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Letter to the Editor

Sarcopenia can be Physiological or Pathological, Primary or Secondary

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Letter to the Editor

We read with interest the review article by Rivera *et al.* on the relationship between sarcopenia and cardiovascular diseases such as atherosclerosis, hypertension, coronary heart disease and heart failure ^[1]. Cardiovascular diseases have been found to trigger sarcopenia through processes such as inflammation, oxidative stress, endothelial dysfunction, neuronal and hormonal changes, malnutrition and reduced physical activity ^[1]. It was concluded that cardiovascular drugs, hormone replacement, changes in diet and nutritional intake, and physical activity can attenuate sarcopenia ^[1]. The study is noteworthy, but some points should be discussed.

The first point is that we disagree with the view mentioned in the introduction that sarcopenia is a disease ^[1]. Sarcopenia can be both a disease and a physiological condition, which is why sarcopenia should be classified as physiological sarcopenia and pathological sarcopenia. Physiological sarcopenia is an age-related regression of skeletal muscles without the presence of a disease that could explain the muscle atrophy. It is characterized by the fact that regular muscle training no longer leads to an increase in muscle volume or only to a marginal increase in muscle size. Pathological sarcopenia is characterized by the fact that, in addition to physiological sarcopenia, muscle atrophy is caused by an underlying disease that causes muscle atrophy. Diseases associated with muscle wasting include neuropathies, myopathies, central nervous system diseases that cause muscle weakness, previous surgery, rheumatologic and orthopedic diseases, decreased blood supply, endocrinologic diseases and malignancies ^[2].

Since physiological and pathological sarcopenia can coexist, it is not always easy to distinguish the extent to which one or the other contributes to the loss of muscle mass.

The second point is that sarcopenia can also be classified as primary or secondary. Primary sarcopenia is due to genetic causes or remains without cause, while secondary sarcopenia is due to comorbidities that manifest with muscle wasting. The distinction between the two is crucial, as secondary sarcopenia may be amenable to treatment if the underlying cause is treatable.

Thirdly, it has not been considered that other factors in addition to comorbidities contribute to muscle wasting in older people. These include diet, level of physical activity, whether or not someone uses whole body electrical stimulation (WBE), lifestyle and current medication. In particular, people on a low-protein diet are at risk of losing muscle mass because essential amino acids are not sufficient to meet the protein requirements needed to produce adequate amounts of muscle proteins, especially those of the contractile apparatus and those involved in signalling, pore functions and energy production. Although physical activity is no guarantee that muscle mass will remain unchanged with regular exercise, it helps to maintain muscle volume in the event of physiological sarcopenia.

WBE is known to be clinically effective in influencing sarcopenia and is well accepted by the non-athletic cohort of older people ^[3]. For older people who are unable or unwilling to perform dynamic strength exercises, WBE may be a less daunting alternative to maintain muscle mass and strength ^[3]. In order to assess whether sarcopenia is physiologic/pathologic or primary/secondary, it is crucial to know the current medication of a person affected by sarcopenia. Medications that can cause muscle wasting include statins, fibrates, alcohol, amiodarone, procainamide, glucocorticoids, beta-blockers, furosemide, chlorthalidone, propofol, antiepileptic drugs (e.g. lamotrigine, phenytoin), omeprazole, colchicine, D-penicillamine, immune checkpoint inhibitors (nivolumab, pembrolizumab, atezolizumab), antiretroviral drugs (e.g. zidovudine), immunosuppressants (e.g. cyclosporine), tumor necrosis factor inhibitors (e.g. etanercept, adalatcept).

The fourth point is that factors such as vegetative innervation, viral reservoirs, copy number variants, reduction in the number

of satellite cells, inability of muscle cells to divide or replicate, ethnicity, haplotype, mtDNA copy number, oxidative stress and mtDNA polymorphisms should also be considered in the assessment of sarcopenia.

In summary, this interesting study has limitations that affect the results and their interpretation. Addressing these limitations could strengthen the conclusions and support the message of the study. In people with sarcopenia, it must be clarified whether it is physiological or pathological and whether it is primary or secondary sarcopenia before intervention can be recommended. Secondary sarcopenia is multicausal and not only due to cardiovascular disease.

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