

Title: Vitamin D for healthy aging

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To the Editor,

Buta et al., in a longitudinal cohort study, have recently reported that women (70-79 years of age) with lower serum concentrations of 25-hydroxyvitamin D (25(OH)D) (<10 ng/mL) had a three-fold increased risk of developing frailty than those with the higher 25(OH)D (≥ 30 ng/mL) levels. Authors found that 32.2 per 1,000 person-years in participants with 25(OH)D <10 ng/mL suffered frailty compared with an incidence of 12.9% per 1,000 person-years in those women with 25(OH)D ≥ 30 ng/mL. The association was no longer significant after accounting cardiometabolic diseases.¹

As we reviewed, this results can be explained because low levels of 25(OH)D have been found in patients with cardiovascular disease, hypertension, carotid atherosclerosis, atrial fibrillation, heart failure and myocardial infarction.² This deficiency has been associated with all-cause mortality.² Vitamin D play also an important role on skeletal muscle,³ and the expression of it receptor declines with aging in this tissue.⁴ 25(OH)D deficiency reduces physical function (through grip strength evaluation),⁵ physical performance,⁶ increases sarcopenia,⁷ and the risk of recurrent falls and fractures in older people.⁸

Bischoff-Ferrari et al. estimated that 30 ng/mL is the optimal concentration of 25(OH)D in relation to bone mineral density, lower-extremity function, dental health, risk of falls, fractures, cancer prevention, incident hypertension and mortality, while 25(OH)D levels <20 ng/mL are associated with adverse effects.⁹ We previously found that healthy centenarians showed higher serum 25(OH)D levels than younger patients with acute myocardial infarction (27-39 years) and even with healthy adults (28-39 years). Thereby we concluded that serum 25(OH)D is associated with successful exceptional longevity.²

Buta et al. concluded that serum circulating vitamin D may partially predict frailty onset and could represent a biomarker for the identification of frailty risk and other adverse outcomes.¹ Supporting the detrimental effects of low level of vitamin D, a recent systematic review and meta-analysis concluded that compared to the highest level of 25(OH)D, the association between frailty and the lowest level of 25(OH)D was significant.¹⁰

Considering all the above mentioned, we highlight the importance of the correction of vitamin D deficiencies through an appropriate supplementation. An intake of vitamin D ≥ 40 $\mu\text{g/day}$ is needed to reach at least 50% of the aforementioned 25(OH)D optimal concentrations,⁹ and safe sunlight exposure may be highly recommended to promote healthy aging and longevity avoiding cardiometabolic disturbances and musculoskeletal alterations such as frailty.¹⁰

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References

- [1] Buta B, Choudhury PP, Xue QL, *et al.* The Association of Vitamin D Deficiency and Incident Frailty in Older Women: The Role of Cardiometabolic Diseases. *J Am Geriatr Soc.* 2016.
- [2] Pareja-Galeano H, Alis R, Sanchis-Gomar F, Lucia A, Emanuele E. Vitamin D, precocious acute myocardial infarction, and exceptional longevity. *Int J Cardiol.* 2015;**199**: 405-406.
- [3] Montero-Odasso M, Duque G. Vitamin D in the aging musculoskeletal system: an authentic strength preserving hormone. *Mol Aspects Med.* 2005;**26**: 203-219.
- [4] Bischoff-Ferrari HA, Borchers M, Gudat F, Dürmüller U, Stähelin HB, Dick W. Vitamin D receptor expression in human muscle tissue decreases with age. *J Bone Miner Res.* 2004;**19**: 265-269.
- [5] Haslam A, Johnson MA, Hausman DB, *et al.* Vitamin D status is associated with grip strength in centenarians. *J Nutr Gerontol Geriatr.* 2014;**33**: 35-46.
- [6] Wicherts IS, van Schoor NM, Boeke AJ, *et al.* Vitamin D status predicts physical performance and its decline in older persons. *J Clin Endocrinol Metab.* 2007;**92**: 2058-2065.
- [7] Visser M, Deeg DJ, Lips P, Amsterdam LAS. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass

(sarcopenia): the Longitudinal Aging Study Amsterdam. *J Clin Endocrinol Metab.* 2003;**88**: 5766-5772.

[8] Snijder MB, van Schoor NM, Pluijm SM, van Dam RM, Visser M, Lips P. Vitamin D status in relation to one-year risk of recurrent falling in older men and women. *J Clin Endocrinol Metab.* 2006;**91**: 2980-2985.

[9] Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr.* 2006;**84**: 18-28.

[10] Zhou J, Huang P, Liu P, *et al.* Association of vitamin D deficiency and frailty: A systematic review and meta-analysis. *Maturitas.* 2016;**94**: 70-76.