Vitamin D deficiency (VDD): the culprit of cardiometabolic diseases?

Deficiência de vitamina D (DVD): o responsável por doenças cardiometabólicas?

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It’s commonly believed that vitamin D only plays a role in bone health maintenance and calcium phosphate homeostasis regulation. This limited recognition of vitamin D’s function can be traced back to its discovery through the fight against rickets almost a century ago. Further studies revealed several other roles vitamin D plays in the human body; its importance in bone related health is merely the tip of the iceberg.

Until now, studies have highlighted that the receptor for vitamin D is quite ubiquitous, residing in almost all the major human organs, including the heart, brain, livers, kidneys, bones, urinary system, and parathyroid glands.\(^1,2\) It’s worth noting that vitamin D receptors are expressed in some seemingly unrelated tissues, for example, all kinds of immune cells, pancreatic \(\beta\) cells, neurons, as well as vascular smooth cells, epithelial cells, and cardiomyocytes in the cardiovascular system. Through those widely distributed receptors, vitamin D regulates the expression of over 200 genes directly or indirectly.\(^3\) It partially explains why vitamin D deficiency has been reported to be associated with different kinds of diseases, such as hypertension, multiple sclerosis, colon cancer, and diabetes. Due to the gene polymorphism of vitamin D receptors, there is individual variation in vitamin D reaction. Recent progress in the study of the vitamin D receptor regulating mechanism has greatly advanced the understanding of diseases related to this vitamin.

Among all research on the role of vitamin D beyond the bone system, the correlation between vitamin D deficiency (VDD) and cardiometabolic diseases has been a hotspot. Is there any causative relationship between VDD and cardiometabolic diseases? If so, which is the cause and which is the consequence? Although there is not yet a definitive answer, accumulating evidence clearly points to the close correlation between the two.

Research from different fields and perspectives provides evidence supporting the conclusion that VDD and cardiometabolic diseases are closely related. Firstly, combined results from the NHANES III cross-sectional study, the HPFS cohort study, and the NHS I research revealed a reverse correlation between serum 25(OH) D levels and blood pressure.\(^4,5\) Another detailed randomized control study further confirmed that vitamin D lowered the systolic pressure, while leaving the diastolic pressure unaffected.\(^6,7\) Secondly, the current knowledge of VDD and diabetes mellitus type 2 (DMT2) is largely derived from epidemic studies. A cross-sectional study indicated that serum 25(OH)D levels in DMT2 were dramatically reduced.\(^8\) A cohort study demonstrated that low levels of 25(OH)D could be used as a biomarker to predict the development and progress of DMT2.\(^9\) It is believed that vitamin D supplementation could regulate insulin sensitivity, and thus ameliorate insulin resistance and even benefit pancreatic \(\beta\) cell secretion.\(^10\) It has also been demonstrated that adult VDD baseline levels are reversely correlated with ten-year risk of metabolic syndrome, and independent of factors such as gender, age, weight, season of the year, and smoking.\(^9\) A cross-sectional study confirmed that VDD was linked to the development of metabolic syndrome.
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Vitamin D deficiency (VDD) is a growing concern, with evidence linking it to various cardiometabolic diseases. However, the role of VDD in these diseases is still under investigation. It is hypothesized that VDD may play a significant role in the development of cardiometabolic diseases, such as cardiovascular disease, type 2 diabetes, and metabolic syndrome, among others. 

The relationship between VDD and cardiometabolic diseases is not fully understood. This is partly due to the inconsistency of the baseline for different studies, which makes it challenging to compare results. Additionally, the length of vitamin D supplementation treatment and validity of the statistical analysis are potential factors that affect the study result. For example, it would be better to first confirm their result with larger samples pools and more careful study designs if necessary. For instance, Kelishadi et al. 15 mentioned that there are several reports on the irrelevance of VDD and cardiometabolic diseases in different age populations. A similar result was reported by the author in another article. 19 By summarizing the available animal model or human research on this issue, regardless of the method used (simple observation or systematic random control study), a great discrepancy was observed regarding the final conclusion, i.e., it is still poorly understood whether there is a causative relationship between VDD and cardiometabolic diseases. Better-designed, large randomized control trials of higher quality are necessary to further address the true role of VDD in cardiometabolic diseases. 

To summarize, although there are limitations to the study by Kelishadi et al., 15 their results are still valuable to the field and advance the VDD research by expanding the analysis to the younger obese population, which is more prone to cardiovascular diseases. It is a pioneering exploration on the benefits of vitamin D supplementation to insulin resistance and obesity-related cardiovascular risk factors in a non-adult population. Not only does it meet the current need to strengthen the study and prevention of chronic non-infectious diseases worldwide, it also opens a window to help pave the road for further study on VDD and cardiometabolic diseases.

Conflicts of interest

The author declares no conflicts of interest.

References


