Journal of Health Study and Medicine
2020, No. 1
pp. 5-21
DOI 10.36145/JHSM2020.01

Dietary Vitamin D Intake Does Not Significantly Affect Plasma 25(OH)D Concentration in Patients with Ischaemic Heart Disease

Małgorzata Godala[1]
https://orcid.org/0000-0003-3579-8537

Ewelina Gaszyńska[1]
https://orcid.org/0000-0001-7568-3502

Izabela Materek-Kuśmierkiewicz[2]
https://orcid.org/0000-0001-5912-4516

Dariusz Moczulski[2]
https://orcid.org/0000-0002-0926-9909

Jan Kowalski[3]
https://orcid.org/0000-0003-0621-1768

[1] Department of Nutrition and Epidemiology, Medical University of Lodz, Poland
[2] Department of Internal Medicine and Nephrodiabetology, Medical University of Lodz, Poland
[3] Department of Internal Medicine and Cardiac Rehabilitation, Medical University of Lodz, Poland

Address for correspondence

Małgorzata Godala
Department of Nutrition and Epidemiology
Medical University of Lodz
7/9 Żeligowskiego Str., 90-752 Lodz, Poland
e-mail: malgorzata.godala@umed.lodz.pl

Abstract

Background: *Cardiovascular diseases are one of the main public health issues in developed and developing countries. Many recent studies indicate pleiotropic diverse functions of vitamin D.*

Aim: *The objective of this study was to evaluate 25(OH)D concentration in plasma of patients suffering from different types of ischaemic heart disease (STEMI, NSTEMI, stable angina pectoris), prevalence of its deficiencies in these patients and relations between 25(OH)D plasma level and traditional biomarkers for cardiovascular diseases.*

Results: *In the conducted study a mean 25(OH)D concentration was 13.7±3.8 and was below the recommended normal limit. The lowest mean concentration, 7.5±3.2 ng/ml, was observed in patients with NSTEMI, in those with STEMI – 13.4±2.1 ng/ml, and in patients with SAP – 19.6±4.2 ng/ml. No correlation was found between plasma vitamin D concentration and its dietary intake in all groups of patients. 25(OH)D concentration negatively correlated with age (r=-0.27), BMI (r=-0.31) and waist circumference (r=-0.29) in the studied group. Patients with normoglycaemia had a significantly higher 25(OH)D concentration than those with glucose intolerance and type 2 diabetes (p=0.02), in patients with type 2 diabetes and glucose intolerance 25(OH)D concentration correlated negatively with serum glucose level (r=-0.29) and TG concentration (r=-0.31), and positively with HDL level (r=0.27).*

Conclusion: *A non-supplemented well-balanced diet does not significantly affect plasma 25(OH)D concentration. Occurrence of vitamin D deficiencies in patients with ischemic heart disease should be regarded as an independent factor increasing the risk of cardiovascular diseases.*

Introduction

Cardiovascular diseases are one of the main public health issues in developed and developing countries. Many recent studies indicate pleiotropic and diverse functions of vitamin D and its deficiency correlates positively with a higher risk of cardiovascular diseases, arterial hypertension, dyslipidaemia, obesity or metabolic syndrome. Moreover, it has been proved that vitamin D deficiency affects progress of the atherosclerotic process [1,2].

Ischaemic heart disease includes all conditions involving ischaemia of the cardiac muscle related to lesions in coronary arteries. We may distinguish stable coronary syndromes, e.g. stable angina pectoris (SAP) and acute coronary syndromes (ACS) – with or without ST segment elevation (STEMI or NSTEMI). The most common cause of ischemic heart disease is coronary atherosclerosis and the cause of ACS – a sudden blockage of the coronary artery by a thrombus which forms on damaged atherosclerotic plaque.

Vitamin D regulates many mechanisms that have impact on the cardiovascular system, and its active form is 1.25 dihydroxy vitamin D with a peculiar intracellular receptor VDR. Most (90%) of the recommended daily intake is obtained from synthesis in the skin, the remaining part should be supplemented by proper diet. The amount of vitamin D production in the skin depends on the season of the year, degree of cloudiness and air pollution, geographic latitude or skin pigmentation [1,3].

Vitamin D regulates homeostasis of calcium and phosphates, increases calcium absorption from the intestines and takes part (together with parathormone) in calcium resorption in the kidneys. It is also associated with arterial blood pressure regulation, and its level correlates inversely with plasma renin activity. Moreover, vitamin D deficiencies increase the risk of diabetes development since it may affect intracellular calcium concentration in pancreatic cells, which stimulates insulin production. It is also believed to have an impact on lipids metabolism, as its deficiency increases the systemic insulin resistance deteriorating the lipid profile, as well as the process of atherosclerotic plague formation. Therefore, there are reasonable grounds for evaluating its level in patients with coronary disease [4,5,6].

The objective of this study was to evaluate 25(OH)D concentration in plasma of patients suffering from different types of ischaemic heart disease (STEMI, NSTEMI, stable angina pectoris), prevalence of its deficiencies in these patients and relations between 25(OH)D plasma level and traditional biomarkers for cardiovascular diseases.

Material and methods

Study population

The study included 192 patients, 112 males and 80 females, aged 41-65 (mean 54.4±4.3 years).

Biochemical analyses

Fasting blood glucose was determined with a reaction between glucose and ATP catalysed by hexokinase; TG concentration was enzymatically measured with coupled reactions in which TG was hydrolysed to produce glycerol; TC was measured with reactions using cholesteryl ester hydrolase, cholesterol oxidase, and peroxidase; HDL was measured using a heparin-manganese precipitation method; LDL was assessed using Friedewald rule.

The concentration of 25-hydroxy vitamin D (25-OH-D) was evaluated with the application of the LIAISON® test using chemiluminescent immunoassay (CLIA) technology. The plasma level of 25(OH)D ≥30 ng/ml was considered normal, between 20 ng/ml and 30 ng/ml – suboptimal (hypovitaminosis) and ≤20 ng/ml – insufficient (deficiency) [7].

Anthropometry analyses

Body mass index (BMI) was calculated as weight (kilograms) divided by height in meters squared. Waist circumference was measured at the midpoint between the bottom of the rib cage and above the top of the iliac crest during minimal respiration.

Nutritional evaluation

The food intake was assessed using a twenty-four-hour dietary recalls (24HR), in accordance with the guidelines of the National Food and Nutrition Institute in Warsaw [8,9]. A total of 576 24HR (three 24HR for each patient) were obtained from subjects by the interviewer and means of consumption were calculated for each nutrient. The "Album of photographs of food products and dishes" of the National Food and Nutrition Institute of Warsaw was used to determine normal size of the consumed portions [9]. The vitamin D intake was determined with "Charts of nutritive values of products and foods" and "Standards of Human Nutrition" using Diet 5.0 software (license No: 52/PD/2013), accorded to the National Food and Nutrition Institute of Warsaw. The degree of insufficient intake of vitamin D was estimated according to the adequate intake standards (AI=15μg per day) [8,10].

Statistical analyses

Statistical analysis was performed using Statistica 7.1 PL and Office 2010 software. The normal distribution was determined using the Shapiro-Wilk test. Continuous variables are presented as the mean value ± standard deviation (SD). The comparison between averages of two independent groups was made using Student's t test and Mann-Whitney U test for continuous variables, chi-square and Fisher's exact tests were applied for dichotomic ones. Correlations were assessed by Spearman's and Pearson's coefficient. One-way analysis of variance (ANOVA) with the post-hoc Bonferroni test for multiple comparisons was used to determine if differences exist between means of patients belonging to different groups, $p<0.05$ was considered to be significant.

The study was approved by the Bioethics Committee of the Medical University in Lodz (No. RNN/556/10/KB). A written consent was obtained from all research participants.

Results

Baseline groups characteristics

Characteristics of the studied groups are shown in Table 1. The three subgroups did not differ with regard to age, gender and smoking habits. Exactly 25% of the studied group were diagnosed with diabetes mellitus, 17.71% – impaired glucose tolerance and 88.54% – hypertension. The three subgroups differ according to anthropometric and lipid profile parameters except for TC. The highest TG and LDL concentration was found in NSTEMI patients whereas the highest HDL – in SAP patients. Patients with NSTEMI were characterised by the highest BMI and waist circumference.

Table 1. Characteristics of the study group

	NSTEMI (n=56)	STEMI (n=62)	SAP (n=74)	p-value
	Mean ±SD / %(n)	Mean ±SD / %(n)	Mean ±SD / %(n)	
Age [years]	53.2±4,2	57.4±5.3	52.7±3,7	sn
Sex [% females]	42.9 (24)	41.9 (26)	40.5 (30)	sn
Current smokers [%]	39.3 (22)	29.0 (18)	32.4 (24)	sn
T2D [%]	28.6 (16)	22.6 (14)	24.3 (18)	<0.001[c]
IGT [%]	17.9 (10)	16.1 (10)	18.9 (14)	sn
HT [%]	96.4 (54)	80.6 (50)	89.2 (66)	sn
BMI [kg/m^2]	32.5±2.6	27.4±6.9	29.7±3.4	<0.0001[a]
Waist [cm]	104.54±8.9	96.66±12.3	101.8±8.2	<0.0001[a]
Glc [mmol/l]	5.7±0.9	5.7±1.2	5.8±0.35	<0.0001[b]
TG [mmol/l]	1.9±1.9	1.7±0.7	1.6±0.2	<0.0001[b]
TC [mmol/l]	4.5±1.8	4.5±0.9	4,6±1.2	sn
HDL [mmol/l]	1.2±0.1	1.3±0.2	1.4±0.4	<0.0001[a]
LDL [mmol/l]	2.9±0.8	2.7±0.7	2.7±0.2	<0.0001[a]
25(OH)D [ng/ml]	7.5±3.2	13.4±2.1	19.6±4.2	<0.00001[a]

a – Student's t test, b – Mann-Whitney U test, c – $\chi 2$ test, sn – statistically non important

Nutritional characteristics

The studied groups were well nourished according to the total energy intake, total protein, carbohydrates and fats intake, as well as dietary fibre (Table 2). The groups did not differ according to the absolute values of the energy obtained from macronutrients intake, also several similarities were found between the groups regarding minerals intake (sodium, potassium, phosphorus, magnesium, iron, copper, zinc, iodine) and vitamins (B vitamins, vitamin A, vitamin D).

The percentage of the group with deficient of the vitamin D consumption of the AI standard was 81.25% (n=156). A detailed analysis of the kind of products commonly chosen by the study group indicated dairy products, meat and fish.

Table 2. Dietary intake in the study group

	NSTEMI (n=56)	STEMI (n=62)	SAP (n=74)	p-value
	Mean ±SD	Mean ±SD	Mean ±SD	
Total energy [kcal/d]	1957±405	1896 ±348	2005±316	sn
Proteins [g/d]	107±29	96 ±28	99±27	sn
Fats [g/d]	84 ±33	76 ±31	82±28	sn
Carbohydrates [g/d]	278±38	277±41	269±32	sn
Cholesterol [mg/d]	321 ±85	272 ±95	289 ±43	sn
SFA [g/d]	35±12	31±16	32±12	sn
MUFA [g/d]	30±24	31±17	33±21	sn
PUFA [g/d]	12±8	11±6	10±11	sn
Fiber [g/d]	24 ±8	23 ±7	25±5	sn
Vtamin D [µg]	4.9±1.2	5.3±1.7	4.7±1.6	sn

sn – statistically non important

25(OH)D concentration and its correlations

In the conducted study a mean 25(OH)D concentration was 13.7±3.8 and was below the recommended normal limit. The lowest mean concentration, 7.5±3.2 ng/ml, was observed in patients with NSTEMI, in those with

STEMI – 13.4±2.1 ng/ml, and in patients with SAP – 19.6±4.2 ng/ml. There was a statistically significant difference between the values. No correlation was found between plasma vitamin D concentration and its dietary intake in all groups of patients.

Plasma 25(OH)D concentration below 20 ng/ml was observed in 53.12% (n=102) of the subjects, significantly more frequently in NSTEMI patients than in the other groups, whereas hypovitaminosis (25(OH)D concentration of 20-30 ng/ml) – in 46.88% (n=90), most often in patients with stable coronary diseases. In none of the subjects the recommended 25(OH)D concentration, over 30 ng/ml, was observed. Moreover, among those with 25(OH)D deficiency as many as 43.14% (n=44) had 25(OH)D concentration below 10 ng/ml (Table 3).

Table 3. Prevalence of 25(OH)D deficiencies and hypovitaminosis in various types of ischaemic heart disease

Plasma 25(OH)D concentration (ng/ml)	NSTEMI (n=28)	STEMI (n=31)	SAP (n=37)	p
	% (n)	% (n)	% (n)	
0-19 (deficiency)	78.57 (22)	54.84 (17)	32.4 (12)	$\chi2=108.16$, $p<0.00001$
20-30 (hypovitaminosis)	21.43 (6)	45.16 (14)	67.6 (25)	

Seasonality of changes in plasma 25(OH)D levels was observed. Patients admitted in the first quarter of the year (January-March) had the lowest mean 25(OH)D concentration, whereas the highest one in the fourth quarter (October-December) (7.24±2.1 ng/ml vs. 15.78±2.9 ng/ml, p=0.008). In the second quarter the mean 25(OH)D concentration was 11.37±3.1 ng/ml, and in the third quarter – 13.56±2.4.2ng/ml (p=0.005).

25(OH)D concentration negatively correlated with age (r=-0.27), BMI (r=-0.31) and waist circumference (r=-0.29) in studied group. Patients with normoglycaemia had a significantly higher 25(OH)D concentration than those with glucose intolerance and type 2 diabetes (p=0.02 (Table 4)). Moreover, in patients with type 2 diabetes and glucose intolerance 25(OH)D concentration correlated negatively with serum glucose level (r=-0.29) and TG concentration (r=-0.31), and positively with HDL level (r=0.27). Such relations were not observed in the group of patients with normoglycaemia.

Table 4. Mean 25(OH)D concentration with respect to sex and carbohydrate metabolism disorders

Females (n=40)	Males (n=56)	All (n=96)	p
10.7±2.6	13.5±4.2	12.9±3.1	0.12
NG (n=55)	IGT (n=17)	T2D (24)	p
19.2±4.7	11.3±4.2	8.6±1,7	0.02

Discussion

Epidemiologic studies show that cardiovascular system diseases are the main cause of deaths in industrialised countries, and in developing countries rate of deaths due to these diseases will increase [11]. Recent data indicates that acute cardiovascular syndromes NSTEMI occur more often than STEMI [12], and mortality in both groups is similar [13,14,15]. The inflammatory process is a factor that initiates atherosclerotic plague rupture and development of acute coronary syndrome. Other factors include vitamin D deficiency and hyperglycaemia which is a strong predictive factor of death in NSTEMI patients, and persistent increased fasting blood glucose level indicate poor prognosis [16,17].

In the conducted study it was proved that patients with ischemic heart disease have lower than recommended plasma 25(OH)D level, and in none of the patients the optimal level was observed. Whereas, a significantly lower 25(OH)D concentration was recorded in the group of patients with acute coronary syndrome NSTEMI. Seasonal variations in 25(OH)D concentration were found and the lowest values were recorded in the first quarter of the year. There was also a relation shown between disturbed carbohydrate metabolism and lipid profile and low 25(OH)D concentration. Moreover, the risk of 25(OH)D deficiencies in the studied types of ischemic heart disease was estimated, and the highest predictive values were observed in the group of NSTEMI patients.

In many studies it has been proven that vitamin D deficiencies are a common phenomenon occurring in many populations, particularly among obese people with metabolic disturbances and circulatory system diseases [18,19,20], despite the general awareness of recommended vitamin D supplementation, particularly in autumn and winter seasons [21,22]. It has not been clearly defined yet what 25(OH)D concentration may be considered optimal. In European populations the established recommended range is 30-50 ng/ml [22]. According to Polish and European recommendations 25(OH)D level of 20-30 ng/ml is considered as hypovitaminosis (suboptimal concentration), whereas below 20 ng/ml is defined as vitamin D deficiency in the body [22,23]. Global recommendations are less restrictive – vitamin D concentration below 10 ng/ml is regarded as deficiency [6]. In the conducted study we observed too low 25(OH)D concentration in all the patients with ischemic heart disease, and in over 50% of the subjects the concentration was below 20 ng/ml. These results correspond to those obtained by other researchers [4,23]. It must be emphasised that very low 25(OH)D concentration occurred significantly more often in the group of NSTEMI patients than among those with STEMI and stable angina pectoris. The results were not confirmed in De Metrio study in which no differences in 25(OH)D concentration were identified between STEMI and NSTEMI patients [24].

Despite very low 25(OH)D concentrations in the patients, seasonal variations were found with the highest level being recorded in the first quarter of the year (January-March). Variations in 25(OH)D concentration depending on seasons of the year were confirmed by many studies [2,25,26]. It is particularly evident in Northern countries where sunshine exposure, especially in autumn and winter, is insufficient for vitamin D synthesis in the skin. It may be particularly important for people with a high risk of cardiovascular diseases, mainly the elderly, in whom a decreased vitamin D synthesis in the skin may be expected.

In literature, many epidemiologic studies, both Polish and European, indicate very common occurrence of 25(OH)D deficiencies [27,28,29], particularly in patients with cardiovascular diseases [3,5,23,30]. Among factors increasing the risk of vitamin D deficiencies there are being a representative of dark-skinned ethnic groups, a distance of one's place of living from the equator, obesity or being female [3,4,31]. However, in the conducted study this data was not confirmed. Females had lower 25(OH)D concentrations than males but those differences were not statistically significant. Due to the fact that the group was not very diversified in respect of nutrition level (all the patients were overweight or obese), it was not possible to estimate the impact of this factor vitamin D nutrition.

On the other hand, a negative correlation was shown between 25(OH) D and TG concentrations and a positive correlation with HDL level. Moreover, a significant relation was found to exist between diabetes occurrence and glucose intolerance and 25(OH)D concentration, which corresponds to the results obtained by other researchers [4,32]. The patients suffering from diabetes and glucose intolerance had lower 25(OH)D concentrations than those with normal glucose level. Diabetes and glucose intolerance are common in patients with ischemic heart disease, nevertheless, it has not been established yet whether vitamin D deficiency affects carbohydrate metabolism and whether vitamin D supplementation may improve it. Regardless of vitamin D mechanism of action analysed in the light of carbohydrate metabolism balance, it appears necessary to monitor vitamin D nutrition in these patients.

Vitamin D plays an important role in cardiovascular diseases prophylaxis, among others by regulating arterial blood pressure, insulin sensitivity or condition of blood vessels. Many studies confirmed a strong relation between vitamin D deficiencies and a high risk of cardiovascular diseases resulting both from modification of known risk factors as well as a direct impact on the vascular endothelium. Although there is still a need to conduct further studies on the relation of vitamin D with incidence and mortality due to cardiovascular diseases and many other conditions, vitamin D deficiencies should be regarded as a significant threat to public health.

Conclusion

A non-supplemented well-balanced diet does not significantly affect plasma 25(OH)D concentration. Occurrence of vitamin D deficiencies in patients with ischemic heart disease should be regarded as an independent factor increasing the risk of cardiovascular diseases.

References

1. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. Diabetes Care 2005; 28(5): 1228-1230. https://doi.org/10.2337/diacare.28.5.1228.

2. Muscogiuri G, Sorice GP, Ajjan R, Mezza T, Pilz S, Prioletta A et al. Can vitamin D deficiency cause diabetes and cardiovascular diseases? Present evidence and future perspectives. Nutr Metab Cardiovasc Dis 2012; 22(2): 81-87.

3. Lips P. Vitamin D status and nutrition in Europe and Asia. J Steroid Biochem Mol Biol 2007; 103(3-5): 620-625.

4. Tokarz A, Kuśnierz-Cabała B, Kuźniewski M, Gacoń J, Mazur-Laskowska M, Stępień EŁ. Seasonal effect of vitamin D deficiency in patients with acute myocardial infarction. Kardiol Pol 2016; 74(8): 786-792. https://doi.org/10.5603/KP.a2016.0002.

5. Skaaby T, Husemoen LL, Pisinger C, Jørgensen T, Thuesen BH, Fenger M et al. Vitamin D status and changes in cardiovascular risk factors: a prospective study of a general population. Cardiology 2012; 123(1): 62-70. https://doi.org/10.1159/000341277.

6. Huotari A, Herzig KH. Vitamin D and living in northern latitudes: an endemic risk area for vitamin D deficiency. Int J Circumpolar Health 2008; 67(2-3): 164-178.

7. Płudowski P, Karczmarewicz E, Bayer M, Carter G, Chlebna-Sokół D, Czech-Kowalska J et al. Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe – recommended vitamin D intakes in the general population and groups at risk of vitamin D deficiency. Pol J Endocrinol 2013; 64(4): 319-327.

8. Jarosz M. Standards of Human Nutrition. Warsaw: National Food and Nutrition Institute; 2012.

9. Szponar L, Wolnicka K, Rychlik E. Album of photographs of food products and dishes. Warsaw: National Food and Nutrition Institute; 2000.

10. Kunachowicz H, Nadolna I, Przygoda B, Iwanow K. Charts of nutritive values of products and foods. Third edition expanded and updated. Warsaw: PZWL; 2005.

11. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997; 349: 1498-1504.

12. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. N Engl J Med 2010; 362(23): 2155-2165. https://doi.org/10.1056/NEJMoa0908610.

13. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatoset G et al. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment and outcome of patients with ACS in Europe and Mediterranean Basin in 2004. Eur Heart J 2006; 27(19): 2285-2293.

14. Savonitto S, Ardissino D, Granger CB et al. Prognostic value of the admission electrocardiogram in acute coronary syndromes. JAMA 1999; 281(8): 707-713. https://doi.org/10.1001/jama.281.8.707.

15. Lindahl B, Toss H, Siegbahn A, Venge P, Wallentin L. Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. FRISC study group. Fragmin during instability in coronary artery disease. N Engl J Med 2000; 343(16): 1139-1147.

16. Aronson D, Hammerman H, Suleiman M, Markiewicz W. Usefulness of changes in fasting glucose during hospitalization to predict long-term mortality in patients with acute myocardial infarction. Am J Cardiol 2009; 104(8): 1013-1017. https://doi.org/10.1016/j.amjcard.2009.05.053.

17. Suleiman M, Hammerman H, Boulos M, Kapeliovich MR, Suleiman A et al. Fasting glucose in an important independent risk factor for 30-daymortality in patients with acute myocardial infarction: a prospective study. Circulation 2005; 111(6): 754-760.

18. Muldowney S, Lucey AJ, Paschos G, Martínez JA, Bandarra N, Thorsdottir I et al. Relationship between vitamin D status and cardio-metabolic risk factors in young European adults. Ann Nutr Metab 2011; 58(2): 85-93. https://doi.org/10.1159/000324600.

19. Tamer G, Mesci B, Tamer I, Kilic D, Arik S. Is vitamin D deficiency an independent risk factor for obesity and abdominal obesity in women? Endokrynol Pol 2012; 63(3): 196-201.

20. Vacek JL, Vanga SR, Good M, Lai SM, Lakkireddy D, Howard PA. Vitamin D deficiency and supplementation and relation to cardiovascular health. Am J Cardiology 2012; 109(3): 359-363. https://doi.org/10.1016/j.amjcard.2011.09.020.

21. Ribeiro Mandarino N, das Chagas Monteiro F, Leal Salgado JV, Lages JS, Filho NS. Is vitamin D deficiency a new risk factor for cardiovascular disease? Open Cardiovasc Med J 2015; 9: 40-49. https://doi.org/10.2174/1874192401509010040.

22. Płudowski P, Grant WB, Bhattoa HP, Bayer M, Povoroznyuk V, Rudenka M et al. Vitamin D status in Central Europe. Int J Endocrinol 2014; 589587. https://doi.org/10.1155/2014/589587.

23. Goleniewska B, Kacprzak M, Zielińska M. Vitamin D level and extent of coronary stenotic lesions in patients with first acute myocardial infarction. Cardiol J 2014; 21(1): 18-23. https://doi.org/10.5603/CJ.a2013.0048.

24. De Metrio M, Milazzo V, Rubino M, Cabiati A, Moltrasio M, Marana I et al. Vitamin D plasma levels and in-hospital and 1-year outcomes in acute coronary syndromes. Medicine 2015; 94(19): e857. https://doi.org/10.1097/MD.0000000000000857.

25. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol 2008; 52(54): 1949-1956. https://doi.org/10.1016/j.jacc.2008.08.050.

26. Lee JH, Gadi R, Spertus JA, Tang F, O'Keefe JH. Prevalence of vitamin D deficiency in patients with acute myocardial infarction. Am J Cardiol 2011; 107(11): 1636-1638. https://doi.org/10.1016/j.amjcard.2011.01.048.

27. Forrest KYZ, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. Nutr Res 2010; 31(1): 48-54. https://doi.org/10.1016/j.nutres.2010.12.001.

28. Lu L, Yu Z, Pan A, Hu FB, Franco OH, Li H et al. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. Diabetes Care 2009; 32(7): 1278-1283. https://doi.org/10.2337/dc09-0209.

29. Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. Am J Clin Nutr 2007; 85(3): 860-868.

30. Pera Ł, Sygitowicz G, Białek S, Łukaszkiewicz J, Sitkiewicz D. Vitamin D and statins: action in preventing cardiovascular events. Kardiol Pol 2012; 70(12): 1296-1298.

31. Schierbeck LL, Rejnmark L, Tofteng CL, Stilgren L, Eiken P, Mosekildeet L et al. Vitamin D deficiency in postmenopausal, healthy women predicts increased cardiovascular events: a 16-year follow-up study. Eur J Endocrinol 2012; 167: 553-560.

32. Verdoia M, Schaffer A, Barbieri L, Di Giovine G, Mariono P, Suryapranata M et al. Impact of gender difference on vitamin D status and its relationship with the extent of coronary artery disease. Nutr Metab Cardiovasc Dis 2015; 5(25): 464-470. https://doi.org/10.1016/j.numecd.2015.01.009.