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Daily sunshine hours as determinant of 25-hydroxyvitamin D concentration among diabetic cardiac patients who experienced myocardial infarction hospitalized due to acute coronary syndrome: a cross-sectional study

Dzienne nasłonecznie jako determinant stężenia 25-hydroksywitaminy D u pacjentów z cukrzycą i chorobami serca po hospitalizacji z powodu zawału serca z powodu ostrego zespołu wieńcowego — badanie przekrojowe

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Abstract

Introduction. Vitamin D deficiency is a worldwide problem with a variety of health consequences. Vitamin D may reduce the risk of heart failure, however, evidence of the impact of vitamin D treatment on maintenance of cardiovascular health (i.e., preventing cardiovascular diseases) is conflicting due to lack of support from clinical trials. The reason for the failure of clinical trials to confirm an effect of vitamin D supplementation could be at least threefold: 1) too little vitamin D given to the participants or 2) lack of inclusion of only severely vitamin D-deficient populations or 3) study duration. The aim of this study was to characterize a group of cardiac patients who presented the lowest concentrations of 25-hydroxyvitamin D [25(OH)D].

Material and methods. Results of 92 diabetic cardiac patients aged between 41 and 89 years who experienced myocardial infarction, with significant coronary arteries changes, hospitalized due to acute coronary syndrome living in Warsaw were analyzed.

Results. Patients presented median 25(OH)D concentration value of 11 ng/mL (range: 4–28 ng/mL). The only significant determinant of 25(OH)D concentration was the date of examination, with higher concentrations in summer than in winter.

Conclusions. Vitamin D treatment in Polish cardiac patients aimed at reaching the optimal level of 30 ng/mL (75 nmol/L) seems to be necessary and implemented as soon as possible.

Key words: vitamin D, vitamin D deficiency, cardiovascular disease

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Introduction

Cardiovascular diseases (CVDs) are expected to be the main cause of mortality in most developing nations by 2020 [1]. More than ninety million American adults have at least one type of CVD, and more than forty percent of this population is projected to have some form of CVD by 2030 [2]. In Poland, CVDs are still one of the most common causes of death despite significant advancements in treatment [3]. Previously conducted clinical trials like e.g. POLSCREEN [4], POLKARD [5] and WOBASZ [6] illustrated the social significance of the problem.

Vitamin D plays an important role in the cardiovascular system by regulating blood pressure [7] and modulating vascular tone [8], facilitating stabilization of endothelial and smooth muscle cells through vitamin D receptors in the blood vessels and the heart [9–11]. The scientific debate on the association between 25-hydroxyvitamin D [25(OH)D] concentration and risk of CVD is ongoing. In recent years, an increasing number of studies has been published suggesting associations between vitamin D deficiency and increased risk of heart failure, adverse cardiac events, and cardiovascular-related deaths in various populations [12–16]. Based on Hill's criteria for causality in a biological system [17], it was approved that evidence supports confirms a causal association between serum 25(OH)D concentrations and increased risk for CVD for all criteria except experiment (i.e., vitamin D supplementation clinical trials) [18]. In contrast, it was also pointed out that data on the impact of vitamin D on cardiovascular health is conflicting [19] and that the link between vitamin D deficiency and cardiovascular disease may be an epiphenomenon [20]. As well as at present it is pointed out that the protective effect of vitamin D concerns only a specific range of its serum concentration and it suggests the negative impact of not only too low but also very high concentrations of 25(OH)D, which have been shown to increase cardiovascular risk [21]. Such U-shaped 25(OH)D relationships are suspect since participants are seldom questioned about when they began to supplement with vitamin D [22].

Therefore, it is essential to evaluate whether vitamin D supplementation (or vitamin D status correction) may play a role in the prevention of heart diseases and to defined groups of patients who benefited mostly from vitamin D supplementation as the greatest beneficial effects are observable in subjects with the lowest 25(OH)D concentration [9, 19, 23–25].

Recently, no significant association between the vitamin D status and severity of coronary atherosclerosis (expressed by the number of vessels with significant stenosis) was reported in numerous heterogeneous population of Polish cardiac patients with hypertension, diabetes, and/or hyperlipidemia [26]. A supplementary independent analysis showed that a group of cardiac patients with diabetes, hyperlipidemia, significant coronary arteries stenosis, hospitalized due to acute coronary syndrome (ACS), who experienced a previous myocardial infarction (MI) was identified as a group of patients with the lowest values of 25(OH)D concentration [27].

The primary aim of this study was to find determinants of the vitamin D status in patients with identified (in previous studies) low values of 25(OH)D concentration taking into account clinical factors. The secondary aim was to clinically characterize groups of cardiac patients in relation to vitamin D status.

Material and methods

Details of the study population (exclusion criteria) and measurements [diabetes diagnosis, ACS diagnosis, interview questionnaire, body mass index (BMI), concentration of total cholesterol (TC) and/or triglycerides (TG), systolic and diastolic blood pressure, coronary angiography and total 25(OH)D in participant serum and plasma] were presented elsewhere [26, 27]. The study was approved by the University Bioethical Committee (KB/124/2014) and followed the rules and principles of the Helsinki Declaration.

Population

This cross-sectional study comprises data of Polish patients referred for diagnostic catheter angiography in an evaluation for coronary artery disease to the cardiology department in 2016. The inclusion criteria were as follows: diagnosis of type 2 diabetes mellitus (T2DM), diagnosis of ACS, presence of previous MI, and significant changes in one, two, or three coronary vessels.

Institute of Meteorology and Water Management, National Research Institute from Warsaw, Poland provided detailed results on daily sunshine hours from the region of Warsaw. Thus, only data of Warsaw citizens were included in the final statistical analysis.

Examinations

Fasting blood samples were collected from the antecubital vein into the clot activator tubes. The serum concentration of 25(OH)D was determined with the "DiaSorin LIAISON® 25 OH Vitamin D TOTAL Assay" (DiaSorin, Stillwater, MN, USA) by a chemiluminescent immunoassay; range of detection 4–150 ng/mL, precision 5.0% cardiovascular, accuracy standard deviation 1.2% [28]. 25(OH)D concentrations were measured in ng/mL (1 ng/mL is equivalent to 2.5 nmol/L [29, 30]). Vitamin D External Quality Assessment Scheme (DEQAS) assessed the reliability of 25(OH)D and 1.25(OH)2D assays. The vitamin D status was classified according to the Endocrine Society clinical practice guidelines for vitamin D deficiency: severe deficiency (concentration of 25(OH)D < 10 ng/mL), moderate deficiency (≥ 10 to < 20 ng/mL), mild deficiency (≥ 20 to < 30 ng/mL), and optimal (≥ 30 ng/mL) [31].

Data for the mean daily sunshine hours were obtained from the Institute of Meteorology and Water Management, National Research Institute, Warsaw, Poland. Patients' examinations were performed throughout the whole year on what may influence their 25(OH)D value. National Health and Nutrition Examination Survey (NHANES) reported the season of blood draw as winter months (November to April) and summer months (May to October) [32]. Vitamin D can only be produced when there is ultraviolet B (UVB), which occurs only during 6 months in Poland [33].

Statistics

The Wilk-Shapiro test was used for evaluating the data distribution. Log transformation (ln) was used if the data were not normally distributed. The potential determinants for the magnitude of the 25(OH)D concentration were investigated using multiple regression analysis. A backwards, stepwise regression analysis was used to identify significant predictors of the 25(OH)D concentration from among independent variables in patients examined during winter and summer months separately. Mann–Whitney U test was used to compare the results between the two groups. Pearson's chi-squared test or Fisher's exact test were used to determine differences between prevalence in selected groups. The statistical analysis was carried out with STATISTICA 12.5 software (significance level of 5% — p value < 0.05). GraphPad Prism 5.0 (GraphPad Software Inc., La Jolla, CA, USA) was used to create Figure 1.

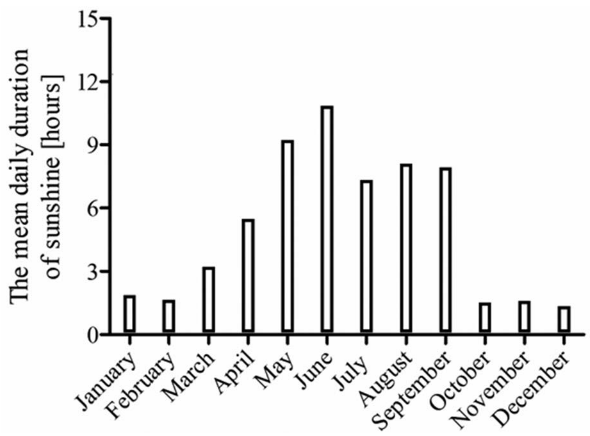

Figure 1. The mean duration of sunshine in all months of the year in Warsaw, Poland. Data for the mean daily sunshine hours were obtained from the Institute of Meteorology and Water Management, National Research Institute, Warsaw, Poland

Results

Participants' characteristics and baseline results

The study group consisted of 92 Caucasian patients (62 males and 30 females) with T2DM, history of previous MI, significant changes in one, two and/or three coronary arteries hospitalized due to ACS living in Warsaw (52°13'N, 21°02'E), Poland. Participants' mean (± standard deviation) age and BMI were: 69 (± 10) years and 29 (± 5) kg/m^2, respectively. Patients were classified into five subgroups based on age: 40–50 years, > 50–60 years, > 60–70 years, > 70–80 years and > 80 years with a following number of patients in consecutive age subgroups: 4, 10, 38, 24, 16. There were no significant differences in sex distribution among the five age subgroups (p = 0.08). Active smoking was declared by 32 patients (35%). TC and TG concentrations of 180 (± 60) mg/dL and 150 (± 90) mg/dL were observed, respectively. Hyperlipidemia was observed in 53 patients (58%) whereas hypertension was observed in most of them (83; 90%).

The median 25(OH)D concentration value in the whole group was 11 ng/mL (27.5 nmol/L), range: 4–28 ng/mL (10–70 nmol/L). All patients presented vitamin D deficiency — there were no patients with optimal 25(OH)D concentration (i.e. equal or greater than 30 ng/mL). Severe deficiency (the value below 10 ng/mL) was noticed in 30 patients (33%). Moderate deficiency (concentration equal or greater than 10 ng/mL and lower than 20 ng/mL) and mild deficiency (concentration equal or greater than 20 ng/mL and lower than 30 ng/mL) weres observed in 43 (47%) and 19 patients (20%), respectively. The mean duration of sunshine in all months of the year is presented in Figure 1.

The median (range) of mean daily duration of sunshine (analysis concerns 3 days before vitamin D measurements) was 1.1 hours (0.0–13.6 hours). The median of mean duration of sunshine per day significantly differed (p < 0.001) between the seasons of the year, and, as expected, was longer during summer months (May to October; median: 5.5 hours, range: 0.0–13.6 hours) and shorter during winter months (November to April: 0.8 hours, range: 0.0–11.8 hours). The examinations during summer months were performed in 49 (53%) patients, whereas during winter months in 43 (47%) patients.

Determinants of 25(OH)D concentration in the whole group

From selected variables examination date appeared as a significant determinant of 25(OH)D concentration (Table 1).

Table 1. Determinants of 25(OH)D concentration for all (n = 92) patients

Determinants		β (SE)	95% CI	p
ln25(OH)D	Age	–0.07 (0.11)	–0.29–0.15	0.54
	Sex (♂/♀)	–0.02 (0.11)	–0.23–0.19	0.83
	BMI	–0.15 (0.11)	–0.36–0.06	0.17
	Smoking (yes/no)	–0.09 (0.10)	–0.29–0.12	0.40
	Hypertension (yes/no)	0.02 (0.10)	–0.18–0.22	0.83
	Hyperlipidemia (yes/no)	–0.17 (0.10)	–0.37–0.03	0.10
	Examination date (May–October/November–April)	–0.40 (0.09)	–0.60–0.20	< 0.001

♂ — male; ♀ — female; β — regression coefficient; BMI — body mass index; CI — confidence interval; SE — standard error

Table 2. Comparison of the selected parameters between the patients examined during the winter and summer months. Results for qualitative variables are presented as number and % of the whole group

	Patients examined during summer months (May–October)	Patients examined during winter months (November–April)	p
N and %	49 (53%)	43 (47%)	–
25(OH)D [ng/mL]	15 (6–28)	9 (4–26)	< 0.001
Age [years)]	70 ± 11	67 ± 10	0.17
Sex (♀/♂)	17 (18%)/32 (35%)	13 (14%)/30 (33%)	0.65
BMI [kg/m^2]	29 ± 4	30 ± 6	0.18
Smoking (yes/no)	14 (15%)/35 (38%)	18 (20%)/25 (27%)	0.18
Hypertension (yes/no)	42 (45%)/7 (8%)	41 (45%)/2 (2%)	0.12
Hyperlipidemia (yes/no)	25 (27%)/24 (26%)	28 (30%)/15 (17%)	0.17

♂ — male; ♀ — female; BMI — body mass index

Table 3. Determinants of 25(OH)D concentration in patients examined during summer months (n = 49)

Determinants		β (SE)	95% CI	p
ln25(OH)D	Age	–0.24 (0.17)	–0.59–0.10	0.16
	Sex (♂/♀)	–0.03 (0.16)	–0.35–0.30	0.88
	BMI	0.01 (0.16)	–0.33–0.33	0.99
	Smoking (yes/no)	–0.11 (0.16)	–0.43–0.22	0.51
	Hypertension (yes/no)	–0.01 (0.16)	–0.33–0.30	0.95
	Hyperlipidemia (yes/no)	–0.24 (0.15)	–0.54–0.06	0.12

♂ — male; ♀ — female; β — regression coefficient; BMI — body mass index; CI — confidence interval; SE — standard error

Taking into account fact that examination date was the most significant determinant of 25(OH)D, and that the vitamin D can only be produced when there is UVB, which occurs only during six months in Poland, the whole group was divided into patients examined during winter and summer months to find significant determinants of the 25(OH)D concentration in these selected group of patients. Table 2 presents a comparison of the results of selected parameters between the patients examined during the winter and summer months.

Besides 25(OH)D concentration there were no significant differences between groups in analyzed clinical parameters.

Determinants of 25(OH)D concentration in patients examined during summer months

Tables 3 and 4 present results of the regression analysis considering selected variables as determinants of 25(OH)D concentration in patients examined during the summer months. There were no significant determinants

Table 4. Final step of the backward stepwise regression analysis considering selected variables as determinants of 25(OH)D concentration in patients examined during summer months (n = 49)

	Determinants	β (SE)	95% CI	p
ln25(OH)D	Age	–0.20 (0.14)	–0.48–0.08	0.16
	Hyperlipidemia (yes/no)	–0.24 (0.14)	–0.52–0.04	0.09

β — regression coefficient; CI — confidence interval; SE — standard error

Table 5. Results of the regression analysis considering selected variables as determinants of 25(OH)D concentration in patients examined during the winter months (n = 43)

	Determinants	β (SE)	95% CI	p
ln25(OH)D	Age	0.25 (0.18)	–0.11–0.60	0.17
	Sex (♂/♀)	0.06 (0.17)	–0.29–0.41	0.74
	BMI	–0.28 (0.17)	–0.63–0.06	0.11
	Smoking (yes/no)	–0.13 (0.16)	–0.46–0.20	0.44
	Hypertension (yes/no)	–0.01 (0.16)	–0.33–0.32	0.96
	Hyperlipidemia (yes/no)	–0.06 (0.17)	–0.41–0.29	0.74

♂ — male; ♀ — female; β — regression coefficient; BMI — body mass index; CI — confidence interval; SE — standard error

Table 6. Final step of the backward stepwise regression analysis considering selected variables as determinants of 25(OH)D concentration in patients examined during winter months (n = 43)

	Determinants	β (SE)	95% CI	p
ln25(OH)D	Age	0.26 (0.15)	–0.03–0.56	0.08
	BMI	–0.24 (0.15)	–0.54–0.06	0.12

♂ — male; ♀ — female; β — regression coefficient; BMI — body mass index; CI — confidence interval; SE — standard error

of ln25(OH)D in patients examined during the summer months. Age and hyperlipidemia were considered in the final step of the stepwise regression as the strongest predictors for the model.

Determinants of 25(OH)D in patients examined during winter months

Tables 5 and 6 present results of the regression analysis considering selected variables as determinants of 25(OH)D concentration in patients examined during winter months. There were no significant determinants of ln 25(OH)D in patients examined during the winter months. Age and BMI were considered in the final step of the stepwise regression as the strongest predictors for the model.

Discussion

The main finding of our study was that the strongest determinant of vitamin D status in Polish cardiac patients with identified (in previous studies [26, 27]) 25(OH)D deficiency is the date of examination. The main aim of our research project included this study and articles published previously [26, 27] was to indicate the group of cardiac patients who presented the lowest 25(OH)D concentration. The outcomes of our research project show that the patients with the most severe clinical characteristic, i.e. diabetic patients who experienced previous MI, with significant alterations in coronary arteries, hospitalized due to ACS, who were examined during winter months present extremely low 25(OH)D concentrations indicating very severe vitamin D deficiency. The median 25(OH)D concentration value in the above-mentioned group was ~9 ng/mL. Our results confirm published data for vitamin D concentration for cardiac patients from another region of Poland (Tarnów; 50°01'45''N, 20°58'18''E). Tokarz et al. [34] presented that median serum 25(OH)D concentration in patients with acute MI was ~7 ng/mL.

Low 25(OH)D concentration in hospitalized cardiac patient group may be associated with their clinical characteristics. Vitamin D plays a role in the whole dynamic process from the initiation of endothelial dysfunction to the development of atherosclerosis. Hypovitaminosis D alters a range of pathways in endothelial cells, extracellular matrix, and vascular smooth muscle, which are implicated in atherosclerosis pathogenesis [35–37]. There have been an increasing number of review papers highlighting that vitamin D deficiency is associated with an increased risk of developing CVD given to the relationship between low vitamin D concentration and e.g. diabetes, dyslipidemia, atherosclerosis, endothelial dysfunction, and hypertension [9, 38–40]. Our results indicated that patients with low 25(OH)D concentration presented more severe conditions than those with higher values of 25(OH)D which is in line with outcomes from, e.g., the NHANES III [41]. The NHANES III study included a representative sample of the American population showed a significant increase in the prevalence of hypertension, diabetes mellitus, obesity, and hypertriglyceridemia in patients with low 25(OH)D concentration (< 21 ng/mL) compared to those with higher concentrations [25(OH)D concentration > 37 ng/mL] [41]. Concentrations below 20 ng/l are linked independently to cardiovascular morbidity and mortality [42]. Diabetic cardiac patients from central Poland achieved lower results compared to the results from the NHANES epidemiological study [41, 43–45]. In the NHANES cohort study, only 5% of participants had values below the cutoff of 11 ng/mL [43]. It confirms intercontinental differences in 25(OH)D concentration [46]. Based on the review of literature, Hilger et al. [46] demonstrated significantly higher 25(OH)D concentration in North America compared to Europe or the Middle East/Africa region.

The results of the presented study (mean, median) are more or less comparable (slightly lower) with the results of epidemiological data on the vitamin D status from general population from central Europe [47] and particularly from Poland, where several authors proved massive vitamin D deficiency [48–51]. Pludowski et al. [47] in 2014 summarized the available data on the supply of vitamin D and the epidemiology of its deficiency in Central European populations, concluded that most people living in Central and Western Europe have serum 25(OH)D concentrations below optimal values (< 30–50 ng/mL). In Poland, the average concentration of 25(OH)D in late winter and early spring in about six thousand healthy residents of 22 Polish cities was about 18.0 ng/mL. In approximately 66% of subjects, the concentration of 25(OH)D was below 20 ng/mL, and optimal values (i.e. > 30 ng/mL) were observed only in less than 10% of the Polish population [48]. Similar results were shown by Kmieć et al. [52], more than 80% of adults living only in the north of Poland (Gdańsk, Gdynia, Sopot) demonstrated the 25(OH)D concentration below 20 ng/mL, only 2.5% presented optimal concentration of 25(OH)D, in winter the 25(OH)D concentration was even about 13 ng/mL [53]. It should be emphasized that this study was also carried out only in the winter months (from February to mid-April) [52]. Such a value was confirmed in an urban population of elderly women living in central Poland (Warsaw) [54]. In the winter months (between December and March) the 25(OH)D concentration in this study sample was 13.6 ng/mL. In addition, 83.2% of the studied women had a concentration of 25(OH)D below 20 ng/mL (in this group 35% were classified as a severe vitamin D deficiency, i.e. 25(OH)D < 10 ng/mL) and only 4% above 30 ng/mL [54]. In another study conducted in Poland, which included more than one hundred residents (82 women and 50 men aged from 41 to 81 years) of Kraków, the southern part of Poland, it was shown that the average concentration of 25(OH)D in the winter months was 16.7 ng/mL, and the deficiency concerned 90.2% of the studied group [55].

Besides many studies confirming the association between low 25(OH)D concentration and adverse cardiac events, results of the several trials aimed at evaluation of the effect of vitamin D supplementation on cardiovascular outcomes have been inconclusive or contradictory [38, 56]. Results from published randomized controlled trials (RCTs) indicated that vitamin D supplementation is ineffective in improving cardiovascular health among different patient populations [57]. Mirhosseini et al. [7] and Raed et al. [8] suggested that the problem was too little vitamin D given to the participants. Mirhosseini et al. [7] stated that at least 100 µg/day of vitamin D is required to achieve and maintain a serum 25(OH)D concentration of 100 nmol/L.

Kennel et al. [24] in their comprehensive review article asked the question: how much vitamin D is needed to correct severe vitamin D deficiency (i.e. values below 10 ng/mL)?; and answered that the usually applied strategy is to prescribe a "loading dose" e.g., 50 000 IU of vitamin D orally once weekly for 2–3 months. The US Endocrine Society suggests 1,500–2,000 IU/day of vitamin D is needed for adults to maintain 25(OH)D above the optimal level of 75 nmol/L [58]. Pilz et al. suggested that the RCTs were not adequately designed to address extraskeletal events, and did not focus on vitamin D-deficient individuals [44, 59]. It was underlined that more emphasis should be placed on well-designed RTCs among severely vitamin D-deficient populations who would mostly benefit from vitamin D treatment [25]. Recent, first individual participant data-derived estimates may offer improved dietary recommendations for vitamin D because the underpinning modeling captures the between-person variability in response of serum 25(OH)D to vitamin D intake [60].

Results from our research project may help in the identification of the severely vitamin D-deficient cardiac population. It should be highlighted here that hypovitaminosis D in our study group of cardiac diabetic patients with severe medical conditions may result from many reasons including environmental and/or clinical reasons. According to the vitamin D supplementation guideline published by Pludowski et al. [11], for patients with a laboratory-confirmed vitamin D deficiency (concentration lower than 20 ng/mL), like our population study group, a vitamin D treatment should be implemented — an age- and body weight-dependent therapeutic dosage should be administered with a treatment duration of 1–3 months.

Treatment including e.g. sun exposure activities and dietary intake may not be enough to achieve and maintain the target — minimum serum 25(OH)D concentration of at least 30 ng/mL (75 nmol/L). Additional vitamin D supplementation could be needed taking into account the fact that with the exception of fatty fish and meat [61] (red meat is also a risk factor for CVD, so should not be recommended [62]) the vitamin D content of most foods, including fortified dairy products, is relatively low to nonexistent [24]. The results of the National Multicentre Health Survey (WOBASZ) showed that the Polish population with established CVD is characterized by a low level of knowledge of non-pharmacological methods of preventing CVD [6] and the quality of dietary habits falls far short of the recommendations relevant for CVD prevention [63]. In Poland, there is a limited number of vitamin D-fortified foods and recommendations of vitamin D supplementation are probably not properly implemented [64].

The report of the European Food Safety Authority [65] indicated that the dietary intake of Vitamin D is commonly too low in European countries. In Poland, vitamin D dietary intake is significantly low — the range of mean daily vitamin D intake was between 2.92 μg/capita/day and 4.16 μg/capita/day in different age groups from 14 to more than 70 years [66]. Additional vitamin D supplementation in Polish cardiac patients seems to be necessary and implemented as soon as possible.

Grant et al. suggested that there could be a significant reduction in many healthcare costs related to diseases that have been associated with vitamin D deficiency [67, 68]. Vitamin D insufficiency is linked to important risk factors of leading causes of death [69]. Clinicians and/or healthcare providers should be aware of the connection and offer adequate interventions to increase 25(OH)D concentration, especially in minority groups [70, 71]. As a good example, recently (2016), the US Food and Drug Agency approved the addition of vitamin D to beverages made from edible plants intended as milk alternatives (also, orange juice) [72]. These are correct steps in the right direction, which can be adapted by e.g. Poland [11]. Programs aimed at improving knowledge level about the benefits of vitamin D supplementation could help reduce widespread vitamin D deficiency. It could be worthwhile to mention here that magnesium should also be supplemented to increase the conversion of vitamin D3 to 25(OH)D3 [73].

The limitations of this study are as follows. Lack of information on the treatment duration of prescribed statins. In each patient, serum phosphate, calcium, and parathyroid hormone concentrations were measured initially to include or exclude consecutive patients. We assessed only whether or not the patient values are in normal values and did not include data for the following variables in our analyses. The examinations were performed in patients living in urban areas of central Poland. To translate the obtained results into the entire Polish population, future examinations should be extended to the inhabitants of other regions of Poland. The study group consisted of 92 patients, however, statistical sub-analyses aimed at finding patients with the lowest values of 25(OH)D concentration limited the sample size in selected patient subgroups leading to reduced statistical power and caution in clinical decision making. Other factors like socioeconomic status (e.g. education level) may influence vitamin D concentration [41, 74], we did not take into account such factors in our analyses.

Conclusions

The population of cardiac patients from central Poland is a vitamin D-deficient group. In these patients, vitamin D treatment seems to be necessary and implemented as soon as possible.

Authors contributions

Conceptualization, EAD; data curation, EAD; investigation, EAD; methodology, EAD; project administration, EAD; resources, EAD; supervision, EAD, PP, WBG, MD; validation, EAD, JSG, PP, WBG, TS, MD; writing — original draft, EAD, JSG, WBG; writing — review and editing, EAD, JSG, PP, WBG, TS, MD. All authors approved the final version of the manuscript prior to submission.

Conflict of interest

WBG receives funding from Bio-Tech Pharmacal, Inc. (Fayetteville, AR, USA). Other authors: EAD, JSG, PP, TS, MD declare no conflict of interest.

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Streszczenie

Wstęp. Niedobór witaminy D jest problemem ogólnoświatowym o różnych konsekwencjach zdrowotnych. Witamina D może obniżać ryzyko niewydolności serca, jednak dowody świadczące o skuteczności suplementacji witaminą D na utrzymanie zdrowia układu sercowo-naczyniowego są sprzeczne z powodu braku odpowiedniej liczby i jakości badań klinicznych. Przyczyny braku jednoznacznych efektów potwierdzających pozytywny wpływ suplementacji witaminy D mogą być co najmniej trzy: 1) suplementacja zbyt małą ilością witaminy D lub 2) brak włączenia do badania tylko populacji z ciężkim niedoborem witaminy D, lub 3) czas trwania suplementacji. Celem pracy była charakterystyka grupy pacjentów kardiologicznych, u których stwierdzono w poprzednich badaniach najniższe stężenia 25-hydroksywitaminy D [25(OH)D].

Materiał i metody. Analizie poddano wyniki 92 chorych kardiologicznych z cukrzycą w wieku 41–89 lat, którzy przeżyli zawał serca z istotnymi zmianami w tętnicach wieńcowych, hospitalizowanych z powodu ostrego zespołu wieńcowego, mieszkających w Warszawie.

Wyniki. Mediana stężenia 25(OH)D w badanej populacji wyniosła 11 ng/ml (zakres: 4–28 ng/ml). Jedynym istotnym determinantem stężenia 25(OH)D był okres badania; stężenie było wyższe latem niż zimą.

Wnioski. Leczenie witaminą D u polskich pacjentów kardiologicznych w celu osiągnięcia optymalnego stężenia, tj. 30 ng/ml (75 nmol/l), wydaje się konieczne i powinno być jak najszybciej wdrożone.

Słowa kluczowe: witamina D, niedobór witaminy D, choroby układu krążenia

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References

1. Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: a review of contemporary guidance and literature. JRSM Cardiovasc Dis. 2017; 6: 2048004016687211, doi: 10.1177/2048004016687211, indexed in Pubmed: 28286646.
2. Benjamin EJ, Blaha MJ, Chiuve SE, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation. 2017; 135(10): e146–e603, doi: 10.1161/CIR.0000000000000485, indexed in Pubmed: 28122885.
3. Turek-Jabrocka R, Szafraniec K, Pach D, et al. Metabolic syndrome as a useful tool in the identification of persons with an increased risk of nonfatal cardiovascular events in the Polish urban population — a prospective study. Folia Cardiologica. 2016; 11(4): 261–267, doi: 10.5603/fc.2016.0067.
4. Cieśliński A, Pająk A, Podolec P, Rynkiewicz A. Ogólnopolski program prewencji choroby wieńcowej POLSCREEN. Termedia Wydawnictwo Medyczne, Poznań 2006: 27–34.
5. Kozela M, Szafraniec K, Broda G, et al. POLKARD Study Group. Detection and treatment of hypercholesterolemia in primary health care. Results of the POLKARD program of the Ministry of Health of the Republic of Poland. Pol Arch Med Wewn. 2012; 122(4): 154–161, doi: 10.20452/pamw.1220, indexed in Pubmed: 22495111.
6. Waśkiewicz A, Piotrowski W, Sygnowska E, et al. Quality of nutrition and health knowledge in subjects with diagnosed cardio-vascular diseases in the Polish population — National Multicentre Health Survey (WOBASZ). Kardiol Pol. 2008; 66(5): 507–13, discussion 514, indexed in Pubmed: 18537058.
7. Mirhosseini N, Vatanparast H, Kimball SM. The association between serum 25(OH)D status and blood pressure in participants of a community-based program taking vitamin D supplements. Nutrients. 2017; 9(11): 1244, doi: 10.3390/nu9111244, indexed in Pubmed: 29135923.
8. Raed A, Bhagatwala J, Zhu H, et al. Dose responses of vitamin D3 supplementation on arterial stiffness in overweight African Americans with vitamin D deficiency: a placebo controlled randomized trial. PLoS One. 2017; 12(12): e0188424, doi: 10.1371/journal.pone.0188424, indexed in Pubmed: 29216203.
9. Muscogiuri G, Annweiler C, Duval G, et al. Vitamin D and cardiovascular disease: From atherosclerosis to myocardial infarction and stroke. Int J Cardiol. 2017; 230: 577–584, doi: 10.1016/j.ijcard.2016.12.053, indexed in Pubmed: 28043680.
10. Wimalawansa SJ. Vitamin D and cardiovascular diseases: causality. J Steroid Biochem Mol Biol. 2018; 175: 29–43, doi: 10.1016/j.jsbmb.2016.12.016, indexed in Pubmed: 28027913.
11. Pludowski P, Holick MF, Grant WB, et al. Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol. 2018; 175: 125–135, doi: 10.1016/j.jsbmb.2017.01.021, indexed in Pubmed: 28216084.
12. Wang TJ, Pencina MJ, Booth SL, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008; 117(4): 503–511, doi: 10.1161/CIRCULATIONAHA.107.706127, indexed in Pubmed: 18180395.
13. Drechsler C, Pilz S, Obermayer-Pietsch B, et al. Vitamin D deficiency is associated with sudden cardiac death, combined cardiovascular events, and mortality in haemodialysis patients. Eur Heart J. 2010; 31(18): 2253–2261, doi: 10.1093/eurheartj/ehq246, indexed in Pubmed: 20688781.
14. Vacek JL, Vanga SR, Good M, et al. Vitamin D deficiency and supplementation and relation to cardiovascular health. Am J Cardiol. 2012; 109(3): 359–363, doi: 10.1016/j.amjcard.2011.09.020, indexed in Pubmed: 22071212.
15. Correia LCL, Sodré F, Garcia G, et al. Relation of severe deficiency of vitamin D to cardiovascular mortality during acute coronary syndromes. Am J Cardiol. 2013; 111(3): 324–327, doi: 10.1016/j.amjcard.2012.10.006, indexed in Pubmed: 23174181.

16. Porto CM, De Lima Silva V, da Luz JS, et al. Association between vitamin D deficiency and heart failure risk in the elderly. ESC Heart Fail. 2018; 5(1): 63–74, doi: 10.1002/ehf2.12198, indexed in Pubmed: 28817241.
17. Hill A. The environment and disease: association or causation? JR Soc Med. 2015; 108(1): 32–37, doi: 10.1177/0141076814562718, indexed in Pubmed: 25572993.
18. Weyland PG, Grant WB, Howie-Esquivel J. Does sufficient evidence exist to support a causal association between vitamin D status and cardiovascular disease risk? An assessment using Hill's criteria for causality. Nutrients. 2014; 6(9): 3403–3430, doi: 10.3390/nu6093403, indexed in Pubmed: 25184368.
19. Trehan N, Afonso L, Levine DL, et al. Vitamin D deficiency, supplementation, and cardiovascular health. Crit Pathw Cardiol. 2017; 16(3): 109–118, doi: 10.1097/HPC.0000000000000122, indexed in Pubmed: 28742648.
20. Al Mheid I, Quyyumi AA. Vitamin D and cardiovascular disease: controversy unresolved. J Am Coll Cardiol. 2017; 70(1): 89–100, doi: 10.1016/j.jacc.2017.05.031, indexed in Pubmed: 28662812.
21. Melamed ML, Michos ED, Post W, et al. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med. 2008; 168(15): 1629–1637, doi: 10.1001/archinte.168.15.1629, indexed in Pubmed: 18695076.
22. Grant WB, Karras SN, Bischoff-Ferrari HA, et al. Do studies reporting 'U'-shaped serum 25-hydroxyvitamin D-health outcome relationships reflect adverse effects? Dermatoendocrinol. 2016; 8(1): e1187349, doi: 10.1080/19381980.2016.1187349, indexed in Pubmed: 27489574.
23. Haines ST, Park SK. Vitamin D supplementation: what's known, what to do, and what's needed. Pharmacotherapy. 2012; 32(4): 354–382, doi: 10.1002/phar.1037, indexed in Pubmed: 22461123.
24. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. Mayo Clin Proc. 2010; 85(8): 752–757, doi: 10.4065/mcp.2010.0138, indexed in Pubmed: 20675513.
25. Grant WB, Boucher BJ, Bhattoa HP, et al. Why vitamin D clinical trials should be based on 25-hydroxyvitamin D concentrations. J Steroid Biochem Mol Biol. 2018; 177: 266–269, doi: 10.1016/j.jsbmb.2017.08.009, indexed in Pubmed: 28842142.
26. Dziedzic EA, Przychodzeń S, Dąbrowski M. The effects of vitamin D on severity of coronary artery atherosclerosis and lipid profile of cardiac patients. Arch Med Sci. 2016; 12(6): 1199–1206, doi: 10.5114/aoms.2016.60640, indexed in Pubmed: 27904508.
27. Dziedzic EA, Gąsior JS, Pawłowski M, et al. Association of vitamin D deficiency and degree of coronary artery disease in cardiac patients with type 2 diabetes. J Diabetes Res. 2017; 2017: 3929075, doi: 10.1155/2017/3929075, indexed in Pubmed: 29230421.
28. Krzywanski J, Mikulski T, Krysztofiak H, et al. Seasonal vitamin D status in Polish elite athletes in relation to sun exposure and oral supplementation. PLoS One. 2016; 11(10): e0164395, doi: 10.1371/journal.pone.0164395, indexed in Pubmed: 27732653.
29. Sahota O. Understanding vitamin D deficiency. Age Ageing. 2014; 43(5): 589–591, doi: 10.1093/ageing/afu104, indexed in Pubmed: 25074537.
30. Heaney RP. Vitamin D in health and disease. Clin J Am Soc Nephrol. 2008; 3(5): 1535–1541, doi: 10.2215/CJN.01160308, indexed in Pubmed: 18525006.
31. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011; 96(7): 1911–1930, doi: 10.1210/jc.2011-0385, indexed in Pubmed: 21646368.
32. Al-Khalidi B, Kimball SM, Rotondi MA, et al. Standardized serum 25-hydroxyvitamin D concentrations are inversely associated with cardiometabolic disease in U.S. adults: a cross-sectional analysis of NHANES, 2001-2010. Nutr J. 2017; 16(1): 16, doi: 10.1186/s12937-017-0237-6, indexed in Pubmed: 28241878.
33. Engelsen O. The relationship between ultraviolet radiation exposure and vitamin D status. Nutrients. 2010; 2(5): 482–495, doi: 10.3390/nu2050482, indexed in Pubmed: 22254036.
34. Tokarz A, Kusnierz-Cabala B, Kuźniewski M, et al. Seasonal effect of vitamin D deficiency in patients with acute myocardial infarction. Kardiol Pol. 2016; 74(8): 786–792, doi: 10.5603/KP.a2016.0002, indexed in Pubmed: 26779851.
35. Brewer LC, Michos ED, Reis JP. Vitamin D in atherosclerosis, vascular disease, and endothelial function. Curr Drug Targets. 2011; 12(1): 54–60, doi: 10.2174/138945011793591617, indexed in Pubmed: 20795937.
36. Kassi E, Adamopoulos C, Basdra EK, et al. Role of vitamin D in atherosclerosis. Circulation. 2013; 128(23): 2517–2531, doi: 10.1161/CIRCULATIONAHA.113.002654, indexed in Pubmed: 24297817.
37. Dalan R, Liew H, Tan W, et al. Vitamin D and the endothelium: basic, translational and clinical research updates. IJC Metabolic & Endocrine. 2014; 4: 4–17, doi: 10.1016/j.ijcme.2014.06.003.
38. McGreevy C, Williams D. New insights about vitamin D and cardiovascular disease: a narrative review. Ann Intern Med. 2011; 155(12): 820–826, doi: 10.7326/0003-4819-155-12-201112200-00004, indexed in Pubmed: 22184689.
39. Pludowski P, Holick MF, Pilz S, et al. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence. Autoimmun Rev. 2013; 12(10): 976–989, doi: 10.1016/j.autrev.2013.02.004, indexed in Pubmed: 23542507.
40. Pilz S, Verheyen N, Grübler MR, et al. Vitamin D and cardiovascular disease prevention. Nat Rev Cardiol. 2016; 13(7): 404–417, doi: 10.1038/nrcardio.2016.73, indexed in Pubmed: 27150190.
41. Martins D, Wolf M, Pan D, et al. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2007; 167(11): 1159–1165, doi: 10.1001/archinte.167.11.1159, indexed in Pubmed: 17563024.
42. Fanari Z, Hammami S, Hammami MB, et al. Vitamin D deficiency plays an important role in cardiac disease and affects patient outcome: Still a myth or a fact that needs exploration? J Saudi Heart Assoc. 2015; 27(4): 264–271, doi: 10.1016/j.jsha.2015.02.003, indexed in Pubmed: 26557744.
43. Yetley EA. Assessing the vitamin D status of the US population. Am J Clin Nutr. 2008; 88(2): 558S–564S, doi: 10.1093/ajcn/88.2.558S, indexed in Pubmed: 18689402.
44. Mazidi M, Michos ED, Banach M. The association of telomere length and serum 25-hydroxyvitamin D levels in US adults: the National Health and Nutrition Examination Survey. Arch Med Sci. 2017; 13(1): 61––65, doi: 10.5114/aoms.2017.64714, indexed in Pubmed: 28144256.
45. Zadshir A, Tareen N, Pan D, et al. The prevalence of hypovitaminosis D among US adults: data from the NHANES III. Ethn Dis. 2005; 15 (4 Suppl 5): 97–101, indexed in Pubmed: 16315387.
46. Hilger J, Friedel A, Herr R, et al. A systematic review of vitamin D status in populations worldwide. Br J Nutr. 2014; 111(1): 23–45, doi: 10.1017/S0007114513001840, indexed in Pubmed: 23930771.

47. Pludowski P, Grant WB, Bhattoa HP, et al. Vitamin D status in Central Europe. Int J Endocrinol. 2014; 2014: 589587, doi: 10.1155/2014/589587, indexed in Pubmed: 24790600.
48. Płudowski P, Ducki C, Konstantynowicz J, et al. Vitamin D status in Poland. Pol Arch Med Wewn. 2016; 126(7-8): 530–539, doi: 10.20452/pamw.3479, indexed in Pubmed: 27509842.
49. Pludowski P, Konstantynowicz J, Jaworski M, et al. Assessment of supply of vitamin D in the adult population in Poland. Standardy Med Pediatria. 2014; 4: 609–617.
50. Rusińska A, Płudowski P, Walczak M, et al. Vitamin D supplementation guidelines for general population and groups at risk of vitamin D deficiency in poland-recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the expert panel with participation of national specialist consultants and representatives of scientific societies — 2018 update. Front Endocrinol (Lausanne). 2018; 9: 246, doi: 10.3389/fendo.2018.00246, indexed in Pubmed: 29904370.
51. Wyskida M, Owczarek A, Szybalska A, et al. Socio-economic determinants of vitamin D deficiency in the older Polish population: results from the PolSenior study. Public Health Nutr. 2018; 21(11): 1995–2003, doi: 10.1017/S1368980017003901, indexed in Pubmed: 29352837.
52. Kmieć P, Żmijewski M, Waszak P, et al. Vitamin D deficiency during winter months among an adult, predominantly urban, population in Northern Poland. Endokrynol Pol. 2014; 65(2): 105–113, doi: 10.5603/EP.2014.0015, indexed in Pubmed: 24802733.
53. Kmieć P, Żmijewski M, Lizakowska-Kmieć M, et al. Widespread vitamin D deficiency among adults from northern Poland (54°N) after months of low and high natural UVB radiation. Endokrynol Pol. 2015; 66(1): 30–38, doi: 10.5603/EP.2015.0006, indexed in Pubmed: 25754279.
54. Napiórkowska L, Budlewski T, JakubasKwiatkowska W, et al. Prevalence of low serum vitamin D concentration in an urban population of elderly women in Poland. Pol Arch Med Wewn. 2009; 119(11): 699–703, doi: 10.20452/pamw.815.
55. Trofimiuk-Muldner M, Kieć-Klimczak M, Hubalewska-Dydejczyk A. Niedobór witaminy D w populacji miasta Krakowa — wyniki wstępne. Endokrynol Pol. 2012; 63(Suppl. A): 160.
56. Carvalho LS, Sposito AC. Vitamin D for the prevention of cardiovascular disease: Are we ready for that? Atherosclerosis. 2015; 241(2): 729–740, doi: 10.1016/j.atherosclerosis.2015.06.034, indexed in Pubmed: 26135478.
57. Veloudi P, Jones G, Sharman JE. Effectiveness of vitamin D supplementation for cardiovascular health outcomes. Pulse (Basel). 2016; 4(4): 193–207, doi: 10.1159/000452742, indexed in Pubmed: 28229054.
58. Pramyothin P, Holick MF. Vitamin D supplementation: guidelines and evidence for subclinical deficiency. Curr Opin Gastroenterol. 2012; 28(2): 139–150, doi: 10.1097/MOG.0b013e32835004dc, indexed in Pubmed: 22274617.
59. Pilz S, Kienreich K, Tomaschitz A, et al. Vitamin D and cardiovascular disease: update and outlook. Scand J Clin Lab Invest Suppl. 2012; 243: 83–91, doi: 10.3109/00365513.2012.681972, indexed in Pubmed: 22536768.
60. Cashman KD, Ritz C, Kiely M, et al. Improved dietary guidelines for vitamin D: application of individual participant data (IPD)-level meta-regression analyses. Nutrients. 2017; 9(5): 469, doi: 10.3390/nu9050469, indexed in Pubmed: 28481259.
61. Crowe FL, Steur M, Allen NE, et al. Plasma concentrations of 25-hydroxyvitamin D in meat eaters, fish eaters, vegetarians and vegans: results from the EPIC-Oxford study. Public Health Nutr. 2011; 14(2): 340–346, doi: 10.1017/S1368980010002454, indexed in Pubmed: 20854716.
62. Bechthold A, Boeing H, Schwedhelm C, et al. Food groups and risk of coronary heart disease, stroke and heart failure: a systematic review and dose-response meta-analysis of prospective studies. Crit Rev Food Sci Nutr. 2019; 59(7): 1071–1090, doi: 10.1080/10408398.2017.1392288, indexed in Pubmed: 29039970.
63. Waśkiewicz A, Szcześniewska D, Szostak-Węgierek D, et al. Are dietary habits of the Polish population consistent with the recommendations for prevention of cardiovascular disease? — WOBASZ II project. Kardiol Pol. 2016; 74(9): 969–977, doi: 10.5603/KP.a2016.0003, indexed in Pubmed: 26779852.
64. Karczmarewicz E, Czekuć-Kryśkiewicz E, Płudowski P, et al. Effect of vitamin D status on pharmacological treatment efficiency: Impact on cost-effective management in medicine. Dermatoendocrinol. 2013; 5(2): 299–304, doi: 10.4161/derm.25279, indexed in Pubmed: 24194969.
65. European Food Safety Authority. Scientific opinion on the tolerable upper intake level of vitamin D. EFSA Journal. 2012; 10(7): 2813, doi: 10.2903/j.efsa.2012.2813.
66. Lichthammer A, Nagy B, Orbán C, et al. A comparative study of eating habits, calcium and vitamin D intakes in the population of Central-Eastern European countries. New Medicine. 2015; 19(2): 66–70, doi: 10.5604/14270994.1169799.
67. Grant WB. An estimate of the global reduction in mortality rates through doubling vitamin D levels. Eur J Clin Nutr. 2011; 65(9): 1016––1026, doi: 10.1038/ejcn.2011.68, indexed in Pubmed: 21731036.
68. Grant WB, Whiting SJ, Schwalfenberg GK, et al. Estimated economic benefit of increasing 25-hydroxyvitamin D concentrations of Canadians to or above 100 nmol/L. Dermatoendocrinol. 2016; 8(1): e1248324, doi: 10.1080/19381980.2016.1248324, indexed in Pubmed: 27942348.
69. Forrest KYZ, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. Nutr Res. 2011; 31(1): 48–54, doi: 10.1016/j.nutres.2010.12.001, indexed in Pubmed: 21310306.
70. Whayne TF. Vitamin d: popular cardiovascular supplement but benefit must be evaluated. Int J Angiol. 2011; 20(2): 63–72, doi: 10.1055/s-0031-1279679, indexed in Pubmed: 22654467.
71. Kühn T. Vitamin D deficiency in urban Poland: what are the implications? Pol Arch Med Wewn. 2016; 126(7-8): 468–470, doi: 10.20452/pamw.3531, indexed in Pubmed: 27578219.
72. Department of Health and Human Services. Food and Drug Administration. Food additives permitted for direct addition to food for human consumption. Federal Register. 2016; 81(137): 46578–46582.
73. Zittermann A. Magnesium deficit ? overlooked cause of low vitamin D status? BMC Med. 2013; 11: 229, doi: 10.1186/1741-7015-11-229, indexed in Pubmed: 24228832.
74. Shirazi L, Almquist M, Malm J, et al. Determinants of serum levels of vitamin D: a study of life-style, menopausal status, dietary intake, serum calcium, and PTH. BMC Womens Health. 2013; 13: 33, doi: 10.1186/1472-6874-13-33, indexed in Pubmed: 23945218.