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RESEARCH ARTICLE

Effect of vitamin D replacement in patients with heart failure on six minute walking test and echocardiographic parameters

Kalp yetmezliği olan hastalarda vitamin D replasmanının altı dakika yürüme testi ve ekokariyografik parametreler üzerine etkisi

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Abstract

Aim: Patients with systolic heart failure frequently exhibit markedly reduced vitamin D levels; however, the clinical benefits of correcting this deficiency remain uncertain. This study aimed to evaluate the effects of high-dose vitamin D replacement therapy on cardiac function and exercise capacity in individuals with reduced ejection fraction and documented vitamin D deficiency.

Methods: In this prospective observational study, patients with low ejection fraction and confirmed vitamin D deficiency received high-dose vitamin D replacement therapy. Throughout the follow-up period, serum vitamin D concentrations, six-minute walk test performance, cardiac imaging parameters (including left ventricular systolic function and chamber dimensions), and laboratory measures such as calcium and parathyroid hormone levels were monitored.

Results: Vitamin D concentrations increased steadily after replacement therapy. Participants demonstrated a significant improvement in functional capacity, walking nearly 100 meters farther on average during the six-minute walk test ($p<0.05$). Echocardiographic evaluation revealed enhanced left ventricular contractility and reduced cavity size ($p<0.05$), whereas atrial and right ventricular parameters remained largely unchanged ($p>0.05$). Serum calcium and parathyroid hormone levels remained stable ($p<0.05$).

Conclusion: Restoration of vitamin D levels in patients with systolic heart failure may lead to improved daily performance and favorable structural remodeling of the left ventricle. Further large-scale studies are warranted to determine whether these benefits translate into improved long-term clinical outcomes.

Keywords: Heart failure, vitamin D, six-minute walk test, echocardiography, remodeling.

Özet

Amaç: Sistolik kalp yetmezliği olan hastalarda D vitamini eksikliğinin sık görülmesine rağmen, bu eksikliğin düzeltilmesinin klinik yarar sağlayıp sağlamadığı belirsizdir. Bu çalışmanın amacı, düşük ejeksiyon fraksiyonu ve D vitamini eksikliği bulunan hastalarda yüksek doz D vitamini replasmanının kardiyak fonksiyonlar ve fonksiyonel kapasite üzerindeki etkilerini değerlendirmektir.

Yöntemler: Prospektif gözlemsel bir tasarımda, D vitamini eksikliği belgelenmiş ve ejeksiyon fraksiyonu düşük bireylere yüksek doz D vitamini replasman tedavisi uygulanmıştır. Takip süresince D vitamini düzeyleri, altı dakikalık yürüme testi performansı, kardiyak görüntüleme bulguları (özellikle sol ventrikül fonksiyonu ve boşluk ölçümleri) ve laboratuvar parametreleri (kalsiyum, paratiroid hormonu) izlenmiştir.

Bulgular: Vitamin D konsantrasyonları replasman tedavisinden sonra düzenli olarak arttı. Katılımcılar fonksiyonel kapasitede anlamlı bir iyileşme gösterdi ve altı dakikalık yürüme testinde ortalama olarak yaklaşık 100 metre daha fazla yürüdü ($p<0,05$). Ekokardiyografik değerlendirme, sol ventrikül kontraktilitesinde artış ve kavite boyutunda azalma olduğunu ortaya koydu ($p<0,05$); buna karşılık atriyal ve sağ ventrikül parametreleri büyük ölçüde değişmeden kaldı ($p>0,05$). Serum kalsiyum ve paratiroid hormon düzeyleri stabil kaldı ($p<0,05$).

Sonuç: D vitamini eksikliği bulunan sistolik kalp yetmezliği hastalarında, replasman tedavisi fonksiyonel kapasiteyi artırmakta ve sol ventrikülün yapısal iyileşmesine katkıda bulunabilmektedir. Bu olumlu değişikliklerin uzun dönem mortalite ve morbiditeye yansıyıp yansımadığını belirlemek için daha geniş ölçekli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Kalp yetmezliği, D vitamini, altı dakikalık yürüme testi, ekokardiyografi, yeniden şekillenme.

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INTRODUCTION

Heart failure (HF) remains a major global health concern, characterized by recurrent hospitalizations, impaired quality of life, and significant mortality despite advances in medical and device-based therapies (1,2). Among the comorbid conditions frequently observed in this population, vitamin D deficiency has gained increasing attention due to its high prevalence and potential cardiovascular effects (3,4).

Although vitamin D is traditionally associated with calcium–phosphate homeostasis and bone metabolism, accumulating evidence suggests that it also plays a role in several cardiovascular pathways. Experimental and clinical studies indicate that vitamin D influences inflammatory responses, modulates the renin–angiotensin–aldosterone system (RAAS), contributes to myocardial calcium handling, and impacts vascular and endothelial function (5–7). Deficiency in vitamin D has been associated with myocardial hypertrophy, interstitial fibrosis, impaired systolic performance, and adverse remodeling in animal models (8,9). Observational studies similarly report higher hospitalization rates, impaired functional capacity, and worse outcomes among patients with HF and low vitamin D levels (10,11).

Clinical trials evaluating vitamin D supplementation in HF have yielded heterogeneous results. While some studies reported no significant improvement in functional or echocardiographic parameters (12), others demonstrated notable gains in exercise performance or left ventricular function (13,14). Recent meta-analyses suggest that these discrepancies may be related to differences in baseline deficiency, dosing regimens, patient characteristics, and follow-up duration (15–18).

Given these uncertainties, there remains a need for further research in patient groups with clearly documented deficiency. Therefore, the present study was designed to investigate whether high-dose vitamin D replacement in patients with systolic HF and confirmed deficiency could lead to measurable improvements in functional capacity and cardiac structure.

METHODS

The study protocol was reviewed and approved by the Local Ethics Committee of Atatürk University Faculty of Medicine (approval number: 7/24, date: 08.12.2016). Written informed consent was obtained from all participants prior to inclusion in the study.

This prospective single-center project included a little more than fifty patients with chronic systolic HF. All participants had a reduced left ventricular ejection fraction, not exceeding 40%, and symptoms consistent with moderate severity as defined by the New York Heart Association classification. Low vitamin D status, with concentrations below 20 ng/ml, was required for inclusion. Patients with advanced liver or kidney disease, active malignancy, or mobility restrictions were excluded. The study was approved by the local ethics committee, and each participant provided written consent.

Patients continued their standard heart failure therapies but also received vitamin D orally in a total dose of 300,000 IU, given as two separate administrations ten weeks apart. Exercise performance was evaluated by a standardized walking assessment lasting six minutes, performed in a flat corridor under supervision. Heart structure and function were assessed with echocardiography at the beginning and end of the study, using two-dimensional measurements of chamber size and Simpson's method to estimate ejection fraction. Blood tests were performed for vitamin D, calcium, parathyroid hormone, and routine chemistry.

Statistical analysis involved comparison of results obtained at baseline with those recorded after supplementation. Continuous variables are expressed as means with standard deviations, and paired tests were applied to examine changes, with significance accepted at $p<0.05$.

RESULTS

The study population was on average 67 years of age, and approximately four out of five participants were male. Ischemic cardiomyopathy was the predominant underlying condition, and all patients were receiving recommended medical therapy.

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After treatment, vitamin D levels in the blood rose substantially. Functional capacity also improved, with participants covering nearly one hundred additional meters during the six-minute walk compared with their initial test. This gain is well above the margin often cited as clinically important in heart failure research. Echocardiography demonstrated improvements in ejection fraction and smaller cavity dimensions in both diastole and systole, findings consistent with beneficial remodeling. By contrast, measures of atrial and right ventricular size remained stable, as did serum calcium and parathyroid hormone levels. The full dataset is summarized in Table 1 and Table 2, with representative changes illustrated in Figure 1.

Table 1. Baseline demographics and clinical characteristics

Characteristic	Value
Age (years)	67±10
Male Gender, n (%)	43 (79.6%)
NYHA Class II/III, n (%)	38 (70.4%) / 16 (29.6%)
Ischemic Cardiomyopathy, n (%)	46 (85.1%)
Diabetes Mellitus, n (%)	16 (29.6%)
Hypertension, n (%)	22 (40.7%)
Atrial Fibrillation, n (%)	19 (35.1%)
Medications: Beta-Blocker	48 (88.8%)
Medications: ACEI/ARB	51 (94.4%)
Medications: Diuretic	54 (100%)

Table 2. Effects of vitamin D replacement on study parameters

Parameter	Baseline	20 Weeks	P-value
25(OH)D (ng/ml)	11.66±5.12	40.72±14.74	<0.001
6-MWT (meters)	461.0±79.97	559.25±71.96	<0.001
LVEF (%)	31.70±3.40	35.50±4.00	<0.001
LVEDD (mm)	60.00±9.67	57.95±9.21	<0.001
LVESD (mm)	50.40±6.40	48.10±6.18	<0.001
Left Atrium (mm)	42.50±6.50	42.40±6.60	0.818
PTH (pg/ml)	62.95±40.40	46.45±32.24	0.120
Calcium (mg/dl)	9.46 ± 0.45	9.64 ± 0.50	0.330

DISCUSSION

This investigation provides evidence that restoring vitamin D in patients with systolic HF can influence both their physical ability and the structure of the heart. An improvement of nearly one hundred meters in walking distance is more than double the threshold often considered clinically relevant (19,20). At the same time, echocardiographic findings indicated better contractile function and reduced cavity dimensions, features that suggest reverse remodeling.

Mechanistic explanations for these results are supported by experimental work, which shows vitamin D to reduce activity of the renin–angiotensin–aldosterone system, limit inflammation, and improve calcium transport within cardiac cells (5,6,8). Clinical studies in the past have yielded divergent findings: some were unable to detect a benefit (12), while others did note significant improvements (13,14). Reviews and meta-analyses suggest that the degree of deficiency and the regimen used may account for these different outcomes (15–18).

A notable observation in this study is that improvements occurred even though calcium and parathyroid hormone levels remained stable, pointing to mechanisms beyond mineral metabolism. Although the study followed patients for a limited duration and involved a relatively small cohort, the magnitude of change observed argues for further large-scale evaluation.

Limitations

The study should be interpreted in light of several limitations. It was conducted in a single institution and involved a modest number of participants, which restricts generalizability. There was no placebo group, so the possibility of unmeasured confounding cannot be ruled out. In addition, the short duration of follow-up and the predominance of older male patients with ischemic disease may limit applicability to broader heart failure populations. Further multicenter randomized studies with longer follow-up are needed to confirm these observations.

CONCLUSION

High-dose vitamin D supplementation in patients with systolic HF and deficiency was associated with better walking performance and favorable changes in ventricular structure. These results suggest that correcting vitamin D status may offer a simple and low-cost adjunct to conventional therapy. Whether these benefits persist in the long term and translate into reduced hospitalization or mortality requires confirmation in larger, rigorously designed clinical trials.

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Ethical Approval: The study protocol was reviewed and approved by the Local Ethics Committee of Atatürk University Faculty of Medicine (approval number: 7/24, date: 08.12.2016). Written informed consent was obtained from all participants prior to inclusion in the study.

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