Journal of Clinical Cardiology and Cardiology Research
2023 Volume 2, Issue 1
DOI: 10.59657/2837-4673.brs.23.003

BioRes Scientia
Value your Research

Research Article

Open Access

# Is there an Association between Vitamin D Status and Left Ventricular Ejection Fraction?

## *Running title: Vitamin D3 and EF*

**Ehsan Shahverdi[1], Mourad Hajabdo[2], Fatemeh Khojastepour [3] , Shadi Kamali[4] , Rojen Manouchehri[5] , Pedram Karami[6], Mahkameh Rasouli[7]***

*[1]Department of Internal Medicine, Niels-Stensen-Kliniken Elisabeth-Hospital Thuine, Thuine, Germany.*
*[2]Department of Cardiology, Ingolstadt Hospital, Ingolstadt, Germany.*
*[3]Hamedan University of Medical Sciences, Hamedan, Iran.*
*[4]Department of Radiology, Ibbenbüren Hospital, Ibbenbüren, Germany.*
*[5]School of Medicine, Tehran Medical, Sciences Branch, Islamic Azad University, Tehran, Iran.*
*[6]Department of Otorhino Laryngology-Head and neck Surgery, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran.*
*[7]Nursing School, University of California, Irvine, California, USA.*
**Corresponding Author: Mahkameh Rasouli.*

## Abstract

**Background and aim**: Some recent studies have shown that vitamin D deficiency was a common finding in patients with cardiovascular disease. Because of the high prevalence of cardiovascular disease and vitamin D deficiency in Iranian population, we examined the correlation between vitamin D blood levels and patients with heart failure (HF).

**Material and Methods**: This analytical cross-sectional study was performed using a randomized sampling technique. One hundred forty-five patients who were admitted to hospitals in Tehran from November 2021 to April 2022 participated in this study. Descriptive analysis and inference tests, including chi-square and t-test were used. Logistic regression tests were also used to find the correlations between variables. A P value less than 0.05 was considered for statistical significance.

**Results:** In aggregate, 145 patients with an average age of 59.91 ± 10.75 years were studied. The average amount of vitamin D was 13.3 ± 12.8 ng/ml. This average was 15.0 ±14.2 ng/ml in patients with normal ejection fraction (EF), 14.6 ± 12.9 ng/ml in patients with mild severity EF, 14.1 ± 11.8 ng/ml and 8.7 ± 5.6 ng/ml in moderate and severe severity EF respectively. (p=0.51)

**Discussion**: Although, in our studies, low levels of serum vitamin D and diabetes were not significantly associated with EF, but preventing them is essential in mitigating risk factors in HF.

**Keywords:** heart failure; hypertension; vitamin d; diabetes; ejection fraction

## Introduction

HF is a heart disorder syndrome that is diagnosed by a reduction of left ventricular ejection fraction (LVEF) in combination with water and sodium retention. Muscle weakness and early fatigue are both common manifestations in HF patients [1,2]. The etiology of HF is not well understood [3]. In a recent observational study in patients with severe HF; vitamin D deficiency was a common finding [4] Severe vitamin D deficiency is associated with cardiovascular dysfunction; death due to HF and sudden cardiac attack; which is common in patients referred to angiography [5].

Vitamin D deficiency is a highly prevalent; global phenomenon. Recently; the incidence of vitamin D deficiency seems to be on the rise and is related in part

due to reduced sun exposure and increased indoor lifestyles along with efforts to minimize sun exposure. Also; there is evidence proposing that the global increase in obesity is also associated with vitamin D deficiency due to its sequestration in adipose tissue [6]. Iran; in keeping with many Mediterranean countries; has high solar radiation during most days of the year. Results of studies in Iran among different age-groups indicate a high prevalence of vitamin D deficiency [7-10].

Ecological evidence suggests an association between vitamin D status and cardiovascular disease (prevalent and incident heart disease; such as coronary disease and HF; stroke; and risk factors for heart disease such as hypertension and coronary artery calcification) [11,12]. To date; several mechanisms for this link have been offered including endothelial dysfunction; vascular compliance; inflammation; and some effects relating to parathyroid hormone (PTH) renin angiotensin system; and others [13-16].

Because of the high prevalence of coronary disease and low blood level of vitamin D in Iran we decided to measure serum serum 25-hydroxycholecalciferol (25(OH)D) concentrations in all patients that underwent coronary arteries bypass grafts to understand the relationship between the blood level of vitamin D and LVEF.

## Methods and Material

This was an analytical cross-sectional study approved by our ethics committee. Patients were asked to sign an informed consent form before blood samples were obtained. All the terms of the Helsinki declaration were considered; and the personal information remained anonymous. This registry collected information on patients admitted for CABG surgery in two University hospitals in Tehran between the period of November 2021 to April 2022. Our sample was restricted to participants aged 18 years and above and enrolled patients were limited to those who presented as suitable candidates for CABG surgery.

One hundred forty-five patients agreed to participate in the study to assess their vitamin D status. Complete data for vitamin D serum levels were available from 137 persons; corresponding to 94.5% of the target population whereas for left ventricular ejection fraction; data from 142 patients was collected; corresponding to 97.9% of the target population.

### Data Collection Vitamin D

serum 25-hydroxycholecalciferol (25(OH)D) concentrations was evaluated by measuring serum 25-hydroxyvitamin D (25 (OH) D) concentration; as this is the primary circulating form of vitamin D. This serum concentration of 25(OH)D is routinely considered as the robust "gold standard" indicator of vitamin D status [17].

After the patients were admitted; we collected serum samples and examined serum levels of 25 (OH) D in all 145 patients. Serum samples were sent to our central laboratory for analysis. Enzyme-linked Immunosorbent Assay (*ELISA*) and Immunodiagnostic System Ltd (IDS ltd) Kit; Boldon-UK with 2 nmol/ml sensitivity measurement for 25 (OH) D assays were performed. We classified serum levels of vitamin D into three groups; group 1 is Levels <=15 ng/ml; group 2 is levels 15-30 ng/ml and group 3 is levels >=30 ng/ml [18,19].

### Left ventricular ejection fraction (LVEF)

We measured left ventricular ejection fraction (LVEF) in all 145 patients by echocardiography using an Epic 7c Philips ultrasound (Manufactured by Philips Ultrasound 22100 Bothell-Everett Highway; Bothell; WA 98021-8431 USA) and classified the measurements into four groups: normal LVEFs are >55%; mild LVEFs are 45-55%; moderate LVEFs are 35-44% and severe LVEFs are <35% [20,21].

### Statistical analyses

Data were analyzed using statistical package for social sciences (SPSS) version 16 (SPSS Inc. Chicago; IL) for windows. Normal distribution variables (approved by one-sample Kolmogorov–Smirnov test) were compared using independent sample t-test between the groups and paired sample t-test within the groups. Chi square test also was used to compare categorical variables in the two groups. P value < 0.05 was considered statistically significant.

## Results

In total; 145 patients with an average age of 59.91 ± 10.75 years were studied. 126 patients (86.9%) were men; and 19 patients (13.1%) were women. A meaningful difference in demographic information among patients with normal; mild; moderate; and severe EF was not observed.

Thirty-eight patients (26.8%) had diabetes. (Table1). There was no significant between the groups. (p=0.176) Fifty-three patients (37.3%) were with hypertension with no significant difference. (p=0.038) (Table1)

Forty-two patients (29.6%) had hyperlipidemia. No significant difference was seen. (Table1) (p=0.121)
There was no significant difference between groups in average hospitalization; average time of CPB (or CABG surgery); average time of cross clamp; average amount of calcium; phosphate; parathyroid hormone and vitamin D. (Table 1) The Average hospitalization was 6.24 ± 1.63 days. (p=0.35); The average time of CPB (or CABG surgery) was 60.9 ± 19.2 minutes. (p=0.107); The average time of cross clamp was 37.6 ± 15.9 minutes. (p=0.351); The average amount of calcium in the blood of patients was 9.15 ± 0.52 mmol/l. (p=0.23); The average amount of phosphate in the blood of patients was 3.85 ± 0.63 mmol/l. (p=0.36); The average amount of parathyroid hormone (PTH) measured in the serum of patients was 78.82 ± 38.25 pg/ml. (p=0.22); The average amount of vitamin D in the blood of patients was 13.31 ± 12.8 ng/ml. (p=0.51).

| | LVEF | | | |
|---|---|---|---|---|
| | Normal | Milde | Moderate | Severe |
| Diabetes Melitus % | 15.7 | 52.6 | 23.6 | 7.8 |
| Hypertension % | 7.5 | 66 | 20.7 | 5.6 |
| Hyperlipidemia % | 11.9 | 73.8 | 7.1 | 7.1 |
| Hospitalization (day) | 6.1±1.9 | 6.3±1.3 | 5.6±1.1 | 7.2±2.9 |
| average time of CPB (or CABG surgery) (minute) | 56.2±9.1 | 59.7±19.2 | 70.2±21.2 | 60.4±22.6 |
| cross clamp (minute) | 35.5±9.1 | 35.5±13.3 | 45.2±20.9 | 41.0±23.5 |
| Calcium mmol/l | 9.1±0.42 | 9.1±0.52 | 9.2±0.61 | 9.4±0.55 |
| Phosphate mmol/l | 3.67±0.58 | 3.84±0.64 | 3.99±0.66 | 3.96±0.65 |
| parathyroid hormone pg/ml | 71.1±32.6 | 81.4±39.2 | 66.8±21.6 | 89.0±50.3 |
| vitamin D ng/ml | 15.0±14.2 | 14.6±12.9 | 14.1±11.8 | 8.7±5.6 |

**Table 1:** Demographic Data of Patients

## Discussion

The highest incidence of heart failure worldwide; is reported in Asian countries [22-24]. One of the most important HF indicators is LVEF which is divided to reduced or preserved. Hypertension and age are considered as important risk factors in both forms of reduced and preserved EF. In this study; many factors regarding the impact on EF are considered; for which we provide a brief analysis of the most important ones.

### *Blood pressure and heart failure with ejection fraction*

According to World Health Organization data; patients with hypertension are 40% more predisposed to heart failure [25]; while aging plays a direct correlation in increasing the risk of HF in hypertensive patients. Coronary Artery Disease (CAD); Diabetes; Left Ventricular Hypertrophy (LVH); and valvular diseases also increase the risk of developing HF [26]. In our study we found that high blood pressure affects EF significantly. This finding in the Iranian population is in concordance with other studies conducted in European populations and in the US as well [27,28]. Also; the study conducted by Rajer et.al. in Poland [29] found the same results in considering the impact of hypertension on HF diagnosed with Heart Failure with preserved EF (HF-PEF) and based on European Society of Cardiology guidelines (ESC) 2012 [30].

### *Diabetes and heart failure with ejection fraction*

Even though diabetes was known to be one of the risk factors of Heart Failure with Reduced EF (HF-REF) in studies conducted by Kristensen et.al; [31] we did not find a significant correlation between diabetes and HF. Of course; this difference can be due to the fact that there was no separation between two forms of preserved and reduced EF in our study.
Although diabetes is proven as an important risk factor for atherosclerosis; it is less recognized regarding HF [32]. Framingham et.al have showed that the incidence of heart failure in men and women with diabetes also confirmed this statement [33]. While there are studies that show almost 30%-50% of patients who have HF-PEF; suffer from diabetes as well [34].

### *Vitamin D and heart failure with ejection fraction*

We investigated the relationship between serum serum 25-hydroxycholecalciferol (25(OH)D) concentrations and EF. Our results showed no significant relation.

Since vitamin D plays a role in the expression of nearly 3000 genes; its deficiency can potentially affect development of various diseases [35]. In many studies; including those conducted by Michaelsson et al. [36]; Joergensen et al. [37]; Pilz et al. [38]; and James et al. [39]; lack of vitamin D lead to HF.

Vitamin D deficiency seems to be a global phenomenon. Even in studies conducted in tropical countries such as Singapore [40]. and Saudi Arabia [41]. this deficiency does exist. BIX studies conducted in Singapore showed that vitamin D deficiency may be due to dyslipidemia and consequently Cardiovascular diseases (CVD) [40]. These results indicate that Vitamin D deficiency is considered as one of the potential risk factors for cardiovascular diseases; including insulin resistance; AD; hypertension and glucose intolerance.

### *the level of serum PTH and heart failure*

We have also investigated the relationship between the factors including calcium and phosphate; bypass time (CPB); clamp time; and lipid profile with EF. No significant relation was observed. These factors may play a role in HF through interactions with each other. It is even possible that they are only involved in HF-PEF which was not investigated in our study.

Studies showed a high level of Parathyroid Hormone (PTH) in HF [42]. However; PTH investigation without measuring 25(OH)-vitamin D may be of value since they are related to each other. Evidence indicates that they have an important role in Cardiovascular diseases [43]. However; our study could not show a significant correlation between Vitamin D and EF but PTH and EF were related as expected.

## Conclusion

we could not show any significant relationship between Vitamin D and EF; which is one of the most important indicators of HF; while hypertension was significantly related to EF. Further studies may be required due to the fact that we did not separate two types of reduced and preserved EF in our study.

**Acknowledgements:** None

**Funding details:** No funding to declare.

**Authors' Contributions:** All authors contributed equally to this study.

## Conflict of Interest

The authors report no conflicts of interest/ No potential conflicts of interest relevant to this article were reported.

## References

1. McKee PA, Castelli WP, McNamara PM, Kannel WB. (1971). The natural history of congestive heart failure: the Framingham study. New England Journal of Medicine. 285(26):1441-1446.
2. McDonald TF, Pelzer S, Trautwein W, Pelzer DJ. (1994). Regulation and modulation of calcium channels in cardiac, skeletal, and smooth muscle cells. Physiological reviews. 74(2):365-507.
3. Krüger C, Erdmann E, Näbauer M, Beuckelmann D. (1994). Intracellular calcium handling in isolated ventricular myocytes from cardiomyopathic hamsters (strain BIO 14.6) with congestive heart failure. Cell calcium. 16(6):500-508.
4. Shane E, Mancini D, Aaronson K, Silverberg SJ, Seibel MJ, Addesso V, et al. (1997). Bone mass, vitamin D deficiency, and hyperparathyroidism in congestive heart failure. The American journal of medicine. 103(3):197-207.
5. Pilz S, Mäŕz W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP, et al. (2008). Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. The Journal of Clinical Endocrinology & Metabolism. 93(10):3927-3935.
6. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. (2000). Decreased bioavailability of vitamin D in obesity. The American journal of clinical nutrition. 72(3):690-693.
7. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. (2004). Vitamin D deficiency and causative factors in the population of Tehran. BMC Public health. 4(1):1-6.
8. Hovsepian S, Amini M, Aminorroaya A, Amini P, Iraj B. (2011). Prevalence of vitamin D deficiency among adult population of Isfahan City, Iran. Journal of health, population, and nutrition. 29(2):149.
9. Shahla A, Charehsaz S, Talebi R, Omrani M. (2005). Vitamin D deficiency in young females with

musculoskeletal complaints in Urmia, northwest of Iran. Iranian Journal of Medical Sciences. 30(2).
10. Salek M, Hashemipour M, Aminorroaya A, Gheiratmand A, Kelishadi R, Ardestani P, et al. (2008). Vitamin D deficiency among pregnant women and their newborns in Isfahan, Iran. Experimental and clinical endocrinology & diabetes. 116(6):352-356.
11. Elamin MB, Abu Elnour NO, Elamin KB, Fatourechi MM, Alkatib AA, Almandoz JP, et al. (2011). Vitamin D and cardiovascular outcomes: a systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 96(7):1931-1942.
12. Boxer RS, Kenny AM, Cheruvu VK, Vest M, Fiutem JJ, Piña II. (2010). Serum 25-hydroxyvitamin D concentration is associated with functional capacity in older adults with heart failure. American heart journal. 160(5):893-899.
13. Mitsuhashi T, Morris R, Ives HE. (1991). 1, 25-dihydroxyvitamin D3 modulates growth of vascular smooth muscle cells. The Journal of clinical investigation. 87(6):1889-1895.
14. Michos ED, Melamed ML. (2008). Vitamin D and cardiovascular disease risk. Current Opinion in Clinical Nutrition & Metabolic Care. 11(1):7-12.
15. London GM, Guérin AP, Verbeke FH, Pannier B, Boutouyrie P, Marchais SJ, et al. (2007). Mineral metabolism and arterial functions in end-stage renal disease: potential role of 25-hydroxyvitamin D deficiency. Journal of the American Society of Nephrology. 18(2):613-620.
16. Dobnig H, Pilz S, Scharnagl H, Renner W, Seelhorst U, Wellnitz B, et al. (2008). Independent association of low serum 25-hydroxyvitamin D and 1, 25-dihydroxyvitamin D levels with all-cause and cardiovascular mortality. Archives of internal medicine. 168(12):1340-1349.
17. Moy F-M, Bulgiba A. (2011). High prevalence of vitamin D insufficiency and its association with obesity and metabolic syndrome among Malay adults in Kuala Lumpur, Malaysia. BMC public health. 11(1):735.
18. Mehrotra R, Kermah DA, Salusky IB, Wolf MS, Thadhani RI, Chiu Y-W, et al. (2009). Chronic kidney disease, hypovitaminosis D, and mortality in the United States. Kidney international. 76(9):977-983.
19. Jablonski K, Jovanovich A, Holmen J, Targher G, McFann K, Kendrick J, et al. (2013). Low 25-hydroxyvitamin D level is independently associated with non-alcoholic fatty liver disease. Nutrition, Metabolism and Cardiovascular Diseases. 23(8):792-798.
20. Broberg CS, Aboulhosn J, Mongeon F-P, Kay J, Valente AM, Khairy P, et al. (2011). Prevalence of left ventricular systolic dysfunction in adults with repaired tetralogy of Fallot. The American journal of cardiology. 107(8):1215-1220.
21. Posch MG, Panek A, Kersten A, Ghadge SK, Geier C, Richter S, et al. (2010). Plasma HER2 levels are not associated with cardiac function or hypertrophy in control subjects and heart failure patients. International journal of cardiology. 145(1):105-106.
22. Chong AY, Rajaratnam R, Hussein NR, Lip GY. (2003). Heart failure in a multiethnic population in Kuala Lumpur, Malaysia. European journal of heart failure. 5(4):569-574.
23. Guo Y, Lip GY, Banerjee A. (2013). Heart failure in East Asia. Current cardiology reviews. 9(2):112-122.
24. Sakata Y, Shimokawa H. (2013). Epidemiology of heart failure in Asia. Circulation Journal. CJ-13-0971.
25. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. (2001). Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. Archives of internal medicine. 161(7):996-1002.
26. Levy D, Larson M, Vasan R, Kannel W. (1997). The progression from hypertension to congestive heart failure. ACC Current Journal Review. 2(6):37.
27. Sato N, Kajimoto K, Asai K, Mizuno M, Minami Y, Nagashima M, et al. (2010). Acute decompensated heart failure syndromes (ATTEND) registry. A prospective observational multicenter cohort study: rationale, design, and preliminary data. American heart journal. 159(6):949-955.
28. Stewart S, Wilkinson D, Hansen C, Vaghela V, Mvungi R, McMurray J, et al. (2008). Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. Circulation. 118(23):2360-2367.
29. Rajzer M, Wojciechowska W, Mikołajczyk U. (2016). Heart failure with preserved ejection fraction. Polskie Archiwum Medycyny Wewnetrznej. 126(1-2):9-11.
30. JV McMurray J, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. (2012). ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Revista Española de Cardiología. 65(10):938.

31. Kristensen SL, Preiss D, Jhund PS, Squire I, Cardoso JS, Merkely B, et al. (2016). Risk related to pre–diabetes mellitus and diabetes mellitus in heart failure with reduced ejection fraction: insights from prospective comparison of ARNI With ACEI to determine impact on global mortality and morbidity in heart failure trial. Circulation: Heart Failure. 9(1):e002560.
32. Nesto RW. (1900). Pharmacological treatment and prevention of heart failure in the diabetic patient. Reviews in cardiovascular medicine. 5(1):1-8.
33. Kannel WB, Hjortland M, Castelli WP. (1974). Role of diabetes in congestive heart failure: the Framingham study. American Journal of Cardiology. 34(1):29-34.
34. Yancy CW, Lopatin M, Stevenson LW, De Marco T, Fonarow GC, Committee ASA, et al. (2006). Clinical presentation, management, and in-hospital outcomes of patients admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. Journal of the American College of Cardiology. 47(1):76-84.
35. Ramagopalan SV, Heger A, Berlanga AJ, Maugeri NJ, Lincoln MR, Burrell A, et al. (2010). A ChIP-seq defined genome-wide map of vitamin D receptor binding: associations with disease and evolution. Genome research. 20(10):1352-1360.
36. Michaëlsson K, Baron JA, Snellman G, Gedeborg R, Byberg L, Sundström J, et al. (2010). Plasma vitamin D and mortality in older men: a community-based prospective cohort study. The American journal of clinical nutrition. 92(4):841-848.
37. Joergensen C, Gall M-A, Schmedes A, Tarnow L, Parving H-H, Rossing P. (2010). Vitamin D levels and mortality in type 2 diabetes. Diabetes Care. 33(10):2238-2243.
38. Pilz S, Dobnig H, Nijpels G, Heine RJ, Stehouwer CD, Snijder MB, et al. (2009). Vitamin D and mortality in older men and women. Clinical endocrinology. 71(5):666-672.
39. Vacek JL, Vanga SR, Good M, Lai SM, Lakkireddy D, Howard PA. (2012). Vitamin D deficiency and supplementation and relation to cardiovascular health. The American journal of cardiology. 109(3):359-363.
40. Bi X, Tey SL, Leong C, Quek R, Henry CJ. (2016). Prevalence of vitamin D deficiency in Singapore: its implications to cardiovascular risk factors. PLoS One. 11(1):e0147616.
41. Alsuwadia A, Farag YM, Al Sayyari AA, Mousa DH, Alhejaili FF, Al-Harbi AS, et al. (2013). Prevalence of vitamin D deficiency in Saudi adults. Saudi Med J. 34(8):814-818.
42. Kestenbaum B, Katz R, de Boer I, Hoofnagle A, Sarnak MJ, Shlipak MG, et al. (2011). Vitamin D, parathyroid hormone, and cardiovascular events among older adults. Journal of the American College of Cardiology. 58(14):1433-1441.
43. Tomaschitz A, Ritz E, Pieske B, Rus-Machan J, Kienreich K, Verheyen N, et al. (2014). Aldosterone and parathyroid hormone interactions as mediators of metabolic and cardiovascular disease. Metabolism. 63(1):20-31.

**Cite this article:** E Shahverdi, S Kamali, F Khojastepour, R Manouchehri, M Rasouli, et al. (2023). Is there an Association between Vitamin D Status and Left Ventricular Ejection Fraction? *Journal of Clinical Cardiology and Cardiology Research*, BRS Publishers. 2(1); DOI: 10.59657/2837-4673.brs.23.003

**Article History** **Received:** August 18, 2022; **Accepted:** September 16, 2022; **Published:** January 02, 2023