

Editorial

Vitamin D status: to be considered in heart failure patients

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Recent data on the world wide high prevalence of vitamin D (Vit. D) deficiency and identification of Vit. D receptor (VDR) expression in almost all human cells raised public health interest in vitamin D. Vitamin D is well known as a major regulator of calcium and bone metabolism, and its supplementation is an established treatment for patients suffering from musculoskeletal diseases^{1,2}. Furthermore it is increasingly recognized that Vit. D and its related mineral metabolism may also play a crucial role in overall and cardiovascular health¹⁻⁷. Two prospective studies published in The European Journal of Heart Failure reported that low Vit. D status is highly prevalent among heart failure patients and indicates an increased risk of mortality^{8,9}. Liu et al⁸ examined 548 heart failure patients and found that after a mean follow-up of 18 months; low and base line 25-hydroxyvitamin D [25(OH)D] plasma concentrations were associated with significantly increased risk of all cause mortality.

Expression of VDR and key enzymes of Vit. D metabolism in both the heart and the arterial vessels argue for an important role of Vit. D in the cardiovascular system^{3,4}. Molecular pathways for Vit. D induced renin suppression have already been clarified and this is in line with the negative association between 25(OH)D and plasma renin activity observed by Liu et al⁸. In the same work C-reactive protein was significantly increased in patients with a poor Vit. D status⁸. This may reflect anti-inflammatory actions of Vit. D which have been observed in previous studies including a randomized Controlled Trial (RCT) of heart failure patients^{3,4}. In addition vitamin D metabolites have been shown to exert various direct effects on cardiomyocytes including anti-hypertrophic actions, regulation of extra cellular matrix turnover, and modulation of contractility^{3,4}. This latter effect seems to be mainly driven by regulation of cardiac calcium flux^{3,4}. Deleterious consequences of Vit. D deficiency on the cardio-vascular system may also be mediated by parathyroid hormone (PTH). Vit. D deficiency contributes to, low serum calcium levels which in turn stimulates PTH secretion in order to maintain serum Calcium within physiological ranges. Schierbeck et al reported that PTH serum concentrations above the median are independent predictor of mortality⁹. This supports previous studies, documenting association of PTH with mortality, cardiovascular events and heart failure hospitalization^{3,4,12,13}. Poor Vit. D status has also been related to classic cardiovascular risk factors such as arterial hypertension, Diabetes mellitus, and chronic kidney disease (CKD)^{1-4,14}.

Interventional studies of the effects of Vit. D supplementation on myocardial structure and functions are sparse and are largely limited by small sample sizes^{3,4}. Some of the reported data show improved myocardial function and reduced myocardial hypertrophy after Vit. D treatment^{3,4}. Studies show that most of the heart failure patients have 25(OH)D levels below the normal range at least 75 nmol/L^{1,3,4,8,9}. Furthermore Vit. D therapy is relatively easy, cheap and

safe^{3,4,6}. Daily Vit. D supplementation of 1000 IU increases 25(OH)D concentrations by 25 nmol/L^{4,6}. There are no respective data for heart failure patients but a meta-analysis of randomized controlled trials that largely included frail elderly patients, showed that Vit. D supplementations significantly reduced all mortality by 7%, compared with placebo¹⁵. Considering the proposed multiple health benefits of Vit. D, we believe that it is reasonable to aim for an adequate Vit. D status. Nevertheless despite accumulating data on the association of Vit. D deficiency with heart disease and related increased mortality, we still need more results from large randomized controlled trials before introducing general recommendations for the treatment of Vit. D deficiency in the heart failure patients.

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