

Editorial



Anti-Inflammatory Effect of Vitamin D via Suppression of YKL-40 Production: One of the Possible Mechanisms for Cardiovascular Protection

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OPEN ACCESS

Received: Jan 26, 2023

Accepted: Jan 29, 2023

Published online: Jan 30, 2023

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Funding

The author received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest

The author has no financial conflicts of interest.

► See the article “Effect of Vitamin D on YKL-40: Rat Hypercholesterolemia Model” in volume 53 on page 92.

It is well known that vitamin D is transformed into an activated form by sunlight and hepatic/renal metabolism, which increases calcium absorption and plays a crucial role in maintaining bone health. In addition to its classical role in influencing bone metabolism, the vitamin D receptor is expressed in almost every tissue in the body and thus has numerous biological effects. In recent years, the function of vitamin D in other organs has become increasingly recognized.

Many studies have demonstrated the pathophysiology of vitamin D's cardiovascular protective effects. Vitamin D lowers renin production and weakens the renin-angiotensin system's activity, leading to delays in the onset of hypertension, atherosclerosis, and heart failure. In addition, vitamin D suppresses inflammatory reactions, thrombosis, and calcification. Vitamin D also inhibits myocardial fibrosis and improves myocardial contractility. Based on these mechanisms, several epidemiological and observational studies have shown the association between low blood levels of vitamin D and high rates of cardiovascular disease (CVD).¹⁾

The inflammatory response is deeply related to CVD, such as causing the endothelial dysfunction, vascular calcification and progression of atherosclerotic plaques and rupture.²⁾³⁾ Vitamin D is known to suppress the inflammatory response through a variety of mechanisms. Vitamin D acts on immune cells to increase the production of antibacterial substances, and regulates T cells to reduce the production of cytokines, such as interleukin (IL)-1, IL-6, IL-12, IL-17, and tumor necrosis factor- α , that cause inflammatory responses.⁴⁾

YKL-40 is a proinflammatory glycoprotein secreted from endothelial cells, vascular smooth muscle cells, and various inflammatory cells.⁵⁾ YKL-40 protein expression is particularly high in atherosclerotic lesions, and is involved in endothelial cell dysfunction and atherosclerosis. Several studies have reported that elevated serum YKL-40 levels were associated with more severe coronary artery disease, and a higher YKL-40 level was an independent predictor all-cause and cardiovascular mortality.⁶⁾

In this issue of the *Korean Circulation Journal*, Kocabas⁷⁾ performed an animal experiment and provided evidence that vitamin D supplementation effectively suppressed serum YKL-40 levels in a hypercholesterolemia rat model. First, the researchers found that blood levels

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

The contents of the report are the author's own views and do not necessarily reflect the views of the *Korean Circulation Journal*.

of YKL-40 were increased in rats fed a high-cholesterol-rich diet compared to rats fed a normal diet. Second, the effect of increasing blood YKL-40 by the high-cholesterol diet was more pronounced when the vitamin D-removed feed was given. Third, when vitamin D was supplied, the increase in blood YKL-40 caused by the high-cholesterol diet was attenuated. Consistent with these findings, several human studies have also reported an association between vitamin D and YLK-40. Can et al.⁸⁾ reported that plasma YKL-40 levels were significantly lower in subjects with vitamin D deficiency compared to age and sex-matched healthy subjects. In another study, Omidian et al.⁹⁾ showed that vitamin D supplementation significantly reduced serum YKL-40 levels in type 2 diabetic patients. All these results suggest that vitamin D may be related to the decrease of YKL-40, leading to the suppression of chronic inflammation.

As mentioned above, both vitamin D and YKL-40 are substances deeply involved in the occurrence of CVDs and have recently attracted attention. Although the effect of vitamin D supplementation on cardiovascular system is less clear,¹⁰⁾ the association between low vitamin D levels and worse cardiovascular outcomes is evident.¹⁾ Therefore, vitamin D deficiency has been suggested as one of the cardiovascular risk factors. However, the mechanisms of the association between vitamin D levels and CVD are still largely unknown. Vitamin D deficiency is frequently identified in various chronic inflammatory diseases, and many studies have shown that vitamin D has anti-inflammatory activity. The anti-inflammatory action of vitamin D is expected to contribute at least to some extent to its cardiovascular protective effect. In this regard, recent animal study has suggested that YKL-40, an inflammatory glycoprotein, is an important target of vitamin D.⁷⁾ Further studies are needed to determine whether vitamin D supplementation also lowers YKL-40 concentrations in human blood and whether the cardiovascular prognosis is affected by the YKL-40 concentrations. Recently, disappointing results have been published that vitamin D supplementation does not improve cardiovascular outcomes in humans.¹⁰⁾ It is also very meaningful and interesting to re-analyze the effect of vitamin D on long-term cardiovascular prognosis based on the individuals' inflammatory status including YKL-40 concentration. Accumulating results from studies in humans suggest that drugs having inhibitory action for YKL-40 production are good treatment options for cardiovascular protection.

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