Vitamin D in COPD with CKD

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Витамин D при ХОББ с ХБЗ

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Abstract:

Introduction: Vitamin D deficiency is common in both patients with chronic obstructive pulmonary disease (COPD), as well as in those with chronic kidney disease (CKD). **Aim:** To investigate the role of vitamin D in patients with COPD and CKD. **Materials and methods:** A prospective study of 90 patients with COPD follow-up during the June 2023 – January 2025 period. They were divided into two groups – patients with COPD and patients with COPD and CKD, according to the estimated glomerular filtration rate (eGFR) indicator. A correlation was sought between vitamin D levels and chronic kidney disease (CKD) in patients with COPD. The data were processed using the statistical software SPSS, version 20.0. A $p < 0.05$ was considered statistically significant. **Results:** At the first visit, 70% of patients had low vitamin D levels and 42.2% had both COPD and CKD. At the second visit, 97.4% were vitamin D deficient and 52.6% had CKD. A statistically significant difference was found regarding vitamin D deficiency between the two groups. In the group with eGFR < 60 mL/min/1.73 m², 54% of cases had low vitamin D levels ($p = 0.0007$). We established a cutoff value of 16.98 ng/mL and agreement between vitamin D and eGFR (AUC) of 41%, Gini index −0.173, sensitivity 79%, and specificity 25%. During dynamic follow-up of vitamin D levels, we found a statistically significant difference between the values at the two visits ($p < 0.01$) and between the two groups ($p = 0.012$). **Conclusion:** Patients with COPD frequently suffer from vitamin D deficiency, which is more pronounced in those with both COPD and CKD.

Key words: chronic obstructive pulmonary disease, chronic kidney disease, vitamin D

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Резюме:

Увод: Дефицитът на витамин D се среща често както при пациенти с хронична обструктивна белодробна болест, така и при тези с хронично бъбречно заболяване. **Цел:** да се проучи ролята на витамин D при пациенти с ХОББ и ХБЗ. **Материал и методи:** Проспективно проучване на 90 пациенти със стабилна ХОББ, периода юни 2023 – януари 2025 г. Разделени в две групи – ХОББ и ХОББ с ХБЗ, според eGFR. Търсена беше корелация между нивата на витамин D и хроничното бъбречно заболяване (ХБЗ) при пациенти с ХОББ. Данните бяха обработени със статистическата програма SPSS, version 20.0. За статистически значимо се приемаше $p < 0.05$. **Резултати:** На първата визита 70% имаха ниски стойности на витамин D и 42,2% бяха с ХОББ и ХБЗ, а на втората 97,4% бяха с витаминен дефицит и 52,6% с ХБЗ. Статистически значима разлика намерихме по отношение дефицита на витамин D при дете групи. В групата с eGFR<60 mL/min/1.73 m^2 54% от случаите бяха с ниски нива на витамин D, ($p=0.0007$). Установихме cutoff value 16,98 ng/mL и съгласуваност на витамин D и eGFR (AUC) – 41%, Gini Index – 0,173, чувствителност 79% и специфичност 25%. При динамично проследяване на витамин D, установихме статистически значима разлика между стойностите на двете визите ($p<0.01$) и двете групи ($p=0.012$). **Заключение:** Пациентите с ХОББ, често страдат от дефицит на витамин D, като той е по-изразен при тези с ХОББ и ХБЗ.

Ключови думи:	ХОББ, ХБЗ, витамин D
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Introduction

Concepts of chronic obstructive pulmonary disease have evolved in recent years. At present, COPD is considered a "heterogeneous lung disease, occurring with chronic symptoms on part of the respiratory system (dyspnea, cough, expectoration, exacerbations) as a result of abnormalities in the respiratory tract (bronchitis, bronchiolitis, emphysema), and leading to persistent, often progressive, obstruction of the airways [1]. It is believed that the basis of these processes is chronic inflammation of the airways, which is most often the result of oxidative stress caused by smoking [2] and harmful external influences. This, in turn, leads to both bronchial obstruction and destruction of the lung parenchyma.

Chronic kidney disease is defined as a clinical and laboratory syndrome of slow and imperceptible decline in kidney function. It is a functional manifestation of reduced nephron mass. The currently used classification for CKD, proposed by the Foundation for Improving Global Outcomes in Kidney Disease (The Kidney Disease Improving Global Outcomes – KDIGO), includes indicators of kidney damage, such as proteinuria, glomerular filtration rate (GFR) and morphological changes in the kidneys. According to this classification, CKD is divided into five stages, based on the estimated GFR (e-GFR) [3].

Vitamin D was discovered in 1922 by the German chemist Adolf Otto Reinhold Windaus. It represents a group of five fat-soluble compounds. The most important for humans are vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol).

Cholecalciferol is converted in the liver to calcifediol (also known as calcidiol or 25-hydroxycholecalciferol), while ergocalciferol is converted to ercalcidiol (25-hydroxyergocalciferol). These two metabolites of vitamin D, collectively called 25-hydroxyvitamin D or 25(OH)D, are measured in serum to assess a person's vitamin D status. Calcifediol is further hydroxylated by the kidneys and certain immune cells to form calcitriol (1,25-dihydroxycholecalciferol; 1,25(OH)2D), the biologically active form of vitamin D. Calcitriol binds to vitamin D receptors, which are nuclear receptors found in various tissues throughout the body [4].

Vitamin D is involved in the absorption of calcium, magnesium, and phosphate in the intestine and in numerous biological processes [5]. It plays an important role in a number of immune processes in the body. The anti-inflammatory effect of vitamin D has been established in many chronic diseases in which its deficiency is confirmed. It has a protective function, both on the epithelial cells of the lung and on immune cells, helping to protect the body against viral and bacterial infections [6].

Comorbidities associated with COPD, such as chronic kidney disease and heart failure, can disrupt the metabolism and storage of vitamin D [7].

Aim: To investigate the importance of Vitamin D in patients with COPD and CKD.

Materials and methods

The study was descriptive-sectional and analytical, with elements of a retro- and prospective nature. 90 outpatients with known COPD, in stable condition, were included, 63 of which were men. The average age of the patients was 67.

All patients were enrolled voluntarily, after signing informed consent forms.

They were followed up in two visits for the period from June 2023 to January 2025 and are from the „Asthma Center" outpatient practice in Pleven.

At the second visit, there were 78 patients – five of them later died and 7 withdrew their informed consent.

The two visits were conducted in two different seasons – the first one was in the summer, and the second one – in the autumn-winter season.

The following methods were used in the study:

1. Sociological methods – document study.
2. Clinical methods for diagnosis and treatment - anamnesis and physical examination of the patient.
3. Laboratory methods. Vitamin D and serum creatinine were tested. For the examination of laboratory parameters, blood was taken by venipuncture from each patient at both visits. The manipulation was performed by qualified personnel, observing all the rules of the procedure. The tests were performed by a certified clinical laboratory with a BioSystems S.A. Costa Brava apparatus. The MDRD formula (Modification of Diet in Renal Disease) was used to calculate glomerular filtration and was followed for over a 3-month period. According to the results of eGFR, patients with COPD were divided into two groups: without CKD – eGFR > 60 mL/min/1.73 m^2 and with CKD – eGFR < 60 mL/min/1.73 m^2.
4. Statistical methods. The data from the study were processed with statistical software packages:

Statistical Package for Social Sciences (SPSS), version 20.0 (IBM Corp., Armonk, NY), and EXCEL for Windows. The results are described by graphs and numerical values (relative share-structure; frequency coefficients; average values; correlation coefficients, etc.). Kolmogorov-Smirnov and Shapiro-Wilk tests were applied to check the distribution of the variables (normal or different from the normal distribution). In the analysis of the results, Analysis of Variance (ANOVA) parametric tests were applied for normal data distribution, while non-parametric tests were applied for abnormal distribution to test hypotheses: Chi-square tests, Pearson test, Kruscal-Wallis test, and Man-Whitney (Wilcoxon) test.

In the dynamic monitoring of the results, Student's t-test was used.

A value of $p < 0.05$ is considered statistically significant.

Results

At the first visit, out of 90 patients examined, 38 (42.2%) had COPD and CKD, and at the second visit, out of 78 patients, 41 (52.6%) had CKD (Fig. 1 and 2).

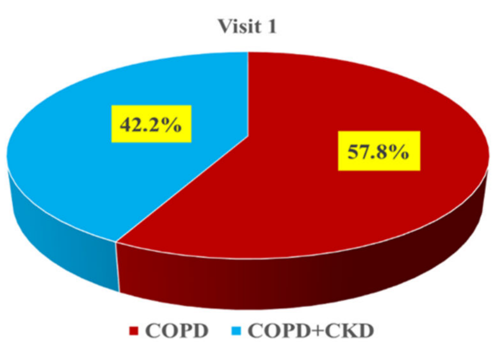

Fig. 1. Patients' distribution on visit 1

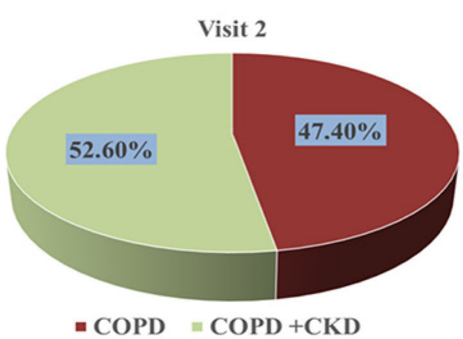

Fig. 2. Patients' distribution on visit 2

Out of the investigated subjects, 70% had low vitamin D levels on visit 1, compared to 97.4% on visit 2 (Fig. 3).

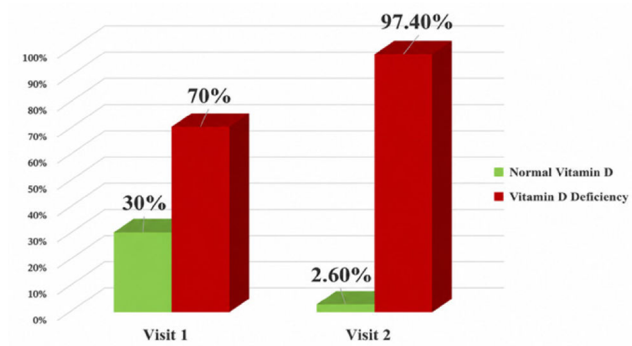

Fig. 3. Vitamin D levels on visits 1 and 2

We found a statistically significant difference in terms of low levels of Vitamin D in patients with COPD and low eGFR. In the group with eGFR < 60 mL/min/1.73 m^2, 54% of cases had low levels of Vitamin D, compared to 29.6% with normal values. In the group with eGFR ≥ 60 mL/min/1.73 m^2, 46% and 70.4% of patients with low levels of Vitamin D were with normal values, respectively (Chi-squared 4.498, df -1, p = 0.04; OR -2.7391, 95% CI 1.5321-4.8972, p = 0.0007) (Fig. 4).

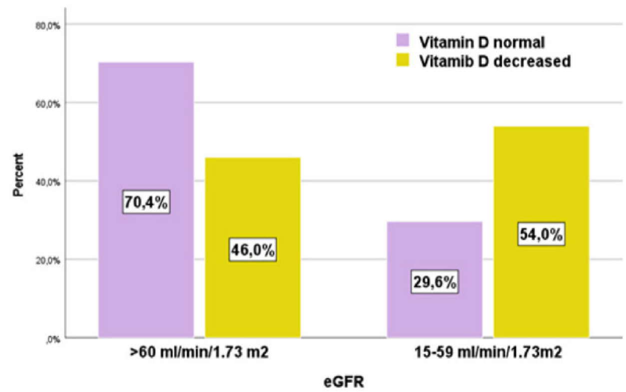

Fig. 4. Vitamin D levels depending on the eGFR

While searching for a relationship between vitamin D values and eGFR, we found a cutoff value of 16.98 ng/mL and a concordance of the two indicators (AUC) of 41%, Gini Index -0.173, sensitivity of 79% and specificity of 25%.

Vitamin D is a biomarker with high sensitivity but low specificity for CKD (Fig. 5).

In the dynamic monitoring of Vitamin D, we found a statistically significant difference, both between the values of the two visas and in relation to the two groups (Fig. 6).

The mean values for vitamin D for the entire study group at the first visit were 26.05 ±10.95 ng/mL, and at the second – 12.77 ± 6.38 ng/mL. We demonstrated a difference in the mean values of vitamin D for the two visits using the paired Student t-test (t = 11.86, df = 77, $p < 0.01$). While comparing the changes in the mean values of laboratory parameters in the two groups: COPD and COPD with CKD, a difference between the values of vitamin D was found (p = 0.012).

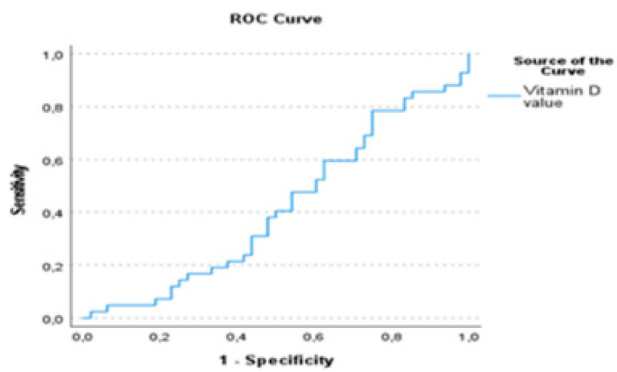

Fig. 5. Specificity and sensitivity of vitamin D in CKD (ROC curve)

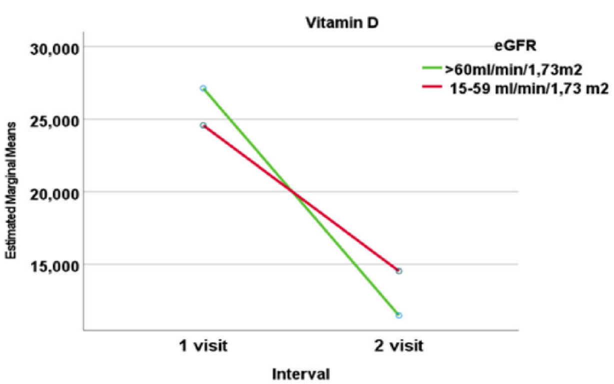

Fig. 6. Changes in vitamin D levels between visits 1 and 2 in patients with COPD with and without CKD

Discussion

Vitamin D deficiency is present in many diseases, and is also significantly more common in old age [8]. More and more studies show that patients with COPD often have a deficiency of Vitamin D. In different reports, the frequency of Vitamin D deficiency varies, but there are publications for 60%-90%, depending on the studied population [9]. In a study from Ireland [10] following 5,356 patients with COPD, the authors reported a higher incidence of Vitamin D deficiency during the winter season. Similar studies have been conducted in Northern Ireland, where the winter season and less outdoor exposure are reported to be factors playing an important role in Vitamin D deficiency in COPD patients [11]. A report from India indicated that Vitamin D deficiency in COPD patients is independent of sunlight exposure. It also occurs in younger patients [12].

In our study, we found a significantly high prevalence of Vitamin D deficiency – 70% – during the summer season. This prevalence increases to 97% during the autumn-winter period.

The data are somewhat consistent with publications from India that Vitamin D deficiency in COPD is not directly related to sunlight exposure. On the other hand, they confirm the data from Ireland and Northern Ireland that the deficiency increases during the autumn-winter season.

The kidneys have a major role in vitamin D metabolism and regulation of its circulating levels. Vitamin D deficiency has been found in more than 80% of patients with CKD [13].

A study from Brazil reported that 77.4% of patients in the pre-dialysis stage of CKD had low levels of Vitamin D [14].

On the other hand, it is stated that low levels of vitamin D are associated with progression of already existing CKD [15]. With increasing life expectancy in the global population, the incidence of CKD in patients with COPD is increasing [16].

A meta-analysis by Sun et al. [17] states that chronic kidney disease in patients with COPD further leads to a decrease in active vitamin D levels, which may occur through different mechanisms.

In our study, we found low levels of Vitamin D in both groups of patients with COPD and COPD with CKD, but in the group with eGFR < 60 ml/min/1.73 m^2, the deficiency of Vitamin D was statistically significantly higher – 54% – compared to the group of patients with eGFR ≥ 60 ml/min/1.73 m^2 – 46% (p = 0.0007).

Our study did not include patients in pre-dialysis stage of CKD.

A study by Bolotova [18], in the follow-up of 338 patients with COPD and early CKD (stage 1-2), indicated that the number of exacerbations, fibrinogen values, the Geriatric Depression Scale (GDS) and the body mass index (BMI) were factors related to Vitamin D levels. We established a Vitamin D value of 16.98 ng/mL as the cut-off for CKD in patients with COPD.

Another report by Bolotova [19] stated that treating Vitamin D deficiency and maintaining a level above 34.3 ng/ml for a period of 12 months in patients with COPD and CKD stage 1-2 is associated with a decrease in the severity of albuminuria, an increase in GFR and a statistically significant decrease in the renal artery resistance index [17]. In a dynamic follow-up of Vitamin D values for an 18-month period, we found not only a higher frequency of deficiency in terms of the time factor, but also in terms of both COPD groups with and without CKD.

Conclusion

Vitamin D deficiency is common among patients with COPD, and this deficiency is significantly higher in COPD and CKD. It is a biomarker with high sensitivity but low specificity for CKD in patients with COPD.

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