Vitamin D and heart: A not so sunny pathway

In their article, Şeker et al. (1) explore the relationship between serum 25-hydroxyvitamin D (25OHD) levels and left ventricular (LV) geometry and function, evaluated through echocardiography, in 151 relatively young subjects with untreated primary hypertension without organ damage. Comorbidities and concomitant therapy were exclusion criteria. Patients were overweight (BMI: 29.7 kg/m^2) and had a borderline-high lipid profile (HDL-cholesterol: 42.4 mg/dL; LDL-cholesterol: 124.0 mg/dL) but only mild hypertension (clinic systolic blood pressure (BP): 146.5 mm Hg; diastolic BP: 91.6 mm Hg). Briefly, the usual phenotype of mild hypertension in primary prevention. Of note, median 25OHD (14.3 ng/mL) was below the cut-off value for vitamin D sufficiency anyhow defined (2, 3).

In vitamin D-deficient patients (25OHD<20 ng/mL), significantly higher (+41%) left ventricular mass index (LVMI) was found, being mean LVMI above the cut-off value for left ventricular hypertrophy (LVH) (4). However, the prevalence of LVH in the two subgroups was not analyzed. Tissue Doppler (TD) examination evidenced a worse systolo-diastolic profile in 25OHD deficiency, with higher mean TD-myocardial performance index (TD-MPI). An altered mean TD-MPI (>0.40) (5) was also present in 25OHD sufficiency subgroup. Multivariate stepwise regressions confirmed the inverse relationship among 25OHD and LVMI, and between 25OHD and TD-MPI. Vitamin D-deficient patients had a better lipid profile (10% lower total and LDL cholesterol), and a positive relationship between 25OHD and LDL persisted after multivariate analysis.

This is the first evidence of a relationship between TD-MPI and 25OHD in adults. Study patients were free from systolic dysfunction (mean ejection fraction: 63.7%) thus an altered TD-MPI implied diastolic disfunction, that is a known early consequence of hypertension A large retrospective study did not confirm the association between 25OHD and TD-MPI: however, confounding factors and co-morbidities were more prevalent (6). LVM and LVH have been previously associated with lower 25OHD levels, particularly in hypertension (7). Given the influence of 25 OHD on parathormone (PTH) and the worse cardiovascular (CV) risk profile of chronic kidney disease (CKD) patients (characterized by elevated PTH values), increased PTH may influence some associations of 25OHD deficiency, including the one with LVH in non-CKD-patients too. In the Cardiovascular Health Study, an association between LVH and PTH, but not with 25OHD, has been reported (8). Furthermore, impaired diastolic LV function evaluated through MPI has been found in primary hyperparathyroidism (9). However, in the present study, PTH was not a significant covariate in multivariate models. The relationship between lipid profile and 25OHD contrasts with most literature findings (10), and given the limited numbers in the study, it should be cautiously considered.

To date, no clear benefits on CV diseases have emerged from randomized clinical trials (RCTs) on vitamin D supplementation (11, 12). Large RCTs, such as the VITAL study (13), are now ongoing; although evidences from CKD patients dampen the enthusiasm on anti-hypertrophic effects of vitamin D (14); this potential relationship is being studied (15). PTH reduction secondary to vitamin D supplementation has to be considered as a possible mediator of supplementation effects.

We are looking forward to these results, hoping to get new insight into this field. Currently, however, vitamin D supplementation for CV prevention and/or treatment is not supported with evidenced and should be avoided.

Alessio Marra

Department of Internal Medicine, IRCCS-AOU San Martino – IST, University of Genova; Genova-*Italy*

References

1. Şeker T, Gür M, Uçar H, Türkoğlu C, Baykan AO, Özaltun B, et al. Lower serum 25-hydroxyvitamin D level is associated with impaired myocardial performance and left ventricle hypertrophy in newly diagnosed hypertensive patients. Anatol J Cardiol 2015; 15: 744-50.
2. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab 2011; 96: 53-8. [CrossRef]
3. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96: 1911-30. [CrossRef]
4. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. Eur J Echocard 2006; 7: 79e108.
5. Feigenbaum H, Armstrong WF, Ryan T. Feigenbaum's echocardiography, 6th ed. Lippincott Williams & Wilkins Ed. 2005. p. 387.
6. Pandit A, Mookadam F, Boddu S, Aryal Pandit A, Tandar A, Chaliki H, et al. Vitamin D levels and left ventricular diastolic function. Open Heart 20141: e000011. doi: 10.1136/openhrt-2013-000011; [CrossRef]
7. Fallo F, Catena C, Camozzi V, Luisetto G, Cosma C, Plebani M, et al. Low serum 25-hydroxyvitamin D levels are associated with left

Address for Correspondence: Dr. Alessio Marra, Di.M.I. - Dipartimento di Medicina Interna, University of Genova
Viale Benedetto XV, 6. 16138, Genova (GE)-*Italy*
Phone: +39-0105552032 E-mail: dott.alessio.marra@gmail.com
Accepted Date: 07.05.2015

DOI:10.5152/AnatolJCardiol.2015.16052

ventricular hypertrophy in essential hypertension. Nutr Metab Cardiovasc Dis 2012; 22: 871-6. [CrossRef]
8. van Ballegooijen AJ1, Visser M, Kestenbaum B, Siscovick DS, de Boer IH, Gottdiener JS, et al. Relation of vitamin D and parathyroid hormone to cardiac biomarkers and to left ventricular mass (from the Cardiovascular Health Study). Am J Cardiol 2013; 111: 418-24. [CrossRef]
9. Baykan M, Erem C, Erdoğan T, Ersöz HO, Gedikli O, Korkmaz L, et al. Assessment of left ventricular diastolic function and the Tei index by tissue Doppler imaging in patients with primary hyperparathyroidism. Clin Endocrinol (Oxf) 2007; 66: 483-8. [CrossRef]
10. Challoumas D. Vitamin D supplementation and lipid profile: what does the best available evidence show? Atherosclerosis 2014; 235: 130-9. [CrossRef]
11. Theodoratou E1, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ 2014; 348: g2035. [CrossRef]
12. Lewis RD, Laing EM. Conflicting reports on vitamin D supplementation: evidence from randomized controlled trials. Mol Cell Endocrinol 2015; 410: 11-8. [CrossRef]
13. Manson JE, Bassuk SS, Lee IM, Cook NR, Albert MA, Gordon D, et al. The VITamin D and OmegA-3 TriaL (VITAL): rationale and design of a large randomized controlled trial of vitamin D and marine omega-3 fatty acid supplements for the primary prevention of cancer and cardiovascular disease. Contemp Clin Trials 2012; 331: 159-71. [CrossRef]
14. Wang AY, Fang F, Chan J, Wen YY, Qing S, Chan IH, et al. Effect of paricalcitol on left ventricular mass and function in CKD--the OPERA trial. J Am Soc Nephrol 2014; 25: 175-86. [CrossRef]
15. Thadani RI, Wang TJ, Picard MH. Vitamin D and Omega-3 Trial: Ancillary Study (VITAL-Echo) on the Impact of Vitamin D Supplementation on Cardiac Structure and Function. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Apr 27] Available from: https://clinicaltrials.gov/ct2/show/NCT01630213. NLM Identifier: NCT01630213.

ERRATUM

In the article by Jonathan Lipton et al., entitled "International Research Interdisciplinary School 8-12 June 2015, Bosteri, Cholpon-Ata, Issyk-Kul, Kyrgyzstan" (Anatol J Cardiol 2015; 15: 694-700) that was published in the August 2015 issue of the Anatolian Journal of Cardiology, two of the contributing authors were erroneously omitted from the author list during the production process. Upon receipt of the written request of the contributing authors, the Editorial Board reviewed the case and approved the author list to be corrected as follows.

Jonathan Lipton[1], Aliina Altymysheva[2], Ljuba Bacharova[3], Aynagul Dzhumagulova[2,4], Çiğdem Koca[5], Taalaibek Kudaiberdiev[6], Ryskul Kydyraliveva[2], Ruslan Sadabaev[6], Adam Stanczyk[7], Galen Wagner[8], Gulmira Kudaiberdieva[9], with contributions of: Berik Bolatbekov[10], Zarema Dzhakipova[6], Samat Kadyrov[11], Gulzada Imanalieva[6], Bakytbek Imanov[2], Inna Lutsenko[12], Tatiana Nekrasova[13], Aleksey Tregubov[13], Kaiyrnisa Tilemanbetova[6], Tatyana Tsivinskaya[12], Zulfiia Radzhapova[2], Iuliana Zalesskaya[2]