

What Are the Effects of Vitamins D3 and K2 on Coronary Artery Disease?

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STORY AT-A-GLANCE

- › Vitamin K2 and vitamin D may reduce the development of coronary artery calcification (CAC), a buildup of calcium in your coronary arteries that's a strong indicator of coronary artery disease
- › Among high-risk patients, those supplementing with vitamins K and D had fewer safety events, including heart attack, procedures and all-cause mortality, compared to those taking a placebo
- › In people taking statin drugs, the combination of vitamins K and D significantly slowed the progression of calcification
- › Vitamin D3 and vitamin K2 must be properly balanced with magnesium and calcium for optimal heart and overall health
- › Foods rich in vitamin K2 include certain fermented foods such as natto or vegetables fermented using a starter culture of vitamin K2-producing bacteria, and cheeses such as Brie, Munster and Gouda

Vitamin K2 and vitamin D may be beneficial for coronary artery calcification (CAC), a buildup of calcium in your coronary arteries that's a strong indicator of coronary artery disease (CAD) and heart attacks.^{1,2}

Vitamin K2 serves the role of regulating calcium through activation of the anticalcific protein, matrix Gla protein. Supplementing with vitamin K2 has been strongly linked to

improving heart disease outcomes by modulating "systemic calcification and arterial stiffness."³ Low vitamin D levels, meanwhile, are associated with an increased risk of heart disease, stroke and all-cause mortality.⁴

Vitamin K2 functions as an important cofactor for calcium and vitamin D. Calcium is important for strengthening bones and overall skeletal health, but it only works when it gets to the right place. Vitamin K2 prevents calcium from being deposited along the walls of your blood vessels and directs it into the bone instead.⁵

Research published in the Journal of the American College of Cardiology (JACC): Advances⁶ revealed that, particularly in high-risk patients, vitamin K2 and vitamin D may reduce the development of CAC,⁷ thereby potentially reducing the risk of heart attack and related mortality.

Vitamins K2 and D Slow Progression of Coronary Artery Calcification

The finding that vitamins K2 and D are beneficial for CAC was revealed due to a subgroup analysis of the Aortic Valve Decalcification Trial.⁸ Known as AVADEC, the study involved 389 patients with a mean age of 71 years who received either vitamins K2 and D or placebo for 24 months.

While the AVADEC study did not find any difference between supplementation and placebo on the progression of aortic valve calcification, a subgroup analysis involving participants with a high baseline CAC score (above 400 AU) and those taking statin drugs had a different outcome.

Among those with a high CAC score, those supplementing with vitamins K and D had fewer safety events, including heart attack, procedures and all-cause mortality, compared to those taking a placebo. In people taking statin drugs, the combination of vitamins K and D significantly slowed the progression of calcification. According to the study:⁹

"No randomized controlled trials have managed to show a reduction in CAC progression to date. It has previously been described that baseline CAC score predicts progression by an annual increase of 20% to 25%.

As expected, the high-risk participants with CAC scores over 400 AU had the highest absolute increase in CAC score, but they also seemed to have the greatest effect of vitamin K2 supplementation. It is possible that the effect is simply most evident in the participants with the most notable progression and that the follow-up period was too short to detect a difference in the participants with lower CAC scores."

The study involved the longer-chained vitamin K2 known as menaquinone-7 (MK-7), which is found in fermented foods. Previous research found that taking 180 micrograms (mcg) per day of vitamin K2 in the MK-7 form for three years improved arterial stiffness in postmenopausal women, especially those who had a high degree of arterial stiffness.¹⁰

Lead AVADEC study author Axel Diederichsen from Odense University Hospital in Denmark said a follow-up study will look into the effects of vitamins K2 and D3 in patients with severe coronary artery calcification, noting, "We were interested in exploring this further, particularly the effects of vitamin K2 deficiency on coronary artery calcifications, which we know is strongly associated with higher risk of heart attack and death."¹¹

Vitamin K2 Is a Powerful Ally for Your Heart Health

Vitamin K's role in heart health is well-noted, particularly for vitamin K2. One of the reasons why vitamin K2 is so important for heart health has to do with a complex biochemistry involving the enzymes matrix Gla protein (MGP, found in your vascular system¹²), and osteocalcin, found in your bone.

"Gla" stands for glutamic acid, which binds to calcium in the cells of your arterial wall and removes it from the lining of your blood vessels. Once removed from your blood

vessel lining, vitamin K2 facilitates the integration of that calcium into your bone matrix by handing it over to osteocalcin, which in turn helps "cement" the calcium in place inside your bone.

Glutamic acid in matrix Gla protein (MGP) plays a crucial role in cardiovascular health, particularly in the regulation of vascular calcification. MGP is a powerful inhibitor of vascular calcification, which is the process where calcium builds up in the arterial walls and forms plaque. This calcification can lead to atherosclerosis, a condition where the arteries become hardened and narrowed, increasing the risk of heart attack and stroke.

MGP contains several glutamic acid residues that need to be carboxylated (a chemical reaction that adds a carboxyl group) to become active. This carboxylation process is where vitamin K2 comes into play. Vitamin K2 acts as a cofactor for the enzyme gamma-glutamyl carboxylase, which facilitates the conversion of glutamic acid residues in MGP to gamma-carboxyglutamate (Gla) residues. This carboxylation process is essential for activating MGP.

Once activated, MGP can bind to calcium ions, preventing them from depositing in the blood vessels. In essence, MGP helps to remove calcium from areas where it shouldn't be (like in arterial plaques) and put the calcium back into circulation where it belongs.

Simultaneously, vitamin K2 also plays a role in promoting the integration of calcium into bones. It activates another protein called osteocalcin, which helps to bind calcium and incorporate it into the bone matrix. This dual action of vitamin K2 – activating MGP to remove calcium from arteries and stimulating osteocalcin to deposit calcium into bones – is crucial for maintaining cardiovascular health as well as healthy bone density.

Glutamic acid in MGP, with the help of vitamin K2, acts to prevent vascular calcification by inhibiting the formation of calcium deposits in the arteries while also facilitating the proper utilization of calcium in strengthening bones. This highlights the importance of adequate vitamin K2 intake for cardiovascular and bone health.

A Dual Approach to Preventing Vascular Calcification and Strengthening Bones

Vitamin K2 activates these two proteins, so without it, this transfer process of calcium from your arteries to your bone cannot occur, which raises your risk of arterial calcification. In fact, in one study, those who had the highest amount of vitamin K2 were 52% less likely to experience severe calcification in their arteries and 57% less likely to die from heart disease over a seven- to 10-year period.¹³

In a subsequent trial called the Prospect Study, 16,000 people were followed for 10 years. It found that each additional 10 mcg of vitamin K2 in the diet resulted in 9% fewer cardiac events.¹⁴ Researchers from Edith Cowan University similarly found that those with a diet rich in vitamin K had a 34% reduced risk of peripheral artery disease (PAD) or PAD-related hospitalization.¹⁵

When the data were separated for vitamin K2, they found those with the highest dietary intake had a 14% lower risk of hospitalization for ASCVD-related illnesses than those eating a diet with the lowest amount of vitamin K2. A 2023 review of clinical studies on the role of vitamin K in cardiovascular diseases further revealed that consumption of vitamin K-rich foods as well as the use of vitamin K supplements may help maintain vascular health, noting:¹⁶

"Optimized intake of vitamin K has been shown to play a crucial role in preventing vascular calcification by regulating the carboxylation of specific VKDPs [vitamin-K-dependent proteins] including MGP and osteocalcin, which are essential for physiological calcium metabolism, with beneficial effects on vascular health and bone mineralization.

MGP appears to be a potent vascular calcification inhibitor produced by vascular smooth muscle cells, chondrocytes, and other cells. In its carboxylated state, MGP binds calcium ions with high affinity and prevents their aberrant deposition, e.g., in the arterial wall."

Vitamin D's Role in Heart Health

Vitamin D, a steroid hormone, is another important player in heart health. One of its benefits lies in significantly reducing oxidative stress in your vascular system,¹⁷ which can prevent the development of heart disease.

A Norwegian study¹⁸ published in the Journal of Clinical Endocrinology and Metabolism also found "a normal intake of vitamin D" significantly reduces your risk of death if you have cardiovascular disease.¹⁹

About 4,000 patients diagnosed with stable angina pectoris – chest pain caused by coronary heart disease – were followed for 12 years. Overall, those with vitamin D blood levels between 16.8 and 40 ng/mL (42 to 100 nmol/L) had the lowest mortality risk. As for the mechanisms behind vitamin D's heart benefits, the researchers explained:²⁰

"Vitamin D activity may affect endothelial function, fibrosis, and inflammation, which are processes relevant to stenosis progression and atheromatous plaque stability ... Vitamin D status is relevant to the regulation of many genes, but the main function is to maintain systemic calcium concentrations.

Genetically elevated serum calcium levels were recently shown to increase the risk for CAD and myocardial infarction, and vitamin D status could play a modifying role by lowering the threshold for safe intake of dietary calcium."

Other research has also highlighted the importance of vitamin D for the prevention and treatment of heart disease, showing it plays a vital role in protecting and repairing damage to your endothelium.²¹ Vitamin D3 helps trigger production of nitric oxide, a molecule known to play an important signaling role in controlling blood flow and preventing blood clot formation in your blood vessels.

The best way to optimize your vitamin D level is through sensible sun exposure. Unfortunately, this can be difficult for many, especially during the winter season and/or if you live in northern regions. If you cannot obtain sufficient amounts of vitamin D through sun exposure, taking a supplement is recommended.

Remember that the only way to determine how much sun exposure is enough and/or how much vitamin D3 you need to take is to measure your vitamin D level, ideally twice a year. Data from GrassrootsHealth's D*Action studies suggest the optimal level for health and disease prevention is between 60 ng/mL and 80 ng/mL, with higher levels recommended for certain conditions like cancer and autoimmune disease.

The cutoff for sufficiency appears to be around 40 ng/mL. In Europe, the measurements you're looking for are 150 to 200 nmol/L and 100 nmol/L respectively.

Vitamins K and D Work Together With Magnesium and Calcium

It's important to understand that magnesium, calcium, vitamin D3 and vitamin K2 must be properly balanced for optimal heart and overall health. Your best and safest bet is to simply eat more calcium-, magnesium- and vitamin K2-rich foods, along with sensible sun exposure.

For instance, excessive vitamin D in combination with lack of vitamin K2 may cause overabsorption of calcium, which in turn may result in calcium deposits in your heart and kidneys. Vascular calcification is also a side effect of low magnesium, so when taking vitamin D3, you need both [vitamin K2 and magnesium](#) to make sure everything is working properly.

Magnesium and vitamin K2 also complement each other, as magnesium helps lower blood pressure,²² which is an important component of heart disease. Magnesium deficiency also decreases the metabolism and synthesis of vitamin D,²³ while researchers wrote in *The Journal of Clinical and Aesthetic Dermatology*, "Research has indicated that magnesium and vitamin K2 enhance absorption of vitamin D and decrease the risk of coronary artery calcium deposition."²⁴

Are You Getting Enough Vitamin K2?

It can be difficult to tell if you're getting enough vitamin K, as there's no easy way to screen or test for vitamin K2 sufficiency. Vitamin K2 cannot, at present, be measured

directly, so it's measured through an indirect assessment of undercarboxylated osteocalcin. This test is still not commercially available, however.

As a general rule, if you have osteoporosis, heart disease or diabetes, you're likely deficient in vitamin K2. Further, it's believed that the vast majority of people are in fact deficient and would benefit from more K2, which you can achieve by eating more of the following foods:

- Certain fermented foods such as natto or vegetables fermented using a starter culture of vitamin K2-producing bacteria
- Certain cheeses such as Brie, Munster and Gouda, which are particularly high in K2
- Grass fed organic animal products such as egg yolks, liver, butter and dairy

If you're taking statin drugs, which are known to deplete vitamin K2,²⁵ you could also be deficient. If you're interested in supplementation, as a general guideline, I recommend getting around 150 mcg of vitamin K2 per day.

Others recommend slightly higher amounts; upward of 180 to 200 mcg. Fortunately, you don't need to worry about overdosing on K2, as it appears to be completely nontoxic. If you opt for a vitamin K2 supplement, make sure it's MK-7. The exception is if you're on vitamin K antagonists, i.e., drugs that reduce blood clotting by reducing the action of vitamin K. If so, you should avoid MK-7 supplements.

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