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Vitamin D Deficiency and Relation to the New York Heart Association Functional Class in Chronic Heart Failure

Kronik Kalp Yetmezliğinde D Vitamini Eksikliği ve New York Kalp Cemiyeti Fonksiyonel Sınıfıyla İlişkisi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Heart failure is an important mortality and morbidity. In this study, we aimed to investigate the frequency of vitamin D deficiency in chronic heart failure patients who live in a sunny region and to evaluate its relationship with the New York Heart Association (NYHA) functional classes.

Methods: The study included 657 patients. Demographic clinical, and laboratory parameters were evaluated according to the NYHA classes. Ordinal regression analysis was used to determine the parameters defining the NYHA class.

Results: The median serum 25-hydroxy-vitamin D [25(OH)D] level of study population was 16.88 ng/mL. It was <20 ng/mL in 63.8% and 20-29 ng/mL in 32.9% of the patients. A 25(OH) D <20 ng/mL was significantly more common in women compared to men (74.1% vs. 60%, *P* < .001). Moreover, 109 patients (16.6%) had severe vitamin D deficiency [25(OH)D <10 ng/mL]. Only 22 (3.3%) patients had a 25(OH)D level >30 ng/mL. 25(OH)D level was positively correlated with eGFR, calcium, albumin, hemoglobin, transferrin saturation, serum iron, while a negative correlation was found with heart rate, parathormon, NT-proBNP, and CRP. Together with dereased ß blocker use, increase in N-terminal pro-brain natriuretic peptide levels and left atrial diameter, a decrease in vitamin D level (OR: 0.970, 95% CI: 0.945-0996, *P*=.024) was independently associated with an increase in the New York Heart Association class.

Conclusion: Vitamin D deficiency and insufficiency are common in patients with chronic heart failure, and vitamin D level is an important determinant of the NYHA functional class in patients with heart failure.

Keywords: Heart failure, Vitamin D, New York Heart Association (NYHA)

ÖZET

Amaç: Kalp yetersizliği, önemli bir ölüm ve morbidite nedenidir. Bu çalışmada kronik kalp yetersizliği olan ve güneşli bir bölgede yaşayan hastalarda D vitamini eksikliği sıklığını ve D vitamini eksikliği ile New York Kalp Cemiyeti fonksiyonel sınıfları arasındaki ilişkiyi araştırmayı amaçladık.

Yöntemler: Çalışmaya 657 hasta dahil edildi. New York Kalp Cemiyeti sınıflarına göre demografik, klinik ve laboratuvar parametreleri değerlendirildi. New York Kalp Cemiyeti sınıflarını belirleyen parametreleri belirlemek için ordinal regresyon analizi kullanıldı.

Bulgular: Çalışma popülasyonunun medyan serum 25-hydroxy-vitamin D [25(OH)D] düzeyi 16,88 ng/mL idi. Hastaların %63.8'inde 25(OH)D <20 ng/mL ve %32.9'unda 20-29 ng/mL arasındaydı. 25(OH)D'nin <20 ng/mL olması kadınlarda anlamlı olarak daha yaygındı (74.1% vs. 60%, *P* < ,001). Ayrıca 109 hastada (%16.6) ciddi D vitamini eksikliği [25(OH)D <10 ng/mL] vardı. Yalnızca 22 (%3,3) hastada 25(OH)D >30 ng/mL idi. 25(OH)D düzeyi tGFH, kalsiyum, albumin, hemoglobin, transferrin satürasyonu, serum demiri ile pozitif, kalp hızı, parathormon, NT-proBNP ve CRP ile negative bağıntılıydı. D vitamini düşüklüğü (OR: 0,970, %95 CI: 0,945-0,996; *P*=,024), ß bloker kullanımının azalması, N-terminal pro-brain natriuretic peptide seviyeleri ve sol atriyum çapındaki artış ile birlikte New York Kalp Cemiyeti sınıfındaki artışla ile bağımsız ilişkiliydi.

Sonuç: Kronik kalp yetersizliği hastalarında D vitamini eksikliği ve yetersizliği yaygın bir durumdur ve D vitamini seviyesi kalp yetersizliği olan hastalarda New York Kalp Cemiyeti fonksiyonel sınıfının önemli bir belirleyicisidir.

Anahtar Kelimeler: Kalp yetmezliği, D vitamini, New York Kalp Cemiyeti (NYHA)

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At the 36th Turkish Cardiology Congress with International Participation, the data of that period were presented as an oral presentation with the title of "Frequency of Vitamin D insufficiency and deficiency in heart failure patients-single center registry in Turkey."

Heart failure (HF) is a major health problem that affects more than 23 million patients worldwide, causing increased mortality and morbidity.[1] Despite significant progress in treatments, the mortality rate of HF is high, between 20% and 40%.[2,3] Therefore, new biomarkers and treatments are needed. One of these biomarkers is vitamin D, a hormone that mainly regulates calcium and phosphate metabolism. Vitamin D deficiency has recently been reported in association with cardiovascular events such as coronary artery disease, myocardial infarction, HF, hypertension, and stroke.[4,5]

In 2011, the Endocrine Society published clinical practice guidelines for the assessment, treatment, and prevention of vitamin D deficiency. Accordingly, it is recommended that vitamin D deficiency be defined as 25-hydroxy-vitamin D [25(OH)D] below 20 ng/mL, and vitamin D insufficiency as 25(OH)D of 21-29 ng/mL.[6] It is estimated that 30%-50% of the world population has vitamin D deficiency in about 1 billion people.[7,8] Heart failure patients become susceptible to vitamin D deficiency due to chronic disease, inadequate ultraviolet B exposure, malnutrition, or impaired vitamin D metabolism.[9,10] Therefore, vitamin D deficiency has been found to be very common in 80%-95% of the HF population.[11]

The association between vitamin D deficiency and higher New York Heart Association (NYHA) functional classes, shorter 6-minute walking distance, increased N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, and poor outcomes such as hospital readmission or all-cause mortality has been reported in patients with HF.[12-15]

The aim of this study was to investigate the frequency of vitamin D deficiency in outpatients with chronic HF in a region (Antalya) that is sunny in all seasons and whether there is a relationship between vitamin D deficiency and NYHA functional classes.

Methods

Patient Population and Clinical/Biochemical Assessment

According to the medical records of the HF outpatient clinic, 745 patients with known vitamin D levels were retrospectively evaluated in our tertiary care hospital between April 2016 and December 2019. Eighty-eight patients were excluded because they received vitamin D replacement, and 657 patients were included in the study. The study complies with the Declaration of Helsinki, was approved by Antalya Training and Research Hospital ethics committee on 03/07/2020 with the decision numbered 10/12.

Inclusion criteria are listed below: (i) diagnosis of HF, (ii) NYHA functional classes I-IV, (iii) left ventricular ejection fraction (LVEF) <50%, (iv) age ≥18 years, (v) both male and female sex.

ABBREVIATIONS

CRP	C-reactive protein
eGFR	Estimates glomerular filtration rate
HF	Heart failure
IQR	Interquartile range
LVEF	Left ventricular ejection fraction
NT-proBNP	N-terminal pro-brain natriuretic peptide
NYHA	New York Heart Association
OR	Odds ratios
PTH	Parathormone

Patients who were already taking vitamin D supplements were excluded. Demographic, echocardiographic, biochemical, and clinical parameters were obtained from medical records. Patients were evaluated for vitamin D deficiency as 25(OH)D <20 ng/mL and vitamin D insufficiency as 25(OH)D of 21-29 ng/mL.[6] The severity of HF was assessed from physical examination notes by evaluating each patient at rest, dressing, walking, and climbing the stairs.[16] NYHA scores ranged from I (no symptoms of HF) to IV (symptoms at rest). The NYHA functional classes of all patients were determined from medical records.

Clinical and biochemical properties of all patients were evaluated including 25(OH)D, body mass index, creatinine, estimates glomerular filtration rate (eGFR), serum electrolytes, albumin, uric acid, hemoglobin, iron profiles, parathormone (PTH), NT-proBNP levels, high sensitive troponin T, C-reactive protein (CRP), electrocardiogram, echocardiography findings, comorbidities, and medications. Vitamin D tests were measured by the chemiluminescence method on the Beckman coulter DxI 800 device (Beckman Coulter Inc. CA, USA). Estimates glomerular filtration rate was calculated as using the following formula: 186.3 × (serum creatinine in mg/dL) – 1.154 × age – 0.203 × (0.742 for women).

Statistical Analysis

The distribution of the data was tested with the Kolmogorov–Smirnov test. Results were expressed as means with standard deviations if normally distributed or medians with interquartile ranges if non-normally distributed. Categorical variables were reported as percentage of observations. Categorical variables between groups were analyzed using chi-square test. Comparisons between groups were performed using analysis of variance and Kruskall–Wallis test or chi-square test for abnormally and normally distributed data, respectively. Correlation was evaluated by the Pearson's or Spearman's rho correlation test. Ordinal regression analysis was used to determine the parameters determining NYHA classes. For this analysis, it was chosen from the parameters previously examined in the literature. Results were presented as odds ratios (OR) with 95% CIs. A *P*-value of .05 was considered statistically significant. Statistical analyses were performed with SPSS software version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Vitamin D Status

The median age of 657 patients included in the study was 63 years [interquartile range (IQR): 54-72 years], 73.5% of them were male (n=483) and 26.5% were female (n=174). Vitamin D deficiency was significantly more common in women than in men. The median serum vitamin D level of study population was calculated as 16.88 [IQR: 11.7-22.6] ng/mL. Vitamin D levels in women were significantly lower than in men (respectively, 13.79 [IQR: 9.09-20.12] ng/mL, 17.75 [IQR: 12.7-23.35] ng/mL, $P < .001$). It was found that 499 patients (63.8%) had vitamin D deficiency [25(OH)D <20 ng/mL] and 216 patients (32.9 %) had vitamin D insufficiency [25(OH)D of 20-29 ng/mL]. Vitamin D deficiency was significantly more common in women than men (74.1% vs. 60%, $P < .001$, respectively) (Figure 1). Vitamin D insufficiency was similar in both genders (23.6% in women vs. 36.2% in men,

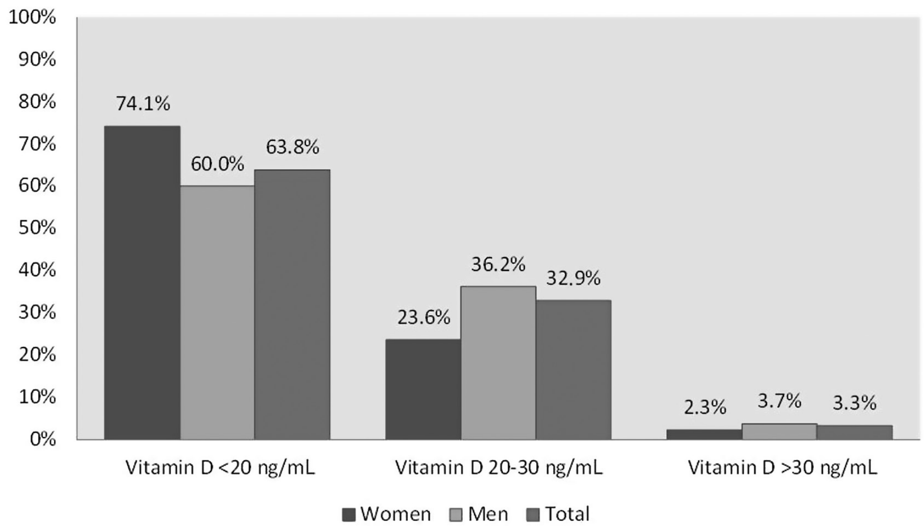

Figure 1. Vitamin D Values by Gender

P=.163). In addition, 109 patients (16.6%) showed severe vitamin D deficiency [25(OH)D <10 ng/mL]. Only 22 (3.3%) patients had normal vitamin D levels [25(OH)D >30 ng/mL]. The majority of patients (96.7%, n=635) had vitamin D deficiency or insufficiency [25(OH)D <30 ng/mL].

Basal Characteristics by NYHA Functional Classes

The patients were classified into 3 groups according to NYHA functional classes. The New York Heart Association class III (n=137) and IV (n=18) patients with severe HF symptoms were evaluated in the same group. The comparison of NYHA classes is presented in Table 1. Vitamin D levels were significantly lower in NYHA class III-IV group compared to NYHA group I and II (14.04 [IQR: 9.45-20.33] ng/mL, 17.51 [IQR: 12.55-23.26] ng/mL, 17.86 [IQR: 12.84-23.38] ng/mL, *P* < .001, respectively). Age, duration of HF, the presence of hypertension, diuretic usage, and heart rate were higher in NYHA class III-IV group. While angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, ß-blockers, and mineralocorticoid receptor antagonists usage rate was lower in NYHA class III-IV group, left atrial size and systolic pulmonary artery pressure were significantly higher. In laboratory tests, a significant difference was found between groups in eGFR, albumin, calcium, uric acid, PTH, hemoglobin, serum iron, transferrin saturation, NT-proBNP, high sensitivity troponin T, and CRP levels (Table 1).

Correlations for Vitamin D

Serum vitamin D levels were significantly correlated in univariate analyses with several parameters (Table 2). Vitamin D was positively correlated with eGFR, calcium, albumin, hemoglobin, transferrin saturation, serum iron, while a negative correlation was found with heart rate, parathyroid hormone, NT-proBNP, and CRP.

Independent Predictors of NYHA Functional Classes

Ordinal regression analyses of echocardiographic, biochemical parameters, and medical treatments to determine NYHA classes are shown in Table 3. The decrease in vitamin D levels was found to be associated with the increase of the NYHA classes (OR: 0.970, 95% CI: 0.945-0996, *P*=.024). However, an increase in NT-proBNP levels (OR: 1.786, 95% CI: 1.184-2.695, *P*=.006) and left atrium diameters (OR: 1.032, 95% CI: 1.006-1.059, *P*=.017) were found to be associated with an increase in NYHA classes. In addition, the reduction in ß blocker use was found to be associated with increased NYHA classes (OR: 2.113, 95% CI: 1.076-4.153, *P*=.03).

Discussion

Our study demonstrated that vitamin D deficiency and insufficiency are common in patients with chronic HF. Although our region has a sunny climate in all seasons, it was observed that the prevalence of vitamin D deficiency was high in HF patients. Therefore, our study provided information for predicting the prevalence of vitamin D deficiency in patients with HF in our country. However, we have seen that vitamin D level is an important determinant in NYHA functional classes of HF patients. Lower vitamin D levels were strongly associated with worse NYHA classes.

Vitamin D, a fat-soluble hormone, can either be taken from dietary sources or synthesized by human skin by exposure to solar ultraviolet B radiation.[17] The role of vitamin D in the pathophysiology of HF is explained by its downregulation of the renin–angiotensin system, its protection against angiogenesis, and its regulatory effects on inflammatory processes.[18,19]

Around 1 billion people worldwide are affected by either vitamin D deficiency or insufficiency.[20] Data from the National Health and Nutrition Examination Survey estimated the prevalence of vitamin D deficiency as 28.9%.[21] In 2 studies that did not include large numbers of patients, the prevalence of vitamin D deficiency [25(OH)D <20 ng/mL] in patients with HF was reported as 56% and 75.6%, respectively.[22,23] In our study, the median 25(OH)D levels were 16.88 ng/mL lower than those generally considered optimal,[6] with the prevalence of vitamin D deficiency [25(OH)D <20 ng/mL] 71.4% in women and 63.8% in all. The fact that the rate of vitamin D deficiency is higher in female patients may be due to women spending less time outdoors than men. In an analysis, the proportion of patients with 25(OH)D <30 ng/mL in 289 patients was 81% in white patients.[24] However, in this study, HF was accepted by the patient's self-report regardless of LVEF. In our study, the rate of patients in this group was

Table 1. Baseline Demographics According to NYHA Functional Classes

Variable	All Patients (n=657)	NYHA Class I (n=205)	NYHA Class II (n=297)	NYHA Class III-IV (n=155)	*P*
Age (years)	63 (54-72)	59 (52-67)	64 (55-72)	68 (57-76)	<.001
Female (%)	26.5	22.4	26.6	31.6	.148
BMI (kg/m²)	26.8 (23.8-30.1)	26.7 (24.2-29.7)	26.9 (23.8-30.3)	26.8 (23.2-31.1)	.777
Disease duration (months)	12 (2-48)	6 (2-24)	12 (2,5-48)	12 (3-60)	.001
Diabetes (%)	37.9	33.7	37	45.2	.077
Hypertension (%)	52.4	43.4	54.2	60.6	.004
ACE-I/ARB (%)	80.5	86.8	83.5	66.5	<.001
β-Blockers (%)	92.1	93.7	93.9	86.5	.012
MRA (%)	68.6	73.7	71.4	56.8	.001
Diuretics (%)	64.8	48.8	67.3	81.3	<.001
Systolic BP (mm Hg)	110 (100-130)	110 (100-130)	110 (110-130)	120 (100-120)	.225
Diastolic BP (mm Hg)	60 (60-80)	65 (60-80)	60 (60-80)	60 (60-70)	.079
Heart rate (bpm)	76 (67-86)	74 (67-84)	75 (66-86)	81 (72-91)	<.001
LVEF (%)	30 (20-35)	30 (22-35)	30 (22-35)	30 (20-35)	.594
Left ventricular diastolic diameter (mm)	57 (53-63)	58 (53-63)	57 (52-62)	57 (53-63)	.675
Left atrial size (mm)	45 (40-49)	44 (39-47)	44 (40-49)	46 (43-51)	<.001
Systolic pulmonary artery pressure (mm Hg)	40 (31-55)	35 (30-50)	40 (30-50)	48 (35-58)	<.001
Creatinine (mg/dL)	1.09 (0.94-1.33)	1.04 (0.92-1.21)	1.08 (0.94-1.31)	1.21 (0.99-1,58)	<0.001
eGFR (mL/min/1.73 m²)	67.2 ± 24 (7.1-201)	73.6 ± 23.6 (9.9-183)	68 ± 24 (52-81.2)	57 ± 21.3 (7.1-114.5)	.029
Sodium (mmol/L)	139 (136-140)	139 (137-140)	139 (137-140)	139 (136-140)	.685
Albumin (g/dL)	4.2 (3.9-4.5)	4.3 (4.1-4.6)	4.2 (4-4.5)	4 (3.7-4.3)	<.001
Calcium (mg/dL)	9.4 (9.1-9.8)	9.4 (9.1-9.8)	9.5 (9.1-9.9)	9.2 (8.9-9.70)	.002
Uric acid (mg/dL)	6.7 (5.7-8.3)	6.2 (5.2-7.6)	6.9 (5.8-8.4)	7.5 (5.8-9.1)	.001
25(OH)D level (ng/mL)	16.88 (11.7-22.6)	17.51 (12.5-23.2)	17.86 (12.8-23.3)	14.04 (9.4-20.3)	<.001
PTH (ng/L)	64 (42.2-95)	52 (36-77)	66 (45-96)	80 (48-119)	<.001
Hemoglobin (g/dL)	13.1 ± 1.8 (8.3-17.5)	3.5 ± 1.8 (9.3-17.4)	13.3 ± 1.7 (8.9-17.5)	12.1 ± 1.7 (8.3-16.5)	.01
Serum iron (µg/dL)	66 (44-92.2)	73.5 (48.7-104)	69 (49-95)	49 (33-71.5)	<.001
Ferritin (µg/L)	62 (31-111)	64.5 (33.75-113.5)	64 (31-114.5)	54.5 (29.7-99)	0.314
Transferrin saturation (%)	19.4 (12.3-27.1)	21.7 (14.2-29.2)	20.5 (13.4-28.4)	13.5 (8.7-21.8)	<.001
NT-proBNP (ng/L)	1653 (632-3992)	1025 (410-2565)	1461 (515-3696)	3294 (1756-8447)	<.001
High sensitive troponin T (ng/L)	18 (11-32)	14 (8-20)	18 (11-32)	29 (16-51)	<.001
CRP (mg/dL)	4.9 (2-11)	3 (1.7-8)	5 (2-10)	6.2 (3-16)	<.001

Normally distributed data are presented as mean ± standard deviation. Non-normally distributed data are presented as median (interquartile range). 25(OH)D, 25-hydroxy-vitamin D; BMI, body mass index; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonists; BP, blood pressure; bpm, beats per minute; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein.

much higher, 96.7% [25(OH)D <30 ng/mL], and diagnosis of HF was made echocardiographically according to the guidelines to assess LVEF.[16] In another study evaluating 25(OH)D levels in 3009 HF patients, vitamin D deficiency [25(OH)D <10 ng/mL] was found to be 28%, while only 8.8% had vitamin D at optimal levels [25(OH)D >30 ng mL].[25] Moreover, similar to our study, the study was conducted in a region receiving solar radiation. But only 3.3% of the patients had normal vitamin D levels [25(OH)D >30 ng/mL]. We also found that the rate of severe vitamin D deficiency was higher than previously reported. While

Table 2. Univariate Correlations for 25-hydroxy-vitamin D

Variables	Correlation Coefficient (Spearman's Rho or Pearson)	*P*
Heart rate	–0.159	<.001
eGFR	0.103	.008
Calcium	0.229	<.001
Albumin	0.276	<.001
Hemoglobin	0.225	<.001
Transferrin saturation	0.183	<.001
Serum iron	0.209	<.001
Parathyroid hormone	–0.270	<.001
NT-proBNP	–0.154	<.001
CRP	–0.122	.002

eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein.

vitamin D levels of <10 ng/mL were reported in 12.2%, we found it to be 16.6% in our study group.[26]

The prevalence of vitamin D deficiency in Turkish adult population has been reported between 33.4% and 74.9% in different studies.[27,28] As far as we know, there is no clear data indicating the prevalence of vitamin D deficiency in HF patients in Turkey. Therefore, our study can provide information for predicting the prevalence of vitamin D deficiency in patients with HF in our country. The lower vitamin D levels seen in patients with HF are explained in part by reduced sun exposure due to limited functional capacity and limited outdoor activities. This is more noticeable in the summer when there is abundant solar radiation.[29] The reason why vitamin D deficiency is observed more prominently in NYHA III-IV patients may be the shorter time spent outside.

Table 3. Ordinal Regression Analysis for NYHA Classes

	Multivariable Analysis	
Variables	**Odds Ratio (95% CI)**	***P***
25(OH)D	0.970 (0.945-0996)	.024
NT-proBNP	1.786 (1.184-2.695)	.006
eGFR	0.996 (0.986-1.005)	.376
Albumin	0.792 (0.492-1.277)	.803
CRP	0.999 (0.992-1.006)	.902
Ferritin	1.000 (0.999-1.001)	.710
Systolic BP	0.992 (0.983-1.002)	.112
Left atrial size	1.032 (1.006-1.059)	.017
Systolic pulmonary artery pressure	1.007 (0.994-1.020)	.305
ACE-I/ARB usage	1.427 (0.879-2.316)	.151
ß-blockers usage	2.113 (1.076-4.153)	.03
MRA usage	1.318 (0.852-2.038)	.214

Values for NT-proBNP were log transformed before analysis.
25(OH)D, 25-hydroxy-vitamin D; NT-proBNP, N-terminal pro-brain natriuretic peptide; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonists.

An activated renin–angiotensin system caused by high levels of renin in vitamin D receptor knockout mice has been shown to induce the development and progression of HF. This situation causes cardiac hypertrophy, hypertension, and increased water intake and sodium retention symptoms of HF.[18,30] A lower concentration of 25(OH) D was associated with higher plasma renin activity and higher CRP and NT-proBNP in mild to moderate HF.[31] Another study showed that, in addition to a poor correlation between 25(OH)D levels and B-type natriuretic peptide levels, vitamin D concentrations were also modestly associated with albumin levels and nutritional status in advanced HF in Japan.[32] Supporting these results, we found that vitamin D was positively correlated with albumin and negatively correlated with NT-proBNP and CRP.

Studies have shown that low 25(OH)D levels in HF patients with low LVEF are associated with shorter 6-minute walking distance and impaired functional capacity as determined by lower peak oxygen uptake in a cardiopulmonary test.[13,33] It has been reported that 25(OH)D levels are negatively associated with the NT-proBNP and inversely associated with higher NYHA classes and impaired LV function. However, when the level of physical exercise was included as a covariant in multivariate modeling, the inverse relationship between vitamin D levels and NYHA class lost significance.[12] In our analysis, a decrease in vitamin D level and use of ß-blockers, an increase in NT-proBNP, and left atrial diameter were significantly associated with NYHA class in multivariate modeling. In our study, medical treatment rates were lower in patients with higher NYHA classes. Because NYHA III-IV patients are more fragile (hypotensive and impaired kidney function), clinicians often may not be in a hurry to initiate and titrate drug doses. In regression analysis, including medical treatments, vitamin D level was independently associated with an increase in NYHA class.

Recent studies have shown that vitamin D deficiency is an important predictor of all-cause mortality and HF rehospitalization in patients with HF.[31,34] But whether supplementation improves outcome is unknown. Several studies have reported that vitamin D suppresses the release of pro-inflammatory cytokines.[35] However, despite a decrease in brain natriuretic peptide, vitamin D supplementation was not found to improve functional capacity or quality of life in elderly HF patients with vitamin D deficiency.[36] It was reported in another study that restoration of serum 25(OH)D level with vitamin D supplementation was associated with significant improvement in NYHA class and 6-minute walking distance.[37] Data on the effects of vitamin D supplementation on NYHA classes, functional capacity, and 6-minute walking distance are limited. Therefore, there is no specific guideline recommendation for the inclusion of vitamin D therapy in the standard care of patients with HF.

Limitations

Limitations of our study are that it was performed retrospectively and the study does not reflect the whole population for it was only performed in a single center in Turkey. Further studies are needed for the whole country and other regions, including vitamin D levels according to the seasons. Although our study was conducted in a sunny city, it is not possible to evaluate how long the patients were outside or their exposure to sunlight, as it is a retrospective study. Similarly, it was not known whether the vitamin D treatment that patients received was sufficient or not and those who received treatment were excluded. Prospective studies are needed to evaluate the effects of vitamin D use on NYHA. In addition, 6-minute walking distance could be used in patients, as it would be more objective, except for NYHA. Another limitation of our study is that medical treatment rates were lower in patients with a high NYHA class at the outpatient clinic admission. Because NYHA III-IV patients are more fragile, clinicians may not be in rush to initiate and titrate drug doses. This rate could have been higher if follow-up data were also evaluated.

Conclusion

Our findings suggest that vitamin D deficiency is common in patients with systolic HF as well as in the general population, even in a geographic area exposed to abundant solar radiation. While low vitamin D levels are associated with decreased functional capacity and increased NYHA classes, more studies are needed on the true clinical benefits of vitamin D supplementation.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Antalya Training and Research Hospital (Approval Date: July 3, 2020; Approval Number: 10/12).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

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