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Body composition analysis in patients with Hashimoto's disease and vitamin D deficiency

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ABSTRACT

Introduction. Hashimoto thyroiditis (HT) is one of the most common organ-specific autoimmune diseases. This autoimmune response disrupts thyroid function, affecting biochemical processes and metabolism, with symptoms often including weight gain and easy fatigue. Vitamin D has so far been considered only a key regulator of calcium-phosphate metabolism. However, it is now considered a pleiotropic substance and increasingly published data indicate that it also plays a role in immune modulation and metabolic health.
Aim. The study aimed to assess anthropometric measures, body composition, and muscle strength in patients with HT, correlate these parameters with serum 25(OH)D levels, and evaluate the impact of vitamin D supplementation.
Material and methods. The study included 80 female patients, aged ≥18 years, divided into an HT group (n = 51) and a Control Group with non-toxic diffuse or nodular goiter (n = 29). Vitamin D supplementation was administered based on the initial 25(OH)D concentration, at a dose of 6000 IU or 4000 IU daily for 3 months to patients with 25(OH)D concentration < 20 ng/ml and ≥ 20 ng/ml, respectively. Anthropometric and body composition measurements, as well as blood tests for 25(OH)D, TSH were performed at baseline and after supplementation.
Results. Both groups showed significant increases in 25(OH)D levels post-supplementation. In the HT group, lean body mass and muscle strength improved significantly (p = 0.002 and p = 0.02, respectively). In the Control Group, muscle strength increased (p = 0.01) and hip circumference decreased slightly (p = 0.03). No significant differences were found in body composition between the groups, although women with HT had larger hip circumferences. Correlation analysis revealed a moderately strong inverse relationship between baseline 25(OH)D levels and BMI in the Control Group (R = -0.44; p = 0.04), with no other significant associations identified.
Conclusion. Vitamin D supplementation effectively increased serum 25(OH)D levels and improved muscle strength and lean body mass in women with HT. Further research is needed to explore the mechanisms by which vitamin D may impact metabolic and immune health in HT patients.

Introduction

Hashimoto thyroiditis (HT), also known as chronic autoimmune thyroiditis, along with Graves' disease, is one of the most common organ-specific autoimmune diseases. HT is associated with the infiltration of the thyroid gland by T lymphocytes and B lymphocytes. The latter cells produce characteristic antibodies against thyroperoxidase (Anti-TPO) and thyroglobulin (Anti-TG), ultimately leading to thyroid dysfunction. The prevalence of the disease increases with age and women have over ten times higher risk of developing it [1].

Thyroid hormones influence many biochemical processes in the body, participating in thermogenesis, controlling the rate of basal metabolism, and regulating the metabolism of carbohydrates, proteins, and fats. Therefore, patients with HT often experience symptoms affecting various organs and systems, including excessive weight gain, loss of energy, decreased physical function, depending on the degree of thyroid dysfunction [2].

Vitamin D performs various essential functions in the body. One of its main tasks is the regulation of calcium-phosphate metabolism. However, its role extends beyond the skeletal system. In the form of calcitriol, a steroid-like hormone, it influences the immune system, muscle function, and may also affect metabolic processes, such as weight regulation [3]. Vitamin D deficiency has been linked to numerous chronic diseases, including obesity, metabolic syndrome, hypertension and type 2 diabetes [4]. Many scientific reports postulate that adipose tissue is a source of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) and stimulation of Th17 lymphocytes involved in the initiation of autoimmune diseases [5]. In opposition to this process is Vitamin D, which contributes to changing the immune state from pro-inflammatory to immunological tolerance. The effect of vitamin D on CD4+ T cells is mainly to inhibit the proliferation of the Th1 line and the cytokines they produce. The response of Th2 line lymphocytes is enhanced by promoting the production of anti-inflammatory cytokines: IL-5, IL-10, TGF-β [6]. Additionally, inhibition of the expression of IL-6, the main factor stimulating Th17 lymphocytes involved in autoimmune reactions was observed [7]. This has a potential beneficial effect in people with abnormal body composition and excess fat tissue.

Aim

The aim of the present study was to analyze selected anthropometric measures and body composition in patients with HT, correlate these parameters with serum 25OHD concentration, and assess the impact of vitamin D supplementation on the aforementioned parameters.

Material and methods

Eighty patients under the care of the Endocrinology Outpatient Clinic at the Regional Center for Menopause and Osteoporosis of the The Military Medical Academy Memorial Teaching Hospital in Lodz – Central Veterans Hospital, aged ≥ 18 years, were enrolled in the study. There were 51 patients diagnosed with Hashimoto's disease (Study Group) and 29 patients with non-toxic diffuse goiter or nodular goiter (Control Group). The patients had not previously supplemented with vitamin D or had a break in supplementation of at least 6 months. The study was conducted from September to May.

Patients were diagnosed based on clinical symptoms and biochemical test results. The diagnosis of Hashimoto's disease was established based on anti-thyroid peroxidase (Anti-TPO) and/or anti-thyroglobulin (Anti-TG) antibody concentrations above the upper limit of reference range (positive result), a typical thyroid ultrasound image, and the exclusion of Graves' disease. The Study Group (with Hashimoto's disease) included patients in a euthyroid clinical state undergoing levothyroxine replacement therapy if necessary. The Control Group (without Hashimoto's disease) comprised patients with diagnosed non-toxic diffuse or nodular goiter with low (negative) concentrations of anti-thyroid antibodies.

Patients with chronic conditions affecting vitamin D absorption and metabolism, such as malabsorption syndrome, chronic kidney disease, liver diseases, hyperparathyroidism, Cushing's syndrome/disease, hypogonadism, hyperprolactinemia, other autoimmune diseases, active

cancer, and/or undergoing chemotherapy, as well as those taking medications affecting vitamin D metabolism were excluded from the study.

After qualification and obtaining consent to participate, basic anthropometric measurements (weight, height, waist and hip circumference) were performed. Body composition analysis was conducted using the Bodystat®1500 device. Blood samples were collected for the determination of Total Vitamin D [25(OH)D total], TSH, anti-TPO, and anti-TG levels.

Following the initial procedures, patients were categorized into two groups based on their serum 25(OH)D levels:

- Group A: Patients with vitamin D levels ≥ 20 ng/mL,
- Group B: Patients with vitamin D levels < 20 ng/mL.

Depending on the initial serum 25(OH)D concentration, patients received oral vitamin D (cholecalciferol) once daily for 3 months, at a dose of 4000 IU/ daily for group A and 6000 IU/ daily for group B.

After 3 months of vitamin D supplementation, anthropometric measurements, body composition analysis and laboratory tests were repeated.

Anthropometric Measurements and Body Composition Analysis

Anthropometric measurements were conducted with patients fasting and wearing light clothing. Weight and height were measured with an accuracy of 0.1 kg and 0.1 cm, respectively, and BMI was calculated as weight (kg)/height (m^2). Obesity was defined as BMI ≥ 30 kg/m^2. Waist circumference was measured halfway between the lowest rib and the iliac crest, and hip circumference was measured at the level of the pubic bone, with the criterion for obesity being a waist circumference ≥ 80 cm and WHR < 0.8 indicating gluteofemoral obesity (pear-shaped), while a waist circumference ≥ 80 cm and WHR ≥ 0.8 indicated abdominal obesity (apple-shaped).

Body composition was assessed using bioimpedance measurements with the Bio-impedance Analyser (Bodystat® 1500). Measurements included: fat mass (kg), percentage fat (%Fat), lean mass (kg), and percentage body water (%Water). Muscle strength measurements were conducted using a spring dynamometer for the dominant hand with results expressed in kilograms.

Laboratory Tests

Vitamin D concentration was determined using an electrochemiluminescence test, while TSH concentration was determined using third-generation immunometric tests. Anti-TPO and anti-TG antibody concentrations were measured using an enhanced chemiluminescence method.

Statistical Analysis

Statistical analysis was performed using R-4.3.0 software. Initial parameter concentrations were compared using the Student's t-test or the non-parametric Mann-Whitney test. The Shapiro-Wilk test was employed to assess the normality of parameter distributions. The significance threshold was $p = 0.05$. To examine correlations Spearman and Pearson correlation coefficients and a test for the significance of correlation were used. Changes in evaluated parameters between two time points (baseline and 3 months) were analyzed using the paired Student's t-test or the Wilcoxon non-parametric test with a significance threshold of $p = 0.05$.

Results

The study included 80 women: 29 in the Control Group (women without Hashimoto's disease) aged 33–73 years and 51 in the Study Group (women with Hashimoto's disease) aged 22–78 years. All women were administered vitamin D (Vitrum D3 forte; Takeda) based on their 25(OH)D initial concentration with doses of 4000 or 6000 IU daily. In the Study Group, 32 women were postmenopausal (63%), while in the Control Group, 17 women were postmenopausal (59%). In the group of patients with HT (Study Group), suboptimal 25(OH)D levels were observed in 50%, while in patients without HT (Control Group), 25(OH)D levels < 20 ng/ml were observed in 49% of participants. No statistically significant difference was found between the groups in this regard. In the conducted study, the mean 25(OH)D concentration in both groups was similar, amounting to 19.97 ng/ml and 21.36 ng/ml, respectively.

Women without HT had a significantly smaller hip circumference compared to patients with HT ($p = 0.049$), but the average BMI in both groups

was similar and within the overweight range (28 kg/m^2 vs. 27 kg/m^2). In the Hashimoto's disease group, 41% of women were obese, whereas in the group without Hashimoto's disease, the percentage of women with BMI ≥ 30 kg/m^2 was lower, constituting 27% (**Figure 1**). WHR values

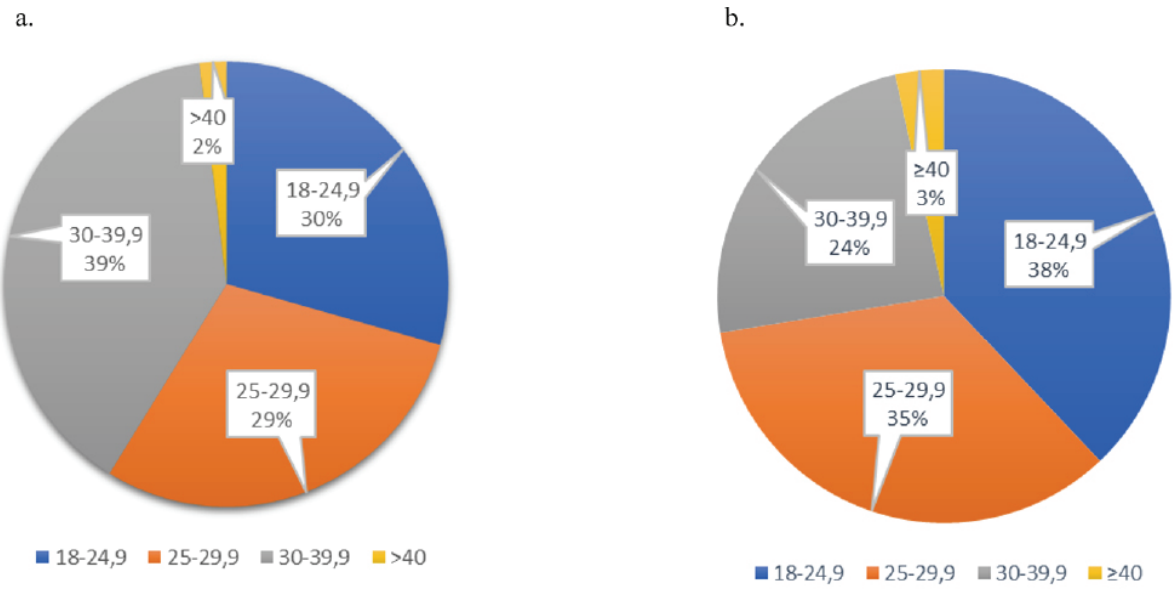


Figure 1. Distribution of BMI (kg/m^2) in the Study Group (a) and Control Group (b).

Table 1. Comparative Characteristics of the Study Group and Control Group at Baseline.

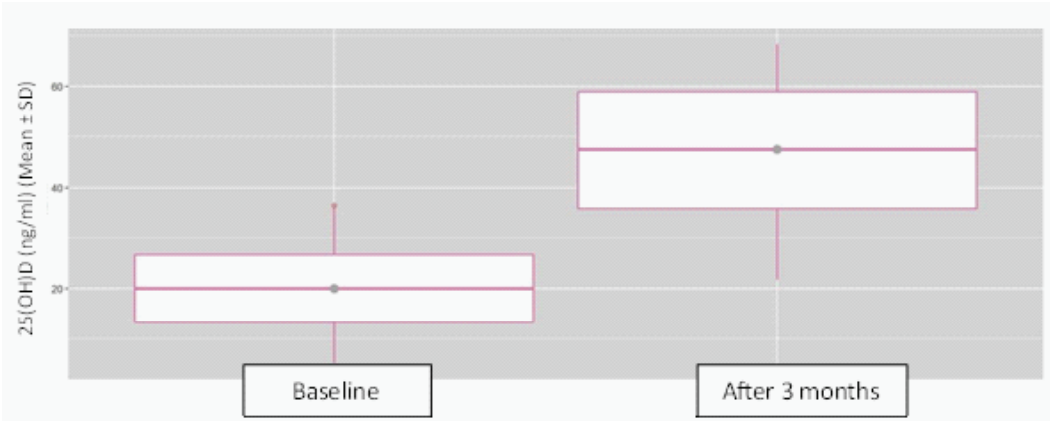
	STUDY GROUP			CONTROL GROUP			
Parameter	**Mean**	**SD**	**Std.error**	**Mean**	**SD**	**Std.error**	**P**
Age	53.98	15.04	29.11	54.35	13.58	2.52	0.93
Weight (kg)	76.40	14.97	2.10	73.13	13.51	2.51	0.32
Height (m)	1.63	0.06	0.01	1.63	0.04	0.01	0.55
BMI (kg/m^2)	28.37	5.44	0.76	27.90	4.92	0.93	0.70
Waist (cm)	87.08	15.51	2.17	81.50	12.30	2.33	0.08
Hips (cm)	106.76	11.75	1.65	102.71	12.47	2.36	**0.049**
WHR	0.81	0.07	0.01	0.79	0.06	0.01	0.20
25(OH)D (ng/ml)	19.97	6.72	0.94	21.36	10.90	2.02	0.54
TSH (U/l)	2.01	1.19	0.17	1.19	0.62	0.12	**0.002**
anti-TPO (IU/ml)	297.98	214.40	30.02	15.83	9.19	1.71	**0.001**
anti-TG (IU/ml)	762.85	1098.48	153.82	31.13	39.18	7.28	**0.001**
Muscle strenght (kg)	37.80	6.08	0.86	36.97	5.88	1.11	0.93
Fat mass (kg)	30.47	11.93	1.67	27.15	10.75	2.03	0.21
Fat mass (%)	38.37	9.12	1.28	36.34	1.54	8.17	0.32
Lean mass (kg)	46.04	5.60	0.79	45.29	5.57	1.05	0.36
Body water (%)	47.34	5.91	0.83	49.40	5.48	1.04	0.13

were comparable between both groups. No differences were observed in terms of body composition and muscle strength between the Study Group and the Control Group. Patient characteristics at baseline are presented in **Table 1**.

After 3 months of vitamin D supplementation, serum 25(OH)D concentrations significantly increased in all women, indicating good compliance (**Figure 2**). In the group of patients with HT, the average concentration was 47.460 ± 1.61 SD ng/dl, while in the group of patients without HT, it was 49.085 ± 2.51 SD ng/dl.

In patients with HT, a statistically significant increase in lean body mass (p = 0.002) and

a.



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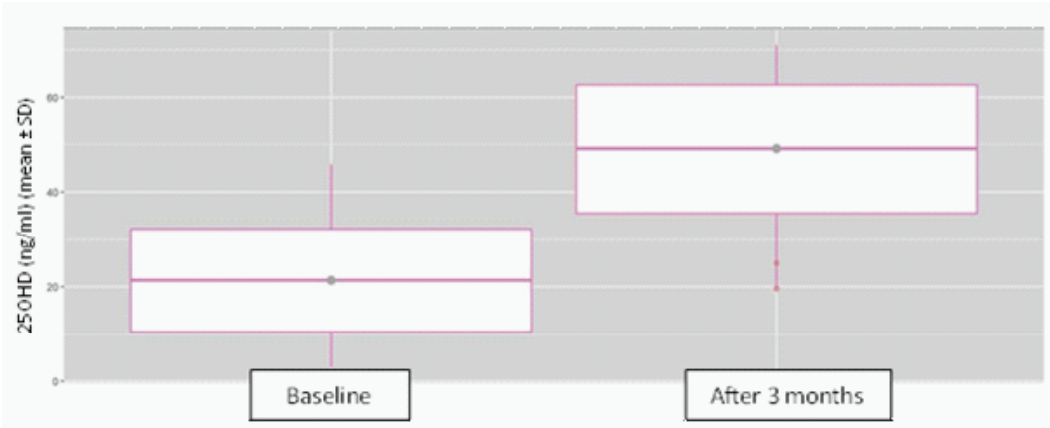

Figure 2. Change in 25(OH)D concentration after 3 months in the Study Group (p = 0.001) (a) and in the Control Group (p = 0.001) (b)

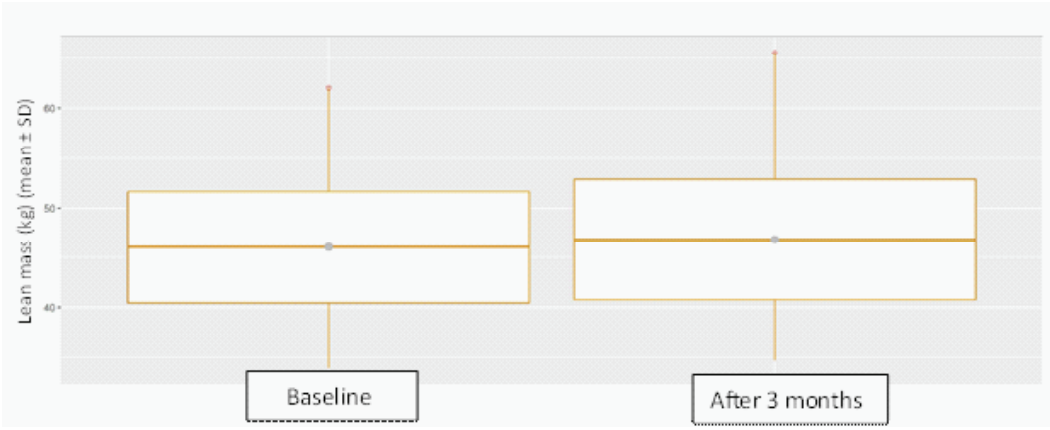

Figure 3. Change in Lean Body Mass (kg) after 3 months in the Study Group (p = 0.002).

muscle strength (p = 0.02) was observed (**Figures 3** and **4**). On the other hand, women without HT showed improvements in muscle strength (p = 0.01) and a reduction in mean hip circumference by 0.5 cm (p = 0.03) (**Figures 4** and **5**), but no impact on parameters related to lean body mass was noted.

Additionally, the correlation analysis between baseline 25(OH)D concentration and anthropometric parameters (waist circumference, hip circumference, BMI, WHR) and body composition parameters did not reveal statistically significant relationships. Only a moderately strong, inverse relationship between 25(OH)D concentration and

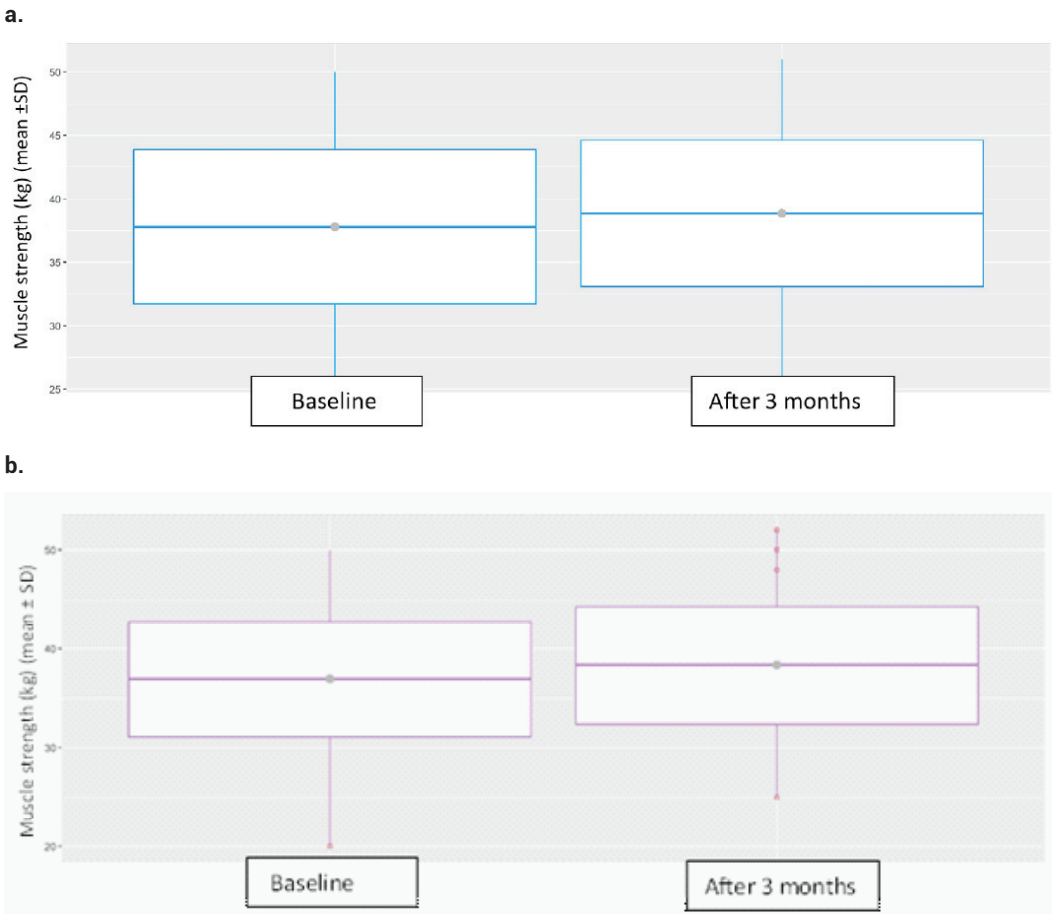

Figure 4. Change in muscle strength (kg) after 3 months in the Study Group (p = 0.02) (a) and in the Control Group (p = 0.01) (b).

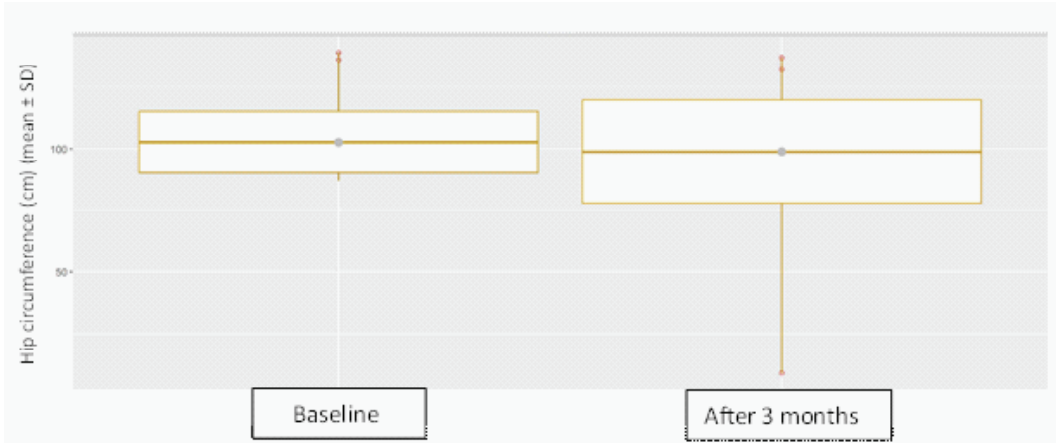

Figure 5. Change in hip circumference (cm) after 3 months in the Control Group (p = 0.03)

BMI in the Control Group was observed (R = -0.44; p = 0.04) (data not shown).

Correlations between the concentration of 25(OH)D and the tested parameters were also analyzed after 3 months of supplementation, showing no statistically significant results.

A correlation analysis between TSH levels and the assessed anthropometric parameters at the baseline and after 3 months was performed, but no statistically significant relationships were observed (data not shown).

Discussion

Vitamin D deficiency is common in the polish population. In a population study by Płudowski et al., involving 5775 adult volunteers from 22 cities in Poland, it was found that 89.9% of them had a deep deficit or insufficient supply of vitamin D, i.e., 25(OH)D levels below 30 ng/ml [8]. In our study suboptimal 25(OH)D levels were observed in 50% patients with HT, while in patients without HT 25(OH)D levels < 20 ng/ml were observed in 49% of participants.

In recent years, many researchers have analyzed the role of vitamin D in the etiopathogenesis of obesity. Studies have shown lower serum 25-hydroxyvitamin D levels in obese individuals compared to those with normal body weight [9–11]. This is confirmed by a meta-analysis conducted by Saneei et al., which found a statistically significant inverse relationship between BMI and serum 25(OH)D levels [12]. Vimaleswaran et al., using Mendelian randomization, suggested a relationship between BMI and serum 25(OH) D levels. It was shown that an increase in BMI is linearly associated with a decrease in the concentration of 25(OH)D in serum. However, there was no evidence of changes in BMI values with an increase in 25(OH)D levels in serum [13]. The mechanism of vitamin D deficiency is explained, among other factors, by increased accumulation of vitamin D in muscle, adipose tissue, and the liver. In obese patients, the content of 25(OH)D in these tissues increases, resulting in a lower level of vitamin D in the serum [14, 15]. Additionally, the stimulation of parathyroid hormone release due to relative vitamin D deficiency leads to calcium influx into adipocytes, stimulating lipogenesis [16]. In our study, the mean 25(OH)D concentration in patients with HT (Study Group) was 19.97 ng/ml, and in patients without HT (Control Group) it was 21.36 ng/ml. We did not find a statistically significant difference between the groups and there was no relationship between BMI and serum 25(OH)D levels in women with HT. However, in women without autoimmune thyroid disease, we observed a moderately strong, negative trend between these parameters. The narrow range of serum vitamin D levels in our patients may have influenced the observation of a possible relationship between 25(OH)D and BMI. Similarly, Baradaran et al. did not confirm such a relationship in a population of 259 healthy adults. The authors concluded that the relationship between BMI and serum 25(OH)D levels should also be considered in correlation with the age of the studied population [17].

Vitamin D deficiency may be also related to an improper body composition, leading to a reduction in lean body mass through the loss of bone mineral density, decreased muscle mass, strength, and function [18]. Randomized, placebo-controlled studies have shown that vitamin D supplementation can slow down the rate of bone loss in older individuals [19]. A study of 341 healthy individuals found that lower vitamin D levels are associated with increased overall body fat mass measured by bioimpedance, regardless of BMI [20]. Karefylakis et al. demonstrated that vitamin D therapy at a dose of 2000 IU per day for 6 months had no effect on final BMI and fat content measured by bioelectrical impedance analysis in 40 overweight and obese patients [21]. The analysis of twenty randomized controlled trials conducted by Karampel et al. concluded that, compared to placebo, vitamin D supplementation did not cause a significant reduction in BMI, WC and WHR. However, in subgroups of women, in studies from the Asian region and with an intervention duration of ≥ 6 months, a favorable and significant reduction of BMI and WC ($p < 0.026$) were observed [22]. Based on scientific evidence and recommendations [23] indicating that the time required to achieve optimal serum 25(OH) D concentrations is 8–12 weeks, the observation period in our study was set to 3 months. Patients received higher doses of vitamin D3 to reach optimal serum levels within this time, then the dosage was reduced to 2000 IU per day. In our population, both in women with HT and in healthy

women, we did not find a relationship between 25(OH)D levels and the amount of body fat. Additionally, cholecalciferol supplementation, similar to the study mentioned above, did not result in significant changes in this regard. This is also confirmed by a meta-analysis conducted by Golzarand et al., which showed that 25(OH)D levels were inversely correlated with the percentage of body fat, but cholecalciferol supplementation had no effect on its reduction over time [24].

Sun et al. investigated the effect of cholecalciferol supplementation on lean body mass in a population of 45 healthy individuals who received 420 IU of vitamin D3 daily, while 47 received a placebo. After a one-year observation period, an increase in lean body mass was observed in the intervention group, but no effect of treatment on other body composition indices was observed [25]. In a population of similar to our group 80 postmenopausal Brazilian women with hypertension, vitamin D supplementation (1000 IU) was observed to be a significant protective factor against the development of sarcopenia, causing a significant increase in muscle strength and counteracting the progressive loss of lean body mass. The intervention period was 9 months, and lean body mass was measured using dual-energy X-ray absorptiometry (DXA) [26]. Similar conclusions were reached by a meta-analysis of 13 randomized, placebo-controlled trials, which showed that vitamin D supplementation increases muscle strength in postmenopausal women [27]. In contrast, Manson et al., in a study involving 25,871 healthy individuals, found no effect of vitamin D supplementation (2000 IU) on body weight, BMI and fat-free mass. The observed effects were independent of gender, race or baseline 25(OH)D concentration [28]. In our study, we demonstrated that in patients with HT, there was a statistically significant increase in lean body mass ($p = 0.002$) and muscle strength ($p = 0.02$), while in healthy women, only improvements in muscle strength were observed ($p = 0.01$). This may play a significant role, particularly in obese patients and those over the age of 75, for whom the recommended prophylactic dose of vitamin D should be higher than in the general population.

In order to eliminate the influence of decompensated hypothyroidism on the studied parameters, all women of study our population with HT remained euthyroid, and both groups showed no differences in the studied anthropometric parameters at the baseline. Wolf et al. found that in patients after thyroidectomy with short-term uncompensated hypothyroidism, the body water content was significantly lower, while the fat tissue percentage was significantly higher compared to a group without these disorders [29]. After the initiation of levothyroxine therapy, body composition did not significantly differ between the study and control groups. In the study by Mousa et al., comparing 99 patients with Hashimoto's thyroiditis (HT) and normal TSH values with 202 healthy women and men, no difference in BMI or fat content measured by bioimpedance was observed [30]. On the other hand, Adamska et al. demonstrated that women with HT had a higher percentage of body fat, measured by bioimpedance, but did not exhibit greater android, gynoid fat, or visceral fat mass compared to the control group, However, the average age of individuals in this study was much lower than in our population [31].

Numerous studies have explored the potential impact of slight changes in thyroid function in euthyroid patients on anthropometric parameters and related indices [32–39]. Findings regarding the relationship between serum Thyroid-Stimulating Hormone (TSH) within reference values and Body Mass Index (BMI) remain conflicting. Some publications confirm a positive correlation between serum TSH levels and BMI [34, 35], while others do not observe such correlations [36–38]. In our study, we also did not find a relationship between TSH concentration and BMI, as well as fat and lean body mass. Analyzing the influence of BMI on the hormonal status of patients, it has been shown that obese individuals have higher TSH levels [39]. This is likely due to increased release of adipokines and proinflammatory cytokines from adipose tissue, promoting the recruitment of additional immune cells and exacerbating systemic inflammation [40–42]. The rise in TSH levels in obese individuals is also associated with the influence of leptin, adiponectin, and resistin on pro-thyrotropin-releasing hormone (pro-TRH) production in the hypothalamus. These adipokines produced by adipose tissue may participate in the interaction between adipocytes and the hypothalamus, resulting in increased release of TRH and TSH and consequently, the production and secretion of free thyroxine (FT4) [42–44].

Our study had some limitations. Blood samples were collected between September and May to avoid interference with sun exposure; therefore, serum 25(OH)D levels did not reflect the full vitamin D status throughout the year. Other limitations include a relatively short observation period, small study population and the use of a less accurate method for assessing body composition, such as bioimpedance measurement, compared to DXA or MRI.

Conclusions

In euthyroid patients with HT, the values of anthropometric parameters and body composition were similar to those in healthy people. Obesity and vitamin D deficiency are common, which is also confirmed in the population of HT patients. Vitamin D supplementation may and even should be recommended to patients with HT due to its potentially beneficial effect on the increase in lean body mass and muscle strength, as well as its anti-inflammatory effect. Further research is needed on the effect of vitamin D on metabolic processes in patients with autoimmune thyroid diseases

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Bioethics Committee approval
The research project was approved by the Bioethics Committee of the Medical University of Lodz (resolution RNN/02/17/KE).

Conflict of interest statement
The authors declare no conflict of interest.

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