damage. Despite successful revascularization procedure, patients with CLI present a high risk of cardiovascular events and death in the short-term follow-up. Coronary heart disease and decompensated heart failure are important prognostic factors for poor outcome. Due to the heterogeneity in patient's characteristics and arterial disease complexity, a personalized care approach and the choice for the revascularization strategy should be discussed in a multidisciplinary team. Further studies would have the potential to focus on the associated effect on quality of life in patients with CLI undergoing revascularization procedure.

Disclosure of interest

The authors declare that they have no competing interest.

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