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VITAMIN D — THE IMPACT ON DEVELOPMENT AND TREATMENT  
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## VITAMIN D — THE IMPACT ON DEVELOPMENT AND TREATMENT OF ATRIAL FIBRILLATION

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**ABSTRACT**

**Introduction:** Atrial fibrillation is the most common cardiac arrhythmia affecting approximately 700 thousand Polish people. In Poland, insufficient vitamin D levels are highly prevalent and concern around 90% of the population. Except the established, modifiable risk factors of AF, new risk factors such as vitamin D deficiency are being described. Some potential mechanisms involving vitamin D in atrial fibrillation pathogenesis include: cardiac remodelling via the vitamin D receptor, modulation of renin-angiotensin-aldosterone system, influence on parathyroid hormone concentration, changes in action potential duration and left atrium contractility, and activation of proinflammatory pathway by low vitamin D levels.

**Aim of the study:** This review aims to analyze the potential relationship between vitamin D concentration and the risk of developing atrial fibrillation based on the current state of knowledge (as of 2025). Moreover, we tried to examine how vitamin D concentration could influence the efficacy of atrial fibrillation treatment methods such as cardioversion or ablation.

**Material and Methods:** This review is based on literature from 2011 to 2024, searched in PubMed, Google Scholar, mp.pl and ClinicalTrials.gov that was describing the results of vitamin D deficiency on atrial fibrillation development and the treatment outcomes.

**Conclusions:** Serum vitamin D concentration may have an impact on both atrial fibrillation onset and its treatment. It is possible that there are several groups of patients among whom the sufficient vitamin D level would be particularly beneficial. Further studies, especially those focusing on vitamin D supplementation, are needed to clarify the role of vitamin D in atrial fibrillation pathogenesis and treatment.

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**KEYWORDS**

Cholecalciferol, Vitamin D Deficiency, Atrial Fibrillation, Cardioversion, Catheter Ablation

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**Introduction**

Atrial fibrillation is the most common type of cardiac arrhythmia affecting around 700 thousand Polish people. Its prevalence rises with age - up to 23% of the population above 65 years old can suffer from this condition. Moreover, there is a group of patients with an undiagnosed disease, which brings a particular risk of AF complications (Medycyna Praktyczna, 2022).

The most serious complication of atrial fibrillation is stroke, with the risk being 4- to 5-fold higher than in the general population (Kornej et al., 2020). The most common mechanisms that link these two diseases are blood clot formation due to contractile dysfunction, especially in the left atrium, and stasis (Kamel et al., 2016). Even so, the most frequent AF complication is heart failure, probably resulting from structural and electrical remodeling that causes left atrium vulnerability. Other atrial fibrillation consequences include myocardial infarction or venous thromboembolism (Kornej et al., 2020).

One of the atrial fibrillation prevention strategies is risk factor modification. The established, modifiable factors of AF include body mass index (BMI), hypertension, diabetes mellitus, obstructive sleep apnea, or smoking (Kornej et al., 2020). However, new risk factors are being described: genetics, ethnic differences, early-life antecedents, lifestyle, and subclinical factors are taken into consideration (Rienstra et al., 2012). Another group of possible factors that could help predict the risk of atrial fibrillation are biomarkers, including vitamin D.

Vitamin D is a fat-soluble vitamin. It occurs naturally in food and is obtained through sun exposure. Its two main forms are ergocalciferol (D2) and cholecalciferol (D3) (Office of Dietary Supplements, 2025; Janoušek et al., 2022). Vitamin D plays important role in calcium and phosphate metabolism, bone growth, and bone remodeling by osteoblasts and osteoclasts. The other roles include modulation of cell growth, neuromuscular and immune function, and glucose metabolism (Office of Dietary Supplements, 2025).

Vitamin D deficiency is a frequent problem in the European population. Limited sun exposure, especially from October to March, and insufficient vitamin intake with food contribute to this issue. Low 25(OH)D levels are widespread among patients with lactose intolerance or those who follow a vegetarian or vegan diet. Vitamin D absorption takes place in the bowels with the aid of bile acids, therefore diseases such as obstructive liver disease, food allergies, celiac disease, cholestasis, biliary obstructions, inflammatory bowel syndrome, and cystic fibrosis lead to deficiency. Other less common reasons include renal disorders, genetic mutations of involved enzymes, tumors, pregnancy, and drug interactions (Office of Dietary Supplements, 2025; Janoušek et al., 2022).

In children, vitamin D deficiency most often manifests itself as rickets, while in adults as osteomalacia or osteoporosis, which is connected to decreased absorption of dietary calcium and phosphate as well as bone demineralization. Other symptoms include muscle weakness, fatigue, increased susceptibility to infectious diseases, and slower healing of epidermal wounds. Some studies also indicate association with cancer, depression, multiple sclerosis, type 2 diabetes, rheumatoid arthritis and cardiovascular disease (Office of Dietary Supplements, 2025; Janoušek et al., 2022).

The vitamin D status is usually based on plasma calcifediol concentration. The 25(OH)D level above 32 ng/mL is considered sufficient (Janoušek et al., 2022). Despite the growing awareness of the results of deficiency and the promotion of products rich in this vitamin, in Poland its concentration < 30 ng/ml is common and affects up to 90% of the population, (Misirowski et al., 2024).

The aim of this article is to analyze the potential correlation between vitamin D and the risk of atrial fibrillation and the influence of vitamin D concentration on the outcomes of AF treatment with methods such as cardioversion and ablation.

### **Review Methods**

This review used literature from 2011–2024, sourced from PubMed, Google Scholar, mp.pl and ClinicalTrials.gov. While investigating the articles, search phrases included: “vitamin D deficiency”, “atrial fibrillation mechanisms”, “vitamin D deficiency in atrial fibrillation”, “vitamin D supplementation”, “vitamin D and cardioversion”, “vitamin D and ablation”. After reviewing the abstracts of the retrieved papers, full-text articles were assessed using the inclusion and exclusion criteria. Inclusion criteria incorporated studies published in English or Polish, not earlier than 2010, that described the results of vitamin D deficiency on the development of atrial fibrillation and treatment outcomes. The authors excluded papers in languages other than the ones mentioned and those, which were not relevantly connected to the topic of this article. Finally, a total of 37 articles were included.

### **Results and discussion**

#### **Vitamin D in atrial fibrillation - the mechanisms**

As vitamin D was claimed to play a significant role in cardiovascular disease pathogenesis, some hypotheses concerning the potential mechanisms were made.

Vitamin D modulates the function of different organs, including the heart, via nuclear vitamin D receptor (VDR) activation. These receptors are expressed in cardiomyocytes and cardiac fibroblasts that play a role in cardiac remodeling. Studies have shown that calcitriol analog can restore the levels of myocardial VDRs, which prolonged action potentials and provided protection against myocardial remodeling associated with increased arrhythmogenic risk. In addition, vitamin D may demonstrate anticoagulant effects through VDRs expressed on monocytes and endothelial cells which are responsible for the increase of thrombomodulin expression and reduce tissue factor expression. The tissue factor is involved in the factor X and thrombin activation that state the targets of active substances of anticoagulant medications (Barsan et al., 2022).

Another mechanism is the modification of the renin-angiotensin-aldosterone system (RAAS) activity. It was reported that vitamin D deficiency caused an increased aldosterone concentration, leading to hypokalemia and consequently increased susceptibility to developing ventricular arrhythmias (Barsan et al., 2022). Furthermore, angiotensin II receptors are involved in atrial pressure conditions and remodeling, which means that RAAS activation may induce the development of AF via induction of cardiomyocyte hypertrophy and interstitial cardiac fibrosis (Ozcan et al., 2015).

Vitamin D deficiency also affects the activation of pro-inflammatory pathways. Elevated C-reactive protein (CRP) levels - a marker of systemic inflammation - have been linked to the higher risk of atrial fibrillation. As mentioned above, vitamin D influences RAAS activation, which also regulates inflammatory responses (Cosentino et al., 2021).

Low vitamin D concentration is also associated with elevated parathyroid hormone (PTH) levels, which are responsible for calcium-phosphorus balance. It was established that disturbed calcium-phosphorus metabolism led to a higher risk of atrial fibrillation (Barsan et al., 2022). Moreover, PTH may have an impact on AF development through release of cytokines mediated by PTH from vascular smooth muscle cells and lymphocytes. The inflammation has been claimed as significant in both electrical and structural remodeling. Furthermore, high PTH levels can contribute to valvular and myocardial calcification, potentially causing valve dysfunction and left atrium enlargement, which increases the AF risk (Trevisan et al., 2019).

Finally, the study by Hanafy et al. reported that vitamin D plays a role in action potential duration and increases left atrium contractility via action potential duration (APD) modulation through calcium release (Hanafy et al., 2014).

### **The effect of vitamin D on the risk of atrial fibrillation**

Studies investigating the impact of serum vitamin D concentration on atrial fibrillation remain inconsistent.

Zhang et al. assessed the association between serum vitamin D concentration and atrial fibrillation by means of Mendelian randomization. This method uses genetic variants as instrumental variables to make causal inferences. The study used single-nucleotide polymorphisms identified from significant genome-wide association. No causal connection between circulating 25(OH)D level and risk of AF was found (Zhang et al., 2022). Similar conclusions were drawn in recent studies. Vitezova et al. conducted a prospective cohort study involving 3,395 elderly participants (median age: 71 years) without AF at baseline. The patients were scanned for arrhythmia within the 12 years of follow-up. The hypothesis that vitamin D status is associated with AF was not supported (Vitezova et al., 2015). Another cohort study by Rienstra et al. evaluated the risk of atrial fibrillation among the group of 2,930 participants in the mean age of 65. It was found that vitamin D status is not a critical contributor to AF in the general population (Rienstra et al., 2011).

A meta-analysis by Alonso et al. did not support a clinically relevant relationship between circulating 25(OH)D and AF risk; however, lower concentrations of 25(OH)D might be linked to increased risk of AF in younger participants (Alonso et al., 2016). Similarly, Huang et al. conducted a meta-analysis of 6 randomized controlled trials, and it was concluded that vitamin D level is unlikely to play a significant role in the development of new-onset AF. Although vitamin D was associated with a significant decrease of left ventricle ejection fraction of patients with new-onset atrial fibrillation, no clear relationship between them was described (Huang et al., 2018).

On the other hand, some studies have found a significant correlation. Zhang et al. reported a possible association between low levels of vitamin D and increased risk of AF (Zhang et al., 2016). Another meta-analysis by Liu et al. drew similar conclusions. It was reported that vitamin D deficiency ( $<20$  ng/ml) or insufficiency ( $<30$  ng/ml) increased the risk of AF by 23% or 14%, respectively. Moreover, the age-based analysis showed that low 25(OH)D levels increased the risk of AF in patients aged  $\geq 65$  years, but not the younger group ( $<65$  years) (Liu et al., 2019).

Other studies have examined a possible relationship between vitamin D concentration and atrial fibrillation among particular groups of patients. Demir et al. compared vitamin D levels among patients with nonvalvular AF, valvular AF, and with sinus rhythm (the control group). Each group of patients between 50 and 70 years old consisted of around 100 participants without any other cardiovascular disease. The group of nonvalvular AF patients had lower vitamin D levels, whereas, the valvular AF and the control group showed no significant difference, which indicates a probable role of vitamin D deficiency in nonvalvular AF (Demir et al., 2014). Chen et al. also focused on patients with nonvalvular AF. The group of atrial fibrillation patients numbered ca. 160 patients without other cardiovascular diseases. The serum 25(OH)D level showed a negative correlation with left atrial diameter, hsCRP level, and pulmonary artery systolic pressure. Moreover, atrial fibrillation was more common in the patients with vitamin D levels at  $<20$  ng/mL than among those with a vitamin D concentrations at  $>30$  ng/mL (Chen et al., 2014).

Tariq et al. focused on the correlation between serum vitamin D concentration and the presence of paroxysmal atrial fibrillation among young adults in the mean age of 28. It was found that patients with vitamin D level deficiency ( $<20$  ng/ml) or insufficiency (20-29 ng/ml) were more likely to develop AF (Tariq et al., 2025). Another study by Chan et al. reported that vitamin D played a protective role against both atrial fibrillation and stroke, especially the young-onset  $<50$  years old. The predominant effect was observed in men (Chan et al., 2024).

Belen et al. examined 180 patients with chronic heart failure who were divided into groups based on sinus rhythm or chronic AF. The study found a strong association of AF with low plasma vitamin D levels. Moreover, the parathormone level and left atrium-to-body surface area ratio were significantly higher among patients with atrial fibrillation. It is worth mentioning that the results were independent of BMI and heart failure stage (Belen et al., 2016).

Ozcan et al. investigated whether vitamin D deficiency is a risk factor for the development of AF in hypertensive patients. The study group consisted of 227 hypertensive patients, of whom 137 had new-onset AF. In this group of patients, vitamin D deficiency was found to be strongly associated with new-onset atrial fibrillation (Ozcan et al., 2015).

### **Vitamin D supplementation—effects on atrial fibrillation**

The abovementioned studies describe the relationship between vitamin D level concentration and atrial fibrillation risk. Another group of researchers has explored the potential benefits of vitamin D supplementation in atrial fibrillation prevention.

Virtanen et al. conducted a randomized, double-blind, placebo-controlled supplementation trial to investigate the effects of vitamin D intake on the incidence of cardiovascular disease. The study group of 2,495 included male participants aged  $\geq 60$  years and postmenopausal female participants aged  $\geq 65$  years without a history of cardiovascular disease. The patients received either 1600 IU/d of vitamin D<sub>3</sub>, 3200 IU/d of vitamin D<sub>3</sub>, or placebo, and were followed-up for 5 years. Compared to the placebo group -in patients who supplemented 1600 IU/d vitamin D<sub>3</sub> AF risk was 27% lower - and in patients who supplemented 3200 IU/d vitamin D<sub>3</sub> - even 32% lower. It is worth mentioning that the risk reduction was more significant after excluding the participants with AF diagnosis during the first 2 years of follow-up. The results show that supplementation of high-dose vitamin D may be beneficial for protection against AF in the examined elderly population (Virtanen et al., 2023).

Acharya et al. described how vitamin D supplementation affects the risk of atrial fibrillation in patients with vitamin D deficiency (25(OH)D level  $< 20$  ng/ml). Thirty-nine thousand eight hundred forty-five individuals without a previous history of AF used vitamin D for  $\geq 6$  months. After supplementation, the risk of AF was lower in the group with vitamin D level  $> 20$  ng/ml. Furthermore, in men  $> 65$  years of age with hypertension or diabetes, this risk decreased even more when the 25(OH)D level was  $> 30$  ng/ml (Acharya et al., 2022).

However, different results were reported by Albert et al. In their study, 25,119 participants aged  $> 50$  without prior cardiovascular disease and AF were given 2000 IU/d of vitamin D or placebo for a median 5.3 years. The number of AF incidents numbered 469 (3.7%) vs. 431 (3.4%) in vitamin D supplemented vs. placebo groups, respectively. It was reported that vitamin D may not play a role in the primary protection against atrial fibrillation (Albert et al., 2021).

Moreover, Boursiquot et al. examined the effects of vitamin D and calcium supplementation on AF risk. The study group included 16,801 postmenopausal women aged 50–79, who were given either 1000 mg/d of elemental calcium and 400 IU/d of vitamin D or a placebo. No significant impact of vitamin D and calcium supplementation on atrial fibrillation risk was found (Boursiquot et al., 2019).

### **The influence on cardioversion and ablation effects**

Vitamin D may influence not only the development of atrial fibrillation but also the outcomes of treatment procedures. The two main strategies for AF management are ventricular rate control and sinus rhythm restoration. The first strategy involves medicines, mainly beta-blockers or calcium channel blockers. The second includes electrical and drug cardioversion with antiarrhythmic medication, as well as more invasive procedures like ablation. Unless the patient is hemodynamically unstable, the treatment method is chosen individually according to the patient's needs and comorbid disorders (Gajewski et al., 2020).

Some studies have examined the role of vitamin D in the success of cardioversion in AF patients. Effat Fakhry and Tawfik Ibrahim described the impact of vitamin D deficiency on cardioversion success in the group of 200 patients with persistent atrial fibrillation qualified to either pharmacological or electrical cardioversion. Based on the effectiveness of cardioversion, participants were divided into two groups. Failure of cardioversion was defined as either detection of AF rhythm in a 12-lead electrocardiogram (ECG) or in ECG Holter monitoring after cardioversion or within the 6-month follow-up. A significant difference in vitamin D concentration was noted between these two groups. It was concluded that cardioversion failure correlated with

vitamin D deficiency, while sufficient and insufficient vitamin D levels were associated with successful cardioversion (Effat Fakhry et al., 2022).

Labib et al. took a similar aim. Their study included 50 patients aged 18–60 who underwent cardioversion, the protocol of which included the administration of 300 mg of amiodarone over 30–60 minutes, then a follow-up dose of 900 mg over 24 hours and a possible electrical cardioversion in case of pharmacological cardioversion failure. Success was claimed if the patient was discharged with sinus rhythm. In the group with successful cardioversion, 57.5% of participants had sufficient vitamin D levels. In comparison, 80% of those in the failure group had deficient vitamin D levels, and 10% had insufficient vitamin D levels. The study found that vitamin D deficiency had a significant impact on cardioversion success. Notably, none of the studies found a statistically significant difference between the two groups in terms of age, gender, BMI and smoking (Labib et al., 2023).

The relationship between vitamin D and atrial fibrillation was also investigated in another study by Askarinejad et al. Similarly to the research as mentioned earlier, it was confirmed that a sufficient level of vitamin D correlated with a better response to electrical cardioversion: the percentage of successful cardioversion was 16.6%, 50%, and 81.8% in case of with vitamin D deficiency, insufficiency, and sufficiency, respectively. Moreover, it was reported that vitamin D deficiency was more common in patients with three-vessel disease as well as in those who needed anticoagulant therapy. Additionally, vitamin D deficiency was associated with a higher prevalence of fatigue and syncope, but not other symptoms like palpitation, dyspnea, dizziness, anxiety, and chest pain. Mortality was also higher in vitamin D-deficient patients with AF (Askarinejad et al., 2024).

While the studies mentioned above focused on the influence of vitamin D level on cardioversion success, Yaman et al. investigated whether vitamin D levels could predict the recurrence of AF after cardioversion. Fifty-one patients qualified for cardioversion were included in the study. Cardioversion was conducted with the amiodarone in the dose of 300 mg intravenous bolus and then 1000 mg continuous intravenous (IV) infusion for up to 24 hours. In case of lack of response, electrical cardioversion was performed. The recurrence of atrial fibrillation was defined as AF detected in 12-lead ECG recorded after cardioversion or in ECG Holter recording at the 6-month follow-up. While the mean vitamin D level was 21.4 ng/ml, the concentration was lower in the AF recurrence group than in the non-recurrence group, and was 18 ng/ml and 26.3 ng/ml, respectively. Therefore, it was concluded that vitamin D level may play a role as a predictor of atrial fibrillation recurrence following cardioversion (Yaman et al., 2020).

Even though some studies noted that vitamin D may serve as a potential factor of cardioversion efficacy, Hussain et al. did not find similar results. In the retrospective study, 100 patients with AF were included, 9% of whom had vitamin D deficiency. Cardioversion failure was defined as the persistence of AF at the time of hospital discharge after cardioversion procedure. At the same time the recurrence was described as the presence of atrial fibrillation in 12-lead ECG during the follow-up period of 6 months up to a year. No significant difference in vitamin D deficiency prevalence was observed between patients who had successful cardioversion and those with an unsuccessful one. Thus, the hypothesis that vitamin D concentration influences cardioversion outcomes was not supported (Hussain et al., 2023). In addition to cardioversion, vitamin D may also influence the success of AF ablation. Cerit et al. aimed to evaluate the value of vitamin D as a factor in preventing recurrence of atrial fibrillation after balloon cryoablation in 63 patients with drug-refractory AF. Significant differences in vitamin D concentration were observed between participants who experienced AF recurrence and those who did not, with a lower level in the recurrence group. It was concluded that vitamin D level may independently forecast the likelihood of AF returning after ablation (Cerit et al., 2018).

In addition, Canpolat et al. investigated the effect of vitamin D levels on left atrial fibrosis. Participants were 48 patients with paroxysmal atrial fibrillation scheduled for catheter balloon cryoablation who underwent delayed-enhancement magnetic resonance imaging (DE-MRI) to assess the degree of left atrial fibrosis, and 48 healthy individuals. Recurrence of AF was defined as detection of AF that lasted >30s during ECG monitoring >3 months following AF ablation. The results showed that in the atrial fibrillation group the 25(OH)D level was lower than in the healthy participants ( $25.8 \pm 7.6$  ng/ml vs.  $31.0 \pm 9.5$  ng/ml). Moreover, serum vitamin D concentrations were associated with moderate to severe left atrial fibrosis which was independent from other measures. The extent of left atrium fibrosis was claimed to be independently associated with late AF recurrence during the follow-up. Lower vitamin D levels have been found to be strongly associated with recurrence of atrial fibrillation after cryoablation, likely due to its effect on left atrial fibrosis (Canpolat et al., 2017).

## Conclusions

Determining the role of vitamin D in atrial fibrillation is crucial. If proven, assessing vitamin D levels and providing appropriate supplementation may improve outcomes in patients with AF, enhance treatment effectiveness, and potentially reduce the need for more invasive therapies. Finally, we conclude that serum vitamin D concentration may have an impact on both AF development and its treatment outcomes. Further research, particularly those focusing on vitamin D supplementation, is needed to clarify its role in atrial fibrillation pathogenesis and treatment.

## Author's Contributions:

**Conceptualization:** Julianna Zielska;

**Methodology:** Julianna Zielska;

**Data curation:** Julianna Zielska;

**Writing – original draft preparation:** Julianna Zielska;

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All authors have read and agreed with the published version of the manuscript.

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