Vitamin D Deficiency and Myocardial Dysfunction

In a recent review, Lee et al. (1) have outlined the role of vitamin D deficiency as a cardiovascular risk factor. In this letter, we want to point out that direct effects of vitamin D on the myocardium might partially explain the link between vitamin D deficiency and adverse cardiovascular outcome. This notion is supported by observations that human cardiomyocytes express enzymes for the metabolism of vitamin D as well as a functional vitamin D receptor, which is up-regulated in myocardial hypertrophy (2,3). In animal models of heart failure, active vitamin D treatment was shown to reduce cardiac hypertrophy and to attenuate myocardial dysfunction (4). Several genes that are up-regulated in the course of cardiac hypertrophy, involving those of natriuretic peptides and renin, are down-regulated by vitamin D (4). Importantly, there exists increasing molecular and clinical evidence that a sufficient vitamin D status is required for maintenance of diastolic function of the heart (3,4). Furthermore, there are several case reports of vitamin D–deficient children with dilated cardiomyopathy that could be successfully treated with vitamin D and calcium (5). In line with this are data from a cohort of over 3,000 patients referred for coronary angiography that showed a significant association of vitamin D deficiency with reduced left ventricular function (6). In the same study cohort, vitamin D deficiency was prospectively associated with deaths caused by heart failure and with sudden cardiac deaths (6). These results fit well with observations that active vitamin D treatment in hemodialysis patients was shown to regress cardiac hypertrophy and to reduce QT interval and dispersion (4,7). In conclusion, there exists compelling evidence that vitamin D supplementation might be useful for the prevention and treatment of myocardial diseases.

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REFERENCES

1. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency: an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol 2008;52:1949–56.
2. Chen S, Glenn DJ, Ni W, et al. Expression of the vitamin D receptor is increased in the hypertrophic heart. Hypertension 2008;52:1106–12.
3. Tishkoff DX, Nibbelink KA, Holmberg KH, Dandu L, Simpson RU. Functional vitamin D receptor (VDR) in the t-tubules of cardiac myocytes: VDR knockout cardiomyocyte contractility. Endocrinology 2008;149:558–64.
4. Bodyak N, Ayus JC, Achinger S, et al. Activated vitamin D attenuates left ventricular abnormalities induced by dietary sodium in Dahl salt-sensitive animals. Proc Natl Acad Sci 2007;104:16810–5.
5. Weber KT, Simpson RU, Carbone LD. Vitamin D and calcium dyshomeostasis-associated heart failure. Heart 2008;94:540–1.
6. Pilz S, März W, Wellnitz B, et al. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. J Clin Endocrinol Metab 2008;93:3927–35.
7. Kim HW, Park CW, Shin YS, et al. Clacitriol regresses cardiac hypertrophy and QT dispersion in secondary hyperparathyroidism on hemodialysis. Nephron Clin Pract 2006;102:21–9.

Vitamin D, Outdoor Happiness, and the Meaning of Deficiency

Lee et al. (1) informatively review the emerging evidence for vitamin D as a lifestyle risk factor for cardiovascular disease. Two overlooked points should be highlighted. First, as the investigators note, the great majority of vitamin D is derived from sun exposure, rather than dietary consumption. Thus, effect estimates in studies of vitamin D levels and cardiovascular risk may be confounded, at least in part, by challenging-to-measure differences in lifestyles, behaviors, dispositions, and opportunities that lead individuals to enjoy and spend time in the sun, such as physical and social activities. Whereas vitamin D itself may still provide benefit, being outside and enjoying these activities are likely to provide additional health benefits that erroneously may be attributed as effects of vitamin D.

Second, vitamin D deficiency has become popularly (and variably) defined by suppression of counter-regulatory hormone levels or by risk of chronic disease, resulting in remarkably high proportions or even majorities of healthy populations being defined as deficient (2,3). Even if vitamin D is convincingly determined to prevent cardiovascular disease or cancer, as may be quite plausible, the departure of such metrics from more typical definitions of deficiency (4) based on prevention of overt deficiency symptoms or comparable biologic indicators must be explicitly recognized. Such novel definitions of deficiency could be arguably justified to reduce risk of chronic disease in the population because policy makers, health providers, and the public each seem to respond much more urgently to concerns over individuals having deficient versus suboptimal exposures. Based on this same logic, however, the strength, consistency, and breadth of scientific evidence would argue for highlighting more strongly the current worldwide pandemics of omega-3 deficiency, whole-grain deficiency, vegetable deficiency, and physical activity deficiency, among others. For example, long-chain omega-3 fatty acids have robust associations with lower risk of coronary heart disease death in numerous well-performed observational studies, including 16 prospective cohort studies of 326,572 generally healthy individuals from the U.S., Europe, and Asia; significant cardiovascular benefits in 4 of 5 large randomized controlled trials of dietary or supplement omega-3s in 36,431 patients with and without established heart disease; and 10-fold differences in risk of sudden cardiac death with modest differences in circulating blood levels (5). At a time when the Institute of Medicine is being urged to revise dietary requirements for vitamin D based on novel definitions of deficiency, these considerations and comparisons cannot be overlooked.