

## Correlation of Diuretic use and Sarcopenia in Elderly Patients with Hypertension

Lídia Zytynski Moura,<sup>1</sup> Camila Hartmann<sup>1</sup>

Pontifícia Universidade Católica do Paraná,<sup>1</sup> Curitiba, PR – Brazil

*Editorial referring to the article: Use of Diuretics is Associated with Higher Risk of Sarcopenia in Older Adults with Hypertension*

Hypertension is a chronic disease with high prevalence in Brazil and worldwide. It is estimated that approximately 31% of the world population has blood pressure levels  $\geq 140/90$  mmHg or uses antihypertensive medication.<sup>1</sup> Hypertension is also the main risk factor with an independent, linear, and continuous association for cardiovascular diseases.<sup>2</sup> Cardiovascular diseases, in turn, are the leading cause of death, hospitalizations, and outpatient care worldwide, including in developing countries such as Brazil.<sup>3</sup>

With aging, hypertension becomes an even more significant health problem. Around 61% of individuals over 60 years old have hypertension.<sup>1</sup> In Brazil, the epidemiological transition with the increase in the number of elderly people ( $\geq 60$  years) in the next decades will lead to a substantial increase in the prevalence of hypertension and its complications.<sup>2</sup> Aging is still associated with other health disorders, including sarcopenia. As with hypertension, the prevalence of sarcopenia is higher in the elderly. It varies from 5% to 13% in people between 60 and 70 years of age, and from 11% to 50% in people  $\geq 80$  years of age.<sup>4</sup>

Sarcopenia is a progressive and generalized skeletal muscular disorder that involves accelerated loss of muscle mass and function (such as muscle strength and physical performance). It is associated with an increase in adverse outcomes, including falls, functional decline, frailty, and mortality<sup>5</sup>. For diagnosis of sarcopenia, the European Working Group on Sarcopenia in Older People (EWGSOP) suggests an algorithm based on

clinical suspicion with measurement of handgrip strength to define probable sarcopenia, which is confirmed by measuring muscle mass.<sup>5</sup>

Recently, an original article was published that evaluated 129 elderly patients with hypertension, concluding that handgrip strength was a good method for evaluating sarcopenia and that the use of diuretics in the treatment of hypertension in these patients was associated with an increase sarcopenia.<sup>6</sup> This was an unprecedented finding in the literature for this population, and it warrants analysis and reflection.

The association of loop diuretics and sarcopenia has already been reported in patients with heart failure (HF).<sup>7</sup> The mechanism potentially involved would be via the  $\text{Na}^+\text{-K}^+\text{-2Cl}^-$  cotransporter (NKCC1), which is highly expressed in mammalian skeletal muscles, where it contributes to the generation of membrane ionic currents and potential. Its elevation when using loop diuretics would worsen the muscular metabolic profile.<sup>8</sup> However, in patients with hypertension, the association of diuretics and sarcopenia had not been previously reported. Differently from what occurs in patients with HF, the main class of diuretics used in the treatment of hypertension are thiazides (hydrochlorothiazide) or thiazide-like diuretics (chlorthalidone and indapamide).

The treatment of hypertension with diuretics in the elderly population has proven benefits in reducing blood pressure and reducing cardiovascular morbidity and mortality.<sup>2</sup> Consistent with this understanding, thiazide diuretics are listed in the hypertension guidelines as one of three equally weighted first-line antihypertensive options alongside calcium channel blockers and renin-angiotensin system blockers.<sup>2</sup> They have electrolytic and metabolic side effects, which are already well known, especially hydrochlorothiazide,

### Keywords

Diuretics; Hypertension; Sarcopenia; Aged.

#### Mailing Address: Lídia Zytynski Moura

Pontifícia Universidade Católica do Paraná, 1060 Jeremias Maciel Perretto St. Postal code: 8121031. Curitiba, Paraná – Brazil  
E-mail: lidia.zyt@gmail.com

a medication that is widely used in the public health system in Brazil. Chlorthalidone and indapamide, on the other hand, have a better metabolic profile for adverse effects. The most common metabolic effect is hypokalemia, which is frequently accompanied by hypomagnesemia. Other known effects are glucose intolerance and increased uric acid.<sup>2</sup>

The pathogenesis of sarcopenia is still not fully understood. Aging disturbs skeletal muscle homeostasis, which requires balance between hypertrophy and regeneration through complex and not yet fully understood mechanisms and pathways.<sup>5</sup> However, chronic inflammation with its relevant catabolic cytokines and even hypomagnesemia continue to be the most widely accepted mechanisms of sarcopenia in hypertension.<sup>9</sup> Accordingly, the adverse effects of thiazide diuretics could, in theory, contribute to sarcopenia in hypertension.

A study published in 2014, however, prospectively evaluated a cohort of 639 elderly patients in the United

Kingdom, with a mean age of 65 years, during a follow-up of 4.4 years.<sup>10</sup> In this study, there was no difference in handgrip strength between users and non-users of the evaluated medications, namely, angiotensin-converting enzyme inhibitors, thiazide diuretics, and statins. Furthermore, the analysis of dropout rates by medication use revealed no evidence of selection bias in this study. The authors concluded that the use of these medications was not associated with differences in the decline in handgrip strength in the elderly without previous sarcopenia.<sup>10</sup>

Therefore, the article is provocative in its findings, but the association of diuretics and sarcopenia is still unclear, especially thiazide diuretics in patients with hypertension. Larger clinical trials, specifically including this population, stratifying age groups, as well as the types and doses of diuretics, are necessary, since the antihypertensive effect of these medications is not directly linked to the doses used; however, the side effects are related to the dose and potency of diuretic action.<sup>2</sup>

## References

- Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation*. 2016;134(6):441-50. doi: 10.1161/CIRCULATIONAHA.115.018912.
- Barroso WKS, Rodrigues CIS, Bortolotto LA, Mota-Gomes MA, Brandão AA, Feitosa ADM, et al. Brazilian Guidelines of Hypertension - 2020. *Arq Bras Cardiol*. 2021;116(3):516-658. doi: 10.36660/abc.20201238.
- GBD 2016 Causes of Death Collaborators. Global, Regional, and National Age-Sex Specific Mortality for 264 Causes of Death, 1980-2016: A Systematic Analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1151-1210. doi: 10.1016/S0140-6736(17)32152-9.
- Alexandre TS, Duarte YA, Santos JL, Wong R, Lebrão ML. Prevalence and Associated Factors of Sarcopenia Among Elderly in Brazil: Findings from the SABE study. *J Nutr Health Aging*. 2014;18(3):284-90. doi: 10.1007/s12603-013-0413-0.
- Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. 2019;393(10191):2636-46. doi: 10.1016/S0140-6736(19)31138-9.
- Martins FAD Jr, Mateo DPA, Silva FJM, Moura SS, Oliveira EC, Coelho DB, et al. Use of Diuretics is Associated with Higher Risk of Sarcopenia in Older Adults with Hypertension. *Int J Cardiovasc Sci*. 2022;35(4):476-485. doi: 10.36660/IJCS.20200279.
- Nakano I, Tsuda M, Kinugawa S, Fukushima A, Kakutani N, Takada S, et al. Loop Diuretic Use is Associated with Skeletal Muscle Wasting in Patients with Heart Failure. *J Cardiol*. 2020;76(1):109-114. doi: 10.1016/j.jcc.2020.01.003.
- Mandai S, Furukawa S, Kodaka M, Hata Y, Mori T, Nomura N, et al. Loop Diuretics Affect Skeletal Myoblast Differentiation and Exercise-Induced Muscle Hypertrophy. *Sci Rep*. 2017;7:46369. doi: 10.1038/srep46369.
- Schrager MA, Metter EJ, Simonsick E, BA, Bandinelli S, Lauretani F, Ferrucci L. Sarcopenic Obesity and Inflammation in the InCHIANTI Study. *J Appl Physiol*. 2007;102(3):919-25. doi: 10.1152/jappphysiol.00627.2006.
- Witham MD, Syddall HE, Dennison E, Cooper C, McMurdo ME, Sayer AA. ACE Inhibitors, Statins and Thiazides: No Association with Change in Grip Strength Among Community Dwelling Older Men and Women from the Hertfordshire Cohort Study. *Age Ageing*. 2014;43(5):661-6. doi: 10.1093/ageing/afu008.

