Measurement of Nutritional Status as Frailty Severity is Indispensable to Treat Patients with Chronic Limb-Threatening Ischemia

Yoshiyuki Ikeda

Department of Cardiovascular Medicine and Hypertension, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan.

In Japan, the older population is increasing because of increasing life expectancy and the prevalence of atherosclerotic cardiovascular disease (ASCVD) increases because of aging society and diffusion of the Western diet. ASCVD is the leading cause of death in the world, and it is noteworthy that a recent investigation has revealed that the years of life lost (YLL), which is a key element in measuring disease burden, due to ASCVD were comparable to those for cancer1).

Peripheral artery disease (PAD) is a manifestation of atherosclerosis, and chronic limb-threatening ischemia (CLTI) is the most advanced form of PAD. CLTI patients have poor vascular condition due to severe arteriosclerosis, and are known to have poor prognosis because of the high prevalence of concomitant vascular disease including coronary artery disease (CAD) and/or cerebrovascular disease2). Since CLTI aggravate YLL, it is important to identify the factors in CLTI patients in order to prevent major adverse cardiac and cerebral events.

Recent accumulation of evidences revealed that frailty is closely associated to the poor clinical outcomes of cardiovascular diseases (CVD), such as CAD, heart failure, aortic stenosis, and atrial fibrillation, and has been identified as a risk factor for mortality3). Frailty is defined as a clinically recognizable state among older adults with increased vulnerability, and consists of three elements; physical, social, and cognitive frailty. Sarcopenia is defined as the loss of skeletal muscle mass and function with age, which contributes to the development of physical frailty. Whereas the identification of frailty is now indispensable for CVD patients who are at higher risks of disability and adverse clinical outcomes, PAD/CLTI has not been well explored relative to frailty due to the insufficiency of clinical studies examining the relationship between PAD/CLTI and frailty.

Takahara et al has been demonstrating the clinical impact of various frailty-related aspects in poor-risk patients undergoing revascularization for CLTI4). They analyzed a clinical database of the Poor-Risk Patients With and Without Revascularization Therapy for Critical Limb Ischemia (PRIORITY) registry5), and a total of 562 CLTI patients, who required assistance for their daily lives and were candidates for revascularization, were examined by measurements of several frailty severity, cardiac function, and inflammatory markers. In this study, frailty-related measures, as well as age and inflammatory markers, had a relatively high variable importance for one-year mortality risk compared to comorbidities and limb severity. Authors also demonstrated that among frailty-related markers, nutrition-related markers, such as cholinesterase, BMI, GNRI, CONUT, and albumin, had valuable importance to predict mortality of patients with CLTI.

Malnutrition is the main factor causing frailty and sarcopenia. In addition, atherosclerosis is accepted inflammatory disease and the concept of malnutrition-inflammation-atherosclerosis (MIA) syndrome has been recently reported6). Therefore, it is conceivable that malnutrition causing frailty is a crucial factor that affects mortality in patients with ASCVD including CLTI (Fig. 1). Given these evidences and the difficulty of assessing frailty status in PAD/CLTI patients who present with gait disturbances, assessment of nutritional status is indispensable to treat patients.
Correlation of MIA syndrome and frailty may play a pivotal role in regulating prognosis of patients with ASCVD including CLTI.

MIA: malnutrition, inflammation and atherosclerosis
ASCVD: atherosclerotic cardiovascular disease
CLTI: chronic limb-threatening ischemia

Conflicts of Interest
None.

References
1) Arai H, Mortaki K, Rane P, Quinn C, Zhao Z, Qian Y. Estimating Years of Life Lost Due to Cardiovascular Disease in Japan. Circ J, 2019; 83: 1006-1010
2) Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, Goto S, Liu CS, Richard AJ, Röther J, Wilson PW; REACH Registry Investigators. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA, 2006; 295: 180-189
3) Uchikado Y, Ikeda Y, Ohishi M. Current Understanding of the Role of Frailty in Cardiovascular Disease. Circ J, 2020; 84: 1903-1908
4) Takahara M, Iida O, Soga Y, Azuma N, Nanto S, on behalf of the PRIORITY investigators. Clinical Impact of Measures for Frailty Severity in Poor-Risk Patients Undergoing Revascularization for Chronic Limb-Threatening Ischemia. J Atheroscler Thromb, 2021; in press. doi: http://doi.org/10.5551/jat.61481
5) Iida O, Takahara M, Soga Y, Azuma N, Nanto S and Uematsu M: Prognostic Impact of Revascularization in Poor-Risk Patients With and Without Revascularization Therapy for Critical Limb Ischemia. JACC Cardiovasc Interv, 2017; 10: 1147-1157
6) Zyga S, Christopoulou G, Malliarou M. Malnutrition-inflammation-atherosclerosis syndrome in patients with end-stage renal disease. J Ren Care, 2011; 37: 12-15