

Heart x Vitamin D Search Abstracts 2013-2015

Cathy Breedon

[Scand Cardiovasc J](#). 2016 Feb;50(1):17-22.

Vitamin D levels predict hospitalization and mortality in patients with heart failure.

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Low levels of vitamin D are closely associated with cardiovascular diseases. Heart failure (HF) is a major health problem globally, occurring with increasing frequency and characterised by poor prognosis despite therapy. We aimed to investigate the effect of vitamin D levels on hospitalisation and mortality in patients with HF. DESIGN: Patients with ejection fraction <50% (n = 219) were included in this prospective study. Demographic, clinical and laboratory parameters were obtained at presentation. Patients were classified into Group 1 (vitamin D level ≤50 nmol/L) and Group 2 (vitamin D level >50 nmol/L). Median follow-up time was 12 months. Hospitalisation rates and overall survival were compared between groups. Independent predictors of hospitalisation and mortality were defined. RESULTS: With a median follow-up period of 12 months, hospitalisation and overall death occurred more frequently in Group 1 than in Group 2 (23.4% vs 7.3% and 16.1% vs 1.2%, respectively; p < 0.005 for both). Vitamin D was defined as an independent predictor of hospitalisation and mortality. Higher levels were found to be associated with decreased hospitalisation (HR 0.89, 95% CI 0.84-0.95, p < 0.001) and mortality (HR 0.83, 95% CI 0.75-0.92, p < 0.001). **CONCLUSIONS: Vitamin D deficiency is highly prevalent in patients with HF, and low vitamin D levels are closely associated with increased hospitalisation and mortality.**

[Am Heart J](#). 2015 Sep;170(3):573-9.e5.

Assessment of serum 25-hydroxy vitamin D improves coronary heart disease risk stratification in patients with type 2 diabetes.

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BACKGROUND: A growing body of evidence suggests an association between lower serum 25-hydroxy vitamin D (25(OH)VitD) levels and adverse cardiovascular events. Patients with type 2 diabetes mellitus (T2DM) are at increased risk for developing coronary heart disease (CHD). 25-Hydroxy vitamin D deficiency is highly prevalent, especially among patients with T2DM. This study aimed to evaluate the predictive value of serum 25(OH)VitD in improvement of CHD risk stratification in patients with T2DM. METHODS: In an open cohort, community-dwelling T2DM patients were followed up for first CHD event. Patients were divided into 4 categories, based on 25(OH)VitD quartiles. Cox regression analysis was used to obtain hazard ratios. RESULTS: A total number of 2,607 T2DM patients were followed up for median time of 8.5 years. During follow-up, 299 patients experienced CHD events. Patients in the lowest quartile experienced more CHD events. Adjusted hazard ratios (95% CI) for developing CHD events were 0.77 (0.55-1.07) for second quartile, 0.52 (0.38-0.73) for third quartile, and 0.43 (0.31-0.60) for fourth quartile, compared with the first quartile. **The incidence rate decreased as serum 25(OH)VitD increased, which remained significant after stepwise adjustments (P value for trend ≤.001). Addition of 25(OH)VitD to traditional risk factors in Framingham Risk Score successfully reclassified 29% of study population.** CONCLUSIONS: Serum 25(OH)VitD is an independent predictor of future adverse CHD events in patients with T2DM. Addition of 25(OH)VitD status to Framingham Risk Score improves CHD risk prediction in patients with T2DM.

[BMC Res Notes](#). 2015 Sep 17;8:449.

Do women with statin-related myalgias have low vitamin D levels?

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BACKGROUND: Statin intolerance is often due to myalgias. Severe vitamin D deficiency is characterized by musculoskeletal pain. We hypothesized that statin-intolerance is associated with vitamin D deficiency. **OBJECTIVES:** To determine whether there is an association between statin-intolerance and vitamin D deficiency in a retrospective observational analysis. **METHODS:** We evaluated 20 female patients with prior myalgia-related daily dose statin intolerance on an alternative day statin dosing protocol of twice weekly for 4 weeks followed by advancement to daily dosing, as tolerated. Fasting baseline and follow-up lipid and 25-hydroxy-vitamin D (25-OHD) levels were obtained by chart review. **RESULTS:** The group median age was 61 ± 13 years old and BMI was 27 ± 7 kg/m². Women who remained on alternative day statin dosing (n = 16) compared to women on daily dosing (n = 4) had a significantly lower group mean 25-OHD (mean 29 ± 11.23 vs. 47.5 ± 23.53 ng/ml p = 0.0307 respectively). **CONCLUSIONS:** In women with prior myalgia-related statin intolerance, vitamin D levels were significantly lower in women who remained on alternative day dosing compared to those who were tolerant of daily dosing.

[J Saudi Heart Assoc](#). 2015 Oct;27(4):264-71.

Vitamin D deficiency plays an important role in cardiac disease and affects patient outcome: Still a myth or a fact that needs exploration?

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There is increasing evidence that a low vitamin D status may be an important and hitherto neglected factor of cardiovascular disease. This review is an overview of the current body of literature, and presents evidence of the mechanisms through which vitamin D deficiency affects the cardiovascular system in general and the heart in particular. Available data indicate that the majority of congestive heart failure patients have 25-hydroxyvitamin D deficiency. Furthermore, the low serum 25-hydroxyvitamin D level has a higher impact on hypertension, coronary artery disease and on the occurrence of relevant cardiac events. A serum 25-hydroxyvitamin D level below 75 nmol/l (30 ng/l) is generally regarded as vitamin D insufficiency in both adults and children, while a level below 50 nmol/l (20 ng/l) is considered deficiency. Levels below 50 nmol/l (20 ng/l) are linked independently to cardiovascular morbidity and mortality.

The Vitamin D Assessment (ViDA) Study: design of a randomized controlled trial of vitamin D supplementation for the prevention of cardiovascular disease, acute respiratory infection, falls and non-vertebral fractures.

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Observational studies have shown that low vitamin D status is associated with an increased risk of cardiovascular disease, acute respiratory infection, falls and non-vertebral fractures. We recruited 5110 Auckland adults, aged 50-84 years, into a **randomized, double-blind, placebo-controlled trial to test whether vitamin D supplementation protects against these four major outcomes. The intervention is a monthly cholecalciferol dose of 100,000IU (2.5mg) for an estimated median 3.3 years (range 2.5-4.2) during 2011-2015.** Participants were recruited primarily from family practices, plus community groups with a high proportion of Maori, Pacific, or South Asian individuals. The baseline evaluation included medical history, lifestyle, physical measurements (e.g. blood pressure, arterial waveform, lung function, muscle function), and a blood sample (stored at -80°C for later testing). Capsules are being mailed to home addresses with a questionnaire to collect data on non-hospitalized outcomes and to monitor adherence and potential adverse effects. Other data sources include New Zealand Ministry of Health data on mortality, hospitalization, cancer registrations and dispensed pharmaceuticals. A random sample of 438 participants returned for annual collection of blood samples to monitor adherence and safety (hypercalcemia), including repeat physical measurements at 12 months follow-up. The trial will allow testing of a priori hypotheses on several other endpoints including: weight, blood pressure, arterial waveform parameters, heart rate variability, lung function, muscle strength, gait and balance, mood, psoriasis, bone density, and chronic pain. **[CB Note: Results not available yet; this just describes the design of the study. The is equivalent of about 833 iu/day for 3 years, assuming that they take the prescribed amount. The monthly dosing should help with compliance, and it also illustrates the safety of high dose supplements given less often. The upper end of safety is a chronic dose of 10,000 iu/day, so overall, this is actually a fairly low supplementation level. Labs will be obtained on a subset at 12 months to confirm actual blood levels and estimate compliance with the prescribed amount.**

[Dis Markers](#). 2015;2015:864370..

Optimal Vitamin D Supplementation Levels for Cardiovascular Disease Protection.

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First described in relation to musculoskeletal disease, there is accumulating data to suggest that vitamin D may play an important role in cardiovascular disease (CVD). In this review we aim to provide an overview of the role of vitamin D status as both a marker of and potentially causative agent of hypertension, coronary artery disease, heart failure, atrial fibrillation, stroke, and peripheral vascular disease. The role of vitamin D levels as a disease marker for all-cause mortality is also discussed. We review the current knowledge gathered from experimental studies, observational studies, randomised controlled trials, and subsequent systematic reviews in order to suggest the optimal vitamin D level for CVD protection.

Amplification of lipotoxic cardiomyopathy in the VDR gene knockout mouse.

[Glenn DJ](#)¹, [Cardema MC](#)², [Gardner DG](#)².

Previous studies demonstrated that the liganded vitamin D receptor (VDR) plays an important role in controlling cardiovascular homeostasis. Both the whole animal VDR gene knockout (VDR^{-/-}) and the myocyte-specific VDR gene deletion result in changes in cardiac structure and function. Clinical states associated with cardiac steatosis (obesity and diabetes mellitus) are also associated with low circulating 25 OH vitamin D levels. We, therefore, examined the effects of VDR deficiency (VDR^{-/-} mouse) in a murine model of cardiac steatosis that expresses the terminal enzyme involved in triglyceride synthesis, diacylglycerol acyltransferase 1 (DGAT1), selectively in the cardiac myocyte. These mice display early cardiac dysfunction and late cardiomyopathy and heart failure. In the present study, we demonstrate that mice harboring both genetic modifications (i.e., MHC-DGAT1 Tg and VDR^{-/-}) exhibit an increase in myocyte size, heart weight/body weight ratio and natriuretic peptide gene expression, all markers of cardiac hypertrophy, that exceed that seen in either VDR^{-/-} or the MHC-DGAT1 Tg mice alone. This was accompanied by a dramatic increase in interstitial fibrosis and increased expression of collagen 1a1 and collagen 3a1, as well as the osteopontin and matrix metalloproteinase 2, genes. At a functional level, this resulted in a 37% reduction in ejection fraction and 55% reduction in fractional shortening in the DGAT1; VDR^{-/-} mice relative to the controls.

Amplification of lipotoxic cardiomyopathy in the VDR gene knockout mouse.

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Previous studies demonstrated that the liganded vitamin D receptor (VDR) plays an important role in controlling cardiovascular homeostasis. Both the whole animal VDR gene knockout (VDR^{-/-}) and the myocyte-specific VDR gene deletion result in changes in cardiac structure and function. Clinical states associated with cardiac steatosis (obesity and diabetes mellitus) are also associated with low circulating 25 OH vitamin D levels. We, therefore, examined the effects of VDR deficiency (VDR^{-/-} mouse) in a murine model of cardiac steatosis that expresses the terminal enzyme involved in triglyceride synthesis, diacylglycerol acyltransferase 1 (DGAT1), selectively in the cardiac myocyte. These mice display early cardiac dysfunction and late cardiomyopathy and heart failure. In the present study, we demonstrate that mice harboring both genetic modifications (i.e., MHC-DGAT1 Tg and VDR^{-/-}) exhibit an increase in myocyte size, heart weight/body weight ratio and natriuretic peptide gene expression, all markers of cardiac hypertrophy, that exceed that seen in either VDR^{-/-} or the MHC-DGAT1 Tg mice alone. This was accompanied by a dramatic increase in interstitial fibrosis and increased expression of collagen 1a1 and collagen 3a1, as well as the osteopontin and matrix metalloproteinase 2, genes. At a functional level, this resulted in a 37% reduction in ejection fraction and 55% reduction in fractional shortening in the DGAT1; VDR^{-/-} mice relative to the controls. **Collectively, these data demonstrate that deficiency in the vitamin D signaling system enhances the pathological phenotype in this experimental cardiomyopathy and suggest an important role for vitamin D in modulating disease severity in common cardiovascular disorders.**

[CB note: This study is about changes in cardiac health with the vitamin D receptor is not present or operating. However, it can also be a model of changes that might occur if the receptor was operational but simply not getting messages from vitamin D hormone because of vitamin D inadequacy.]

[Best Pract Res Clin Endocrinol Metab.](#) 2015 Oct;29(5):773-86.

Behind the scenes of vitamin D binding protein: More than vitamin D binding.

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Although being discovered in 1959, the number of published papers in recent years reveals that vitamin D binding protein (DBP), a member of the albuminoid superfamily, is a hot research topic. Besides the three major phenotypes (DBP1F, DBP1S and DBP2), more than 120 unique variants have been described of this polymorphic protein. The presence of DBP has been demonstrated in different body fluids (serum, urine, breast milk, ascitic fluid, cerebrospinal fluid, saliva and seminal fluid) and organs (brain, heart, lungs, kidneys, placenta, spleen, testes and uterus). Although the major function is binding, solubilization and transport of vitamin D and its metabolites, the name of this glycoprotein hides numerous other important biological functions. In this review, we will focus on the analytical aspects of the determination of DBP and discuss in detail the multifunctional capacity [actin scavenging, binding of fatty acids, chemotaxis, binding of endotoxins, influence on T cell response and influence of vitamin D binding protein-macrophage activating factor (DBP-MAF) on bone metabolism and cancer] of this abundant plasma protein.

[Can J Cardiol.](#) 2015 Dec;31(12):1462-8. doi: 10.1016/j.cjca.2015.07.737. Epub 2015 Aug 21.

Usefulness of Clinical Data and Biomarkers for the Identification of Frailty After Acute Coronary Syndromes.

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Abstract

BACKGROUND:

Frailty predicts mortality after acute coronary syndrome (ACS). The standard frailty scales, such as the Fried score, consist of a variety of questionnaires and physical tests. Our aim was to investigate easily available clinical data and blood markers to predict frailty at discharge, in elderly patients after ACS.

METHODS:

A total of 342 patients older than 65 years, survivors after ACS, were included. A high number of clinical variables were collected. In addition, blood markers potentially linked to frailty and related to the processes of inflammation, coagulation, hormonal dysregulation, nutrition, renal dysfunction, and heart

dysfunction were determined. Frailty was evaluated using the Fried score at discharge. The main outcome was frailty defined by a Fried score ≥ 3 points. Secondary endpoints were mortality and myocardial infarction at 30-month median follow-up.

RESULTS:

A total of 116 patients were frail. Seven clinical variables or biomarkers predicted frailty: age ≥ 75 years, female, prior ischemic heart disease, admission heart failure, haemoglobin ≤ 12.5 g/dL, vitamin D ≤ 9 ng/mL, and cystatin-C ≥ 1.2 mg/L. This model based on clinical data and biomarkers showed an excellent discrimination accuracy for frailty (C-statistic = 0.818). During the follow-up, 105 patients died and 137 died or suffered myocardial infarction. The clinical data and biomarker model (C-statistics = 0.730 and 0.691) performed better than the Fried score (C-statistics = 0.676 and 0.650) for death and death or myocardial infarction, respectively.

CONCLUSIONS:

Easy available clinical data and biomarkers can identify frail patients at discharge after ACS and predict outcomes better than the standard Fried's frailty scale.

[n Chem.](#) 2015 Dec;61(12):1484-94. doi: 10.1373/clinchem.2015.244913. Epub 2015 Oct 28.

Effect of Vitamin D or Activated Vitamin D on Circulating 1,25-Dihydroxyvitamin D Concentrations: A Systematic Review and Metaanalysis of Randomized Controlled Trials.

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BACKGROUND: Evidence is accumulating that circulating 1,25-dihydroxyvitamin D [1,25(OH)₂D] concentrations are inversely related to overall mortality. **METHODS:** We searched PubMed, Embase and ISI Web of Science for randomized controlled trials with a control group receiving a placebo instead of vitamin D/activated vitamin D and performed a metaanalysis to evaluate the effect of oral vitamin D/activated vitamin D on circulating 1,25(OH)₂D concentrations using a random effects model. **RESULTS:** We included 52 vitamin D intervention groups (4796 individuals) and 14 intervention groups with activated vitamin D (668 individuals). Vitamin D supplements increased circulating 1,25(OH)₂D by 12.2 pmol/L (95% CI, 7.8-16.5 pmol/L) and 18.8 pmol/L (95% CI, 9.2-28.4 pmol/L) if only studies with a low risk of bias in study design and reporting were considered (n = 18). There was significant heterogeneity among studies (Cohran's Q P < 0.001, I(2) = 91%). The incremental effect was larger in studies using vitamin D alone compared with coadministration of calcium supplements (18.6 pmol/L; 95% CI, 12.7-24.4 pmol/L vs 4.9 pmol/L; 95% CI, -0.4 to 10.2 pmol/L; P = 0.001), and if quantification was performed with RIA vs other methods (17.1 pmol/L; 95% CI, 11.1-23.1 pmol/L vs 6.9 pmol/L; 95% CI, 1.0-12.8 pmol/L; P = 0.02). Activated vitamin D increased the mean circulating 1,25(OH)₂D by 20.5 pmol/L (95% CI, 8.3-32.7 pmol/L; P = 0.04). Again, there was evidence for significant heterogeneity among studies (Cochran Q = 85.4; P < 0.001; I(2) = 87%), but subgroup analysis did not identify parameters significantly influencing the increment in 1,25(OH)₂D concentrations. **CONCLUSIONS: Both vitamin D and activated vitamin D significantly increase circulating 1,25(OH)₂D concentrations, but in vitamin D users this increase is suppressed by calcium coadministration.**

[J Cardiovasc Nurs.](#) 2015 Nov 5.

Micronutrient Deficiency Independently Predicts Adverse Health Outcomes in Patients With Heart Failure.

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BACKGROUND: Despite growing evidence on the important role of micronutrients in prognosis of heart failure (HF), there has been limited research that micronutrient deficiency predicts health outcomes in patients with HF. **PURPOSE:** The aim of this study was to determine whether micronutrient deficiency independently predicts adverse health outcomes. **METHODS:** A total of 113 consecutive outpatients with HF completed a 3-day food diary to measure intake of 15 micronutrients. The Computer Aided Nutrition Analysis Program for Professionals was used to analyze the food diaries and determine dietary micronutrient deficiencies. Patients completed the Minnesota Living With HF Questionnaire to assess health-related quality of life (HRQoL) and were followed up for 1 year to determine cardiac-related hospitalization or cardiac death. Hierarchical multiple linear regressions and Cox proportional hazard regressions were used to determine whether micronutrient deficiencies predicted health outcomes. **RESULTS:** Fifty-eight patients (51%) had at least 3 micronutrient deficiencies (range, 0-14). **Calcium, magnesium, and vitamin D were the most common micronutrient deficiencies.** Micronutrient deficiency was independently associated with worse HRQoL ($\beta = .187$, $P = .025$) in hierarchical multiple linear regression. Thirty-nine patients were hospitalized or died during 1-year follow-up because of cardiac problems. The number of micronutrient deficiencies independently predicted cardiac event-free survival (hazard ratio, 1.14; 95% confidence interval, 1.02-1.28). **CONCLUSIONS:** These findings show that micronutrient deficiency independently predicted poor HRQoL and earlier cardiac event-free survival in patients with HF. Further research is needed to provide for specific dietary guidelines for better health outcomes in HF patients.

[J Nutr Sci Vitaminol \(Tokyo\)](#). 2015;61 Suppl:S170-2.

Cardiovascular Diseases and Fat Soluble Vitamins: Vitamin D and Vitamin K.

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Recently, the associations between insufficiency of fat soluble vitamins and cardiovascular diseases (CVDs) have been reported. **Vitamin D** affects the cardiovascular system via several pathways, such as suppression of parathyroid hormone, the renin-angiotensin-aldosterone system and vascular endothelial growth and the immune system. Cross-sectional and longitudinal studies have shown the association between the concentration of serum 25-hydroxyvitamin D (25OHD), which is a vitamin D metabolite indicating nutritional vitamin D status, and hypertension, myocardial infarction, heart failure and CVD mortality. On the other hand, the association between **vitamin K** status and CVDs, especially vascular calcification, has been also reported. Cross-sectional and cohort studies show that high vitamin K status is associated with reduced coronary artery calcification, CVDs and mortality risk. Epidemiological and basic studies indicate that vitamin K possesses a benefit in the prevention of the progression of coronary artery calcification via activation of matrix-gla protein (MGP). While these data in epidemiological and basic studies suggest the protective role of vitamin D and K in CVDs, the benefits of supplementation of both vitamins have not been validated in randomized controlled trials. Further basic and interventional studies are needed to confirm the benefit of both vitamins in protection against CVDs.

[BMJ Open](#). 2015 Nov 30;5(11):e009140. doi: 10.1136/bmjopen-2015-009140.

Vitamin D status and associated metabolic risk factors among North Korean refugees in South Korea: a cross-sectional study.

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Abstract

OBJECTIVE:

Vitamin D deficiency is now recognised as a common health problem associated with various chronic diseases; however, it has not been fully elucidated among the minority groups. Here, we aimed to investigate the prevalence of vitamin D deficiency and its associated metabolic risk factors among North Korean refugees living in South Korea.

DESIGN:

Cross-sectional analysis from the longitudinal cohort, the North Korean refugee health in South Korea (NORNS) study.

PARTICIPANTS:

A total of 386 North Korean refugees aged ≥ 30 years, who measured serum 25-hydroxy vitamin D (25(OH)D) level.

RESULTS:

The prevalence of vitamin D deficiency (25(OH)D < 20 ng/mL) was 87% and no participants had an adequate vitamin D level (25(OH)D ≥ 30 ng/mL). Underweight participants (body mass index (BMI) < 18 kg/m²) had significantly lower 25(OH)D levels than individuals with normal BMI (≥ 18.5 and < 23 kg/m²). In the multivariate logistic regression analysis, the lowest 25(OH)D level (< 10 ng/mL) was significantly associated with metabolic syndrome (OR, 6.37, 95% CI 1.34 to 30.3), high triglyceride (OR, 6.71, 95% CI 1.75 to 25.7), and low high-density lipoprotein (OR, 5.98, 95% CI 1.54 to 23.2) compared with 25(OH)D levels ≥ 20 ng/mL after adjusting for age, sex, season, length of residence in South Korea, physical activity and BMI.

CONCLUSIONS:

Vitamin D deficiency is very common among North Korean refugees in South Korea. Despite their lower BMI, vitamin D deficiency was associated with metabolic syndrome in this population.

[Cardiovasc Drugs Ther.](#) 2015 Nov 25. [Epub ahead of print]

The Vitamin D Receptor Activator Maxacalcitol Provides Cardioprotective Effects in Diabetes Mellitus.

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Abstract

PURPOSE:

Recent reports showed a significant association between vitamin D levels and cardiovascular disease events and mortality. In the current study, we investigated the effect of the vitamin D receptor activator maxacalcitol (OCT) on cardiac damage in a rat model of type 2 diabetes.

METHODS:

At 20 weeks of age, the rats were divided into three groups: vehicle-treated (DM), insulin-treated (INS) and OCT-treated (OCT). At 30 weeks, the rats were sacrificed and urinary and blood biochemical analyses and cardiac histological and immunohistochemical analyses were performed. To evaluate the effect of OCT on the renin-angiotensin system, we performed a further study using aliskiren (ALS). At 20 weeks, the diabetic rats were divided into two groups: the ALS-treated group (ALS) and the ALS plus OCT-treated group (ALS + OCT), and we evaluated the renin-angiotensin system (RAS) and cardiac lesions at 30 weeks.

RESULTS:

At 30 weeks, despite comparable blood pressure and renal function, heart volume, intracardiac oxidative stress by immunohistological analysis, cardiac and perivascular fibrosis and urinary excretion of 8-hydroxydeoxyguanosine and serum N-terminal pro-brain natriuretic peptide levels were significantly decreased in the OCT group compared to the DM group. mRNA expressions of dihydronicotinamide adenine dinucleotide phosphate (NADPH) p47 subunit and cardiac injury-related markers in the heart were also significantly decreased in the OCT group compared to the DM group. The cardioprotective effect of OCT was preserved even in the context of RAS inhibition.

CONCLUSION:

Our results suggest that OCT prevents the development of cardiac damage in DM, independent of RAS inhibition.

[Clin Cardiol.](#) 2015 Sep 28. doi: 10.1002/clc.22473. [Epub ahead of print]

Vitamin D Supplementation in the Treatment of Chronic Heart Failure: A Meta-analysis of Randomized Controlled Trials.

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Abstract

BACKGROUND:

In recent years, there has been growing evidence that vitamin D deficiency is associated with the development and progression of chronic heart failure (CHF).

HYPOTHESIS:

Additional supplementation of vitamin D may have protective effects in patients with CHF.

METHODS:

We searched PubMed, Embase, and Cochrane databases through June 2015 and included 7 randomized controlled trials that investigated the effects of vitamin D on cardiovascular outcomes in patients with CHF. Then, we performed a meta-analysis of clinical trials to confirm whether vitamin D supplementation is beneficial in CHF patients. The weighted mean difference (WMD) and 95% confidence interval (CI) were calculated using fixed- or random-effects models.

RESULTS:

Our pooled results indicated that additional supplementation of vitamin D was not superior to conventional treatment in terms of left ventricular ejection fraction, N-terminal pro-B-type natriuretic peptide, and 6-minute walk distance. Moreover, vitamin D supplementation was associated with significant decreases in the levels of tumor necrosis factor- α (WMD: -2.42 pg/mL, 95% CI: -4.26 to -0.57, $P < 0.05$), C-reactive protein (WMD: -0.72 mg/L, 95% CI: -1.42 to -0.02, $P < 0.05$), and parathyroid hormone (WMD: -13.44 pg/mL, 95% CI: -21.22 to -5.67, $P < 0.05$).

CONCLUSIONS:

Vitamin D supplementation may decrease serum levels of parathyroid hormone and inflammatory mediators in CHF patients, whereas it has no beneficial effects on improvement of left ventricular function and exercise tolerance.

[Arch Physiol Biochem.](#) 2015 Nov 24:1-4. [Epub ahead of print]

Effect of vitamin D3 on thyroid function and de-iodinase 2 expression in diabetic rats.

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- ^{3c} Physiology Department, Faculty of Medicine , Ain Shams University , Cairo , Egypt.

Abstract

OBJECTIVE:

This study aimed to assess the effect of vitamin D₃ administration to diabetic rats on thyroid profile and deiodinase 2 (D2).

METHODS:

Thirty male Wistar rats were included into three groups; control, streptozotocin-induced diabetic and diabetic supplemented with vitamin D₃ groups. Ten weeks later, serum levels of free T₄, free T₃ and TSH were measured. Tissue homogenates from liver, kidney, muscle, femur bone, heart and brain were obtained and assessed for D2 mRNA.

RESULTS:

Diabetic rats demonstrated significant increase in free T₄ and significant decrease in free T₃. These changes were ameliorated by vitamin D₃ administration. D2 mRNA was significantly reduced in all tissue homogenates obtained from diabetic rats, while vitamin D₃ treatment significantly enhanced D2 in liver and brain homogenates.

CONCLUSION:

Diabetes mellitus inhibited peripheral conversion of T₄ into T₃ secondary to reduction in D2 expression. Vitamin D₃ greatly corrected the alterations in thyroid profile and D2 expression.

[Eur J Nutr.](#) 2015 Nov 30.

Vitamin D3 supplementation does not modify cardiovascular risk profile of adults with inadequate vitamin D status.

[Important CB Note regarding interpretation follows abstract/]

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PURPOSE: The Nutrition Societies in Germany, Austria, and Switzerland recommend a daily intake of 20 µg vitamin D₃ for adults when endogenous synthesis is absent. The current study aimed to elucidate whether this vitamin D₃ dose impacts cardiovascular risk markers of adults during the winter months. **METHODS:** The study was conducted in Halle (Saale), Germany (51° northern latitude) as a placebo-controlled, double-blinded, randomised trial (from January to April). A total of 105 apparently

healthy subjects (male and female, 20-71 years old) were included. Subjects were randomly allocated to two groups. One group received a daily 20- μg vitamin D₃ dose (n = 54), and the other group received a placebo (n = 51) for 12 weeks. Outcome measures included blood pressure, heart rate, concentrations of renin, aldosterone, serum lipids and vascular calcification markers, and haematologic variables such as pro-inflammatory monocytes. **RESULTS:** Blood pressure and systemic cardiovascular risk markers remained unchanged by vitamin D₃ supplementation, although serum 25-hydroxyvitamin D₃ increased from 38 ± 14 to 73 ± 16 nmol/L at week 12. The placebo and vitamin D groups did not differ in their final cardiovascular risk profile. **CONCLUSION:** Daily supplementation of 20 μg vitamin D₃ during winter is unlikely to change cardiovascular risk profile.

CB note: It is very important to note that they used only 800 iu (the Swiss RDA of 20 μg) and gave it for only four months in the winter among people described as having low vitamin D levels.

This minimal intervention is extremely unlikely to have been enough to make any difference in correcting deficiency or altering cardiovascular biomarkers. I would have been amazed if it showed anything at all. Additionally, actual vitamin D levels or changes within patients are not included in the study.

I am concerned that the title is misleading and makes it sound like “Never mind about all that research you read about vitamin D and heart disease” My interpretation of this result is that it does not at all erase the potential shown elsewhere for a role of assuring vitamin D adequacy in cardiovascular disease. Vitamin D adequacy was never assured or even checked during or after four month test period.

A better title should be **“Four months of providing really puny RDA-level supplementation of Vitamin D3 in the winter does not modify cardiovascular risk profile of adults with inadequate vitamin D status.”**

[Curr Opin Cardiol](#). 2013 Mar;28(2):216-22.

The role of vitamin D in chronic heart failure.

[Pourjabbar A](#)¹, [Dwivedi G](#), [Haddad H](#). Div Cardiol, U of Ottawa Heart Institute, Ottawa, Ontario, Canada.

PURPOSE OF REVIEW: Despite advanced medical and device-based therapies, congestive heart failure (CHF) remains a major medical problem, associated with significant morbidity and mortality. Vitamin D deficiency is prevalent in CHF and is associated with poor outcomes. In this manuscript we review the evidence linking vitamin D deficiency and CHF and discuss potential mechanisms involved, as well the clinical data on vitamin D supplementation in CHF patients.

RECENT FINDINGS: A clear relationship has been established between Vitamin D deficiency and increased mortality and morbidity in CHF. However, the mechanism involved is not clearly understood. Recent clinical and experimental evidence have identified the renin-angiotensin-aldosterone system and inflammatory cytokines as likely mediators that can lead to poor clinical outcomes via the cardiorenal

syndrome. Clinical data on vitamin D supplementation also remain unestablished, with potential clinical benefits recently reported in patients with vitamin D deficiency. Nonetheless, large-scale randomized clinical trials are lacking. **SUMMARY: Vitamin D is an emerging agent with tremendous potential and may represent a novel target for therapy in CHF. Further studies are needed to identify the mechanism(s) involved in the pathophysiology as well as to adequately examine the role of Vitamin D measurement and supplementation in patients with CHF.**

[Int J Clin Pract.](#) 2014 Feb 6. doi: 10.1111/ijcp.12323. [Epub ahead of print]

Severe vitamin D deficiency is associated with frequently observed diseases in medical inpatients.

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INTRODUCTION: Vitamin D deficiency consequences may go beyond altered calcium homeostasis and musculoskeletal disease. Medical inpatients are often vitamin D-deficient, but little information is available about the relation of vitamin D status with extra-skeletal disorders in this population. **METHODS:** We analysed the relationship between the concentrations of 25-hydroxyvitamin D [25(OH)D], the marker of vitamin D status, and the conditions most commonly causing admission in 115 consecutive medical inpatients. **RESULTS:** Sixty-five subjects (56.5%) had severe vitamin D deficiency [25(OH)D < 8 ng/ml]. Age ($\beta = -0.35$, $p = 0.01$) and hepatic disease ($\beta = -0.21$, $p = 0.02$) were significant correlates of 25(OH)D levels. Compared with patients with ≥ 8 ng/ml 25(OH)D, those with < 8 ng/ml 25(OH)D had significantly higher parathyroid hormone (PTH) concentrations [123 (92.7-208.2) ng/l vs. 88 (68.5-129.5) ng/l, $p < 0.001$], were significantly more likely to have arterial hypertension (OR 2.76, 95% CI 1.16-6.58), heart failure (HF) (OR 2.49, 95% CI 1.14-5.47), cerebrovascular disease (OR 3.23, 95% CI 1.41-7.39), and infections (OR 2.44, 95% CI 1.02-5.87), and stayed in hospital significantly longer (10 days vs. 7.5 days, $p = 0.01$). Only the probability of having an infection remained significantly higher in cases with severe vitamin D deficiency after adjustment for age (OR 2.41, 95% CI 1.03-5.68) and persisted after further correcting for presence of hepatic disease and PTH values (OR 2.66, 95% CI 1.03-6.88). A significant association between PTH and HF (OR 2.32, 95% CI 1.05-5.09) and length of hospitalisation ($\beta = 0.22$, $p = 0.04$) emerged in the fully adjusted regression models. **CONCLUSIONS: Severe vitamin D deficiency is associated with commonly presenting extra-skeletal diseases in medical inpatients. With the exception of infections, this association is mainly driven by age. Additional studies are needed to determine whether vitamin D testing on admission may help stratifying specific categories of patients by clinical severity.**

[J Intern Med.](#) 2013 Mar;273(3):253-62..

Relationship between vitamin D status and left ventricular geometry in a healthy population: results from the Baltimore Longitudinal Study of Aging.

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OBJECTIVES: The effects of vitamin D on the heart have been studied in patients with cardiac disease, but not in healthy persons. We investigated the relation between vitamin D status and left ventricular (LV) structure and function in community-dwelling subjects without heart disease. **DESIGN:** The relationship between concentrations of 25-hydroxyvitamin D [25(OH)D], a marker of vitamin D reserve, and LV transthoracic echocardiography measures was analysed in 711 participants in the Baltimore Longitudinal Study of Aging who were without cardiac disease. **RESULTS:** Mean 25(OH)D in the study population was 32.3 ± 11.4 ng mL⁻¹; only 15.5% of subjects had moderate or severe vitamin D deficiency [25(OH)D < 20 ng mL⁻¹]. Adjusting for age, body mass index, cardiovascular disease risk factors,

physical activity, calcium and parathyroid hormone, 25(OH)D was positively correlated with LV thickness (β 0.095, SE 0.039, $P < 0.05$) and LV mass index (β 7.5, SE 2.6, $P < 0.01$). A significant nonlinear relation between 25(OH)D and LV concentric remodelling was observed. LV remodelling was more likely in participants with 25(OH)D levels <30 ng mL⁻¹ [odds ratio (OR) 1.24; 95% confidence interval (CI) 0.83-1.85] or ≥ 38 ng mL⁻¹ (OR 1.73; 95% CI 1.13-2.65), compared with those with 30-37 ng mL⁻¹ 25(OH)D. Consistently, LV relative wall thickness was significantly lower (P for trend=0.05), and LV diastolic internal diameter index (P for trend <0.05) and end-diastolic volume index (P for trend <0.05) were significantly higher in subjects with 30-37 ng mL⁻¹ 25(OH)D compared to the rest of the study population. **There was a significant interaction between 25(OH)D and hypertension on the risk of LV hypertrophy ($P < 0.05$).** **CONCLUSIONS:** In a population-based sample of predominantly vitamin D-sufficient subjects without heart disease, LV geometry was most favourable at intermediate 25(OH)D concentrations.

[J Card Fail.](#) 2014 Feb 4. pii: S1071-9164(14)00062-1.

The Effect of Vitamin D on Aldosterone and Health Status in Patients with Heart Failure.

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BACKGROUND: Vitamin D deficiency is associated with HF events and in animal models vitamin D down-regulates RAAS hormones. **METHODS:** Patients with NYHA II-IV HF and a 25OHD level ≤ 37.5 ng/mL received weekly vitamin D3 50,000 IU ($n=31$) or placebo ($n=33$) for 6 months. Serum aldosterone, renin, echocardiography and health status were collected at baseline and 6 months. **RESULTS:** Mean age of participants 65.9 \pm 10.4 years, women 48%, AA 64%, mean EF 37.6 \pm 13.9, NYHA class III 36 %, II 64%. The vitamin D group increased serum 25OHD (19.1 \pm 9.3 to 61.7 \pm 20.3 ng/ml) and not in the placebo group (17.8 \pm 9.0 to 17.4 \pm 9.8 ng/ml). Aldosterone decreased in the vitamin D group (10.0 \pm 11.9 to 6.2 \pm 11.6 ng/dl) and not in the placebo group 8.9 \pm 8.6 to 9.0 \pm 12.4 ng/dl) ($p=.02$). There was no difference between groups in renin, echocardiographic measures or health status from baseline to 6 months. Modeling indicated that variables which predicted change in aldosterone included receiving vitamin D, increasing age, AA race, and lower GFR. **CONCLUSIONS:** Vitamin D3 repletion decreases aldosterone in patients with HF and low serum vitamin D. Vitamin D may be an important adjunct to standard HF therapy. Further will assess if vitamin D provides long-term benefit for patients with HF. ClinicalTrials.gov Identifier: NCT01125436.

[PLoS One.](#) 2013 Nov 15;8(11):e81120.

Vitamin D status and community-acquired pneumonia: results from the third National Health and Nutrition Examination Survey.

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OBJECTIVE: To investigate the association between serum 25-hydroxyvitamin D [25(OH)D] level and history of community-acquired pneumonia (CAP). **PATIENTS AND METHODS:** We identified 16,975 individuals (≥ 17 years) from the third National Health and Nutrition Examination Survey (NHANES III) with documented 25(OH)D levels. To investigate the association of 25(OH)D with history of CAP in these participants, we developed a multivariable logistic regression model, adjusting for demographic factors (age, sex, race, poverty-to-income ratio, and geographic location), clinical data (body mass index, smoking status, asthma, chronic obstructive pulmonary disease, congestive heart failure, diabetes mellitus, stroke, chronic kidney disease, neutropenia, and alcohol consumption), and season. Locally

weighted scatterplot smoothing (LOWESS) was used to depict the relationship between increasing 25(OH)D levels and the cumulative frequency of CAP in the study cohort. **RESULTS:** The median [interquartile range (IQR)] serum 25(OH)D level was 24 (IQR 18-32) ng/mL. 2.1% [95% confidence interval (CI): 1.9-2.3] of participants reported experiencing a CAP within one year of their participation in the national survey. After adjusting for demographic factors, clinical data, and season, 25(OH)D levels <30 ng/mL were associated with 56% higher odds of CAP [odds ratio 1.56; 95% confidence interval: 1.17-2.07] compared to levels ≥30 ng/mL. LOWESS analysis revealed a near linear relationship between vitamin D status and the cumulative frequency of CAP up to 25(OH)D levels around 30 ng/mL. **CONCLUSION:** Among 16,975 participants in NHANES III, 25(OH)D levels were inversely associated with history of CAP. Randomized controlled trials are warranted to determine the effect of optimizing vitamin D status on the risk of CAP.

[J Vet Intern Med.](#) 2014 Jan;28(1):109-15.

Relation of vitamin d status to congestive heart failure and cardiovascular events in dogs.

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BACKGROUND: Vitamin D plays a pivotal role in cardiac function, and there is increasing evidence that vitamin D deficiency is associated with the development of congestive heart failure (CHF) in people. **HYPOTHESIS:** Serum vitamin D concentration is lower in dogs with CHF compared with unaffected controls and serum vitamin D concentration is associated with clinical outcome in dogs with CHF. **ANIMALS:** Eighty-two client-owned dogs. **METHODS:** In this cross-sectional study, we examined the association between circulating 25-hydroxyvitamin D [25(OH)D], a measure of vitamin D status, and CHF in dogs. In the prospective cohort study, we examined whether 25(OH)D serum concentration was associated with clinical outcome in dogs with CHF. **RESULTS:** Mean 25(OH)D concentration (100 ± 44 nmol/L) in 31 dogs with CHF was significantly lower than that of 51 unaffected dogs (123 ± 42 nmol/L; $P = .023$). The mean calculated vitamin D intake per kg of metabolic body weight in dogs with CHF was no different from that of unaffected dogs (1.37 ± 0.90 µg/kg metabolic body weight versus 0.98 ± 0.59 µg/kg body weight, respectively, $P = .097$). There was a significant association of serum 25(OH)D concentration on time to clinical manifestation of CHF or sudden death ($P = .02$). **CONCLUSION AND CLINICAL RELEVANCE:** These findings suggest that low concentrations of 25(OH)D may be a risk factor for CHF in dogs. Low serum 25(OH)D concentration was associated with poor outcome in dogs with CHF. Strategies to improve vitamin D status in some dogs with CHF may prove beneficial without causing toxicity.

[J Cardiovasc Electrophysiol.](#) 2013 Oct 23.

Electromechanical Effects of 1,25-Dihydroxyvitamin D with Atrial Fibrillation Activities.

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INTRODUCTION: Treatment with 1,25-dihydroxyvitamin D ($1,25[\text{OH}]_2\text{D}$) has several cardiovascular benefits. $1,25[\text{OH}]_2\text{D}$ has direct cellular effects, but its effects on the atrium are not clear. We evaluated the effects of $1,25[\text{OH}]_2\text{D}$ on the atrial electrophysiology and atrial fibrillation (AF). **METHODS:** Conventional microelectrodes were used to record action potentials (APs) and contractility in isolated rabbit left atrium (LA) tissue preparations before and after the administration of 0.01, 0.1, and 1 nM $1,25[\text{OH}]_2\text{D}$ with and without rapid atrial pacing (RAP) and acetylcholine (5 mM)-induced AF. Surface

ECG and intracardiac electrograms were recorded before and after the intravenous administration of 4 units/kg of 1,25[OH]₂ D in heart failure (HF) rabbits (4 weeks after coronary artery ligation) with RAP and acetylcholine-induced AF. **RESULTS:** 1,25[OH]₂ D dose-dependently increased the AP duration in the LA, which was abolished by pretreatment with 0.1 μM ryanodine. RAP and 5 mM acetylcholine-induced fewer (64.3% vs 100%, P < 0.05) AF occurrences in the presence (n = 14) of 1,25[OH]₂ D than those (n = 14) in the absence of 1,25[OH]₂ D. The LA treated with 1,25[OH]₂ D (n = 9) had a slower maximal AF rate (10.9 ± 2.4 Hz vs 13.3 ± 2.7 Hz, P < 0.05) than the LA (n = 14) without 1,25[OH]₂ D. Moreover, 1,25[OH]₂ D caused a lower AF inducible percentage (11.0 ± 1.9% vs 100 ± 0%, P < 0.001) and a shorter duration (4 ± 0.4 seconds vs 309 ± 26 seconds, P < 0.001) with a prolonged LA 90% monophasic AP duration (94.1 ± 0.2 milliseconds vs 98.5 ± 0.1 milliseconds, P < 0.05) in 5 rabbits with HF. 1,25[OH]₂ D did not prolong the QT interval or 90% of the AP duration in isolated Purkinje fibers. **CONCLUSION:** 1,25[OH]₂ D has direct electromechanical effects on the LA and can prevent or terminate AF.

[J Card Fail.](#) 2013 Oct;19(10):692-711. doi: 10.1016/j.cardfail.2013.09.002.

Vitamin D in heart failure.

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Evidence linking vitamin D to cardiovascular (CV) health has accumulated in recent years: numerous epidemiologic studies report deficiency as a significant CV risk factor, and rodent models suggest that active vitamin D can modulate critical remodeling processes, including cardiac hypertrophy and extracellular matrix remodeling. The presence of vitamin D signaling machinery within the human heart implies a direct role for this hormone in cardiac physiology and may explain associations between vitamin D status and CV outcomes. Heart failure (HF) represents a growing social and economic burden worldwide. Myocardial remodeling is central to HF development, and in the context of emerging evidence supporting mechanistic involvement of vitamin D, this review provides critical appraisal of scientific literature related to the role of vitamin D in CV disease, including data from epidemiologic and supplementation studies, as well as novel findings from animal models and in vitro work. Although associative data linking vitamin D and CV outcomes and evidence supporting a role for vitamin D in relevant pathogenic processes are both substantial, there are limited mechanistic data to indicate vitamin D supplementation as a viable therapeutic adjunct for the prevention of HF development following myocardial injury.

[Am Heart J.](#) 2013 Aug;166(2):357-364.e2.

Short-term vitamin D3 supplementation lowers plasma renin activity in patients with stable chronic heart failure: an open-label, blinded end point, randomized prospective trial (VitD-CHF trial).

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BACKGROUND: Many chronic heart failure (CHF) patients have low vitamin D (VitD) and high plasma renin activity (PRA), which are both associated with poor prognosis. Vitamin D may inhibit renin transcription and lower PRA. We investigated whether vitamin D3 (VitD3) supplementation lowers PRA in CHF patients. **METHODS AND RESULTS:** We conducted a single-center, open-label, blinded end point trial in 101 stable CHF patients with reduced left ventricular ejection fraction. Patients were randomized to 6 weeks of 2,000 IU oral VitD3 daily or control. At baseline, mean age was 64 ± 10 years, 93% male, left

ventricular ejection fraction $35\% \pm 8\%$, and 56% had VitD deficiency. The geometric mean (95% CI) of 25-hydroxyvitamin D3 increased from 48 nmol/L (43-54) at baseline to 80 nmol/L (75-87) after 6 weeks in the VitD3 treatment group and decreased from 47 nmol/L (42-53) to 44 nmol/L (39-49) in the control group ($P < .001$). The primary outcome PRA decreased from 6.5 ng/mL per hour (3.8-11.2) to 5.2 ng/mL per hour (2.9-9.5) in the VitD3 treatment group and increased from 4.9 ng/mL per hour (2.9-8.5) to 7.3 ng/mL per hour (4.5-11.8) in the control group ($P = .002$). This was paralleled by a larger decrease in plasma renin concentration in the VitD3 treatment group compared to control ($P = .020$). No significant changes were observed in secondary outcome parameters, including N-terminal pro-B-type natriuretic peptide and fibrosis markers. **CONCLUSIONS: Most CHF patients had VitD deficiency and high PRA levels. Six weeks of supplementation with 2,000 IU VitD3 increased 25-hydroxyvitamin D3 levels and decreased PRA and plasma renin concentration.**

[J Cardiovasc Pharmacol Ther.](#) 2013 Jul;18(4):386-91.

Cardioprotective effect of calcitriol on myocardial injury induced by isoproterenol in rats.

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BACKGROUND: Calcitriol (CAL), an active form of vitamin D, plays a vital role in controlling cardiac hypertrophy and heart failure. The aim of the present study is to explore the effects of CAL and to elucidate its underlying mechanisms on myocardial injury induced by isoproterenol (ISO). **METHODS:** Myocardial impairment was induced by the subcutaneous injection of ISO in adult male Sprague-Dawley rats, and the therapeutic effect of CAL was assessed. Biometric and echocardiographic parameters, interstitial fibrosis, oxidant-antioxidant status, and protein expression relevant to the mitochondrial apoptosis pathway were then measured. **RESULTS:** Calcitriol treatment improved the cardiac injury resulting from excessive ISO stimulation, as supported by the suppression of the development of myocardial hypertrophy, interstitial fibrosis, and H₂O₂ level in heart tissue. The decreased superoxide dismutase and catalase activities induced by ISO were also improved by CAL. Finally, the administration of CAL downregulated the protein expression of Bax and caspase-9. **CONCLUSIONS: This study provides evidence that CAL ameliorated cardiac hypertrophy, interstitial fibrosis, and oxidative stress in ISO-induced cardiac injury and might play a vital cardioprotective role in such injuries.**

[Congest Heart Fail.](#) 2013 Jul-Aug;19(4):E22-8.

Can vitamin D supplementation improve the severity of congestive heart failure?

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The aim of the present study was to investigate whether vitamin D supplementation could improve biochemical findings and functional capacity of patients with heart failure (HF). One hundred patients with New York Heart Association (NYHA) class I through III HF were included in this prospective study and their 25-hydroxyvitamin D levels were evaluated. Only 6% of the participants had a sufficient serum concentration of 25(OH) D >30 nmol/L. Patients with insufficient or deficient serum levels of 25(OH) D (<30 ng/mL and <20 ng/mL, respectively) received oral vitamin D3 (cholecalciferol) for a total

period of 4 months. **Vitamin D supplementation increased mean serum concentration of 25(OH) D from 12.63±7.60 nmol/L to 54.49±18.01 nmol/L (P<.001). After vitamin D supplementation, the serum level of pro-brain natriuretic peptide markedly decreased (P<.001). Cholecalciferol significantly decreased high-sensitivity C-reactive protein level (P<.001). Restoration of serum 25(OH) D level was also associated with substantial improvement in NYHA class (P<.001) and 6-minute walk distance (P<.001).**

[J Clin Endocrinol Metab.](#) 2013 May;98(5):E872-6.

Prevalence and consequences of vitamin D insufficiency in women with takotsubo cardiomyopathy.

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OBJECTIVE: The purpose of this study was to identify the prevalence and clinical consequences of vitamin D insufficiency in patients with takotsubo cardiomyopathy. **BACKGROUND:** Takotsubo cardiomyopathy is a syndrome of acute, transient left ventricular dysfunction seen predominantly in postmenopausal women after acute emotional or physical stress. Postmenopausal women have a high prevalence of bone and musculoskeletal consequences related to hypovitaminosis D. Although rickets is known to cause a reversible dilated cardiomyopathy in children, the importance of vitamin D for adult cardiovascular health is less understood. **METHODS:** We prospectively identified patients diagnosed with takotsubo cardiomyopathy at Danbury Hospital from April 2009 through January 2011, collected demographic, clinical, laboratory, and angiographic data, and performed serum 25 hydroxyvitamin D levels during the index hospitalization. Vitamin D insufficiency was defined as serum 25-hydroxy-vitamin D less than 30 ng/mL. We compared parameters of myocardial damage and heart failure between patients with and without vitamin D insufficiency. A χ^2 test and a Student's t test were used for categorical and continuous variables, respectively. Statistical significance was set at $P < .05$ (2 tailed). **RESULTS:** Twenty-seven women were diagnosed with takotsubo cardiomyopathy during the study period. The mean age was 67.4 years (SD 10.4). The serum 25-hydroxyvitamin D levels were performed on 25 patients, and 17 of these had hypovitaminosis D (68%). A comparison of laboratory and imaging parameters between the 2 groups revealed that patients with hypovitaminosis D had a slightly higher mean left ventricular end-diastolic pressure and lower mean left ventricular ejection fraction ($P < .05$), suggestive of slightly worse heart failure. **CONCLUSIONS: Women diagnosed with takotsubo cardiomyopathy have a high prevalence of vitamin D insufficiency. In our prospective study of 25 women with takotsubo cardiomyopathy, this was associated with worse hemodynamic parameters.**

[Int J Cardiol.](#) 2013 Oct 3;168(3):2341-6.

Vitamin D and prognosis in acute myocardial infarction.

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BACKGROUND: Vitamin D status (VDS) has been linked to mortality and incident acute myocardial infarction (AMI) in healthy cohorts. Associations with recurrent adverse cardiovascular events in those with cardiovascular disease are less clear. **Our objective was to assess the prevalence and prognostic impact of VDS on patients presenting with AMI. METHODS:** We measured plasma 25-(OH)D3 and 25-(OH)D2 using isotope dilution tandem mass spectrometry, in 1259 AMI patients (908 men, mean age 65.7 ± 12.8 years). The primary endpoint was major adverse events (MACE), a composite of death (n=141), heart failure hospitalisation (n=111) and recurrent AMI (n=147) over median follow-up of 550 days (range 131-1095). Secondary endpoints were fatal and non-fatal MACE.

RESULTS: Almost 74% of the patients were vitamin D deficient (<20 ng/ml 25-(OH)D). Plasma 25-(OH)D existed mainly as 25-(OH)D₃ which varied with month of recruitment. Multivariable survival Cox regression models stratified by recruitment month (adjusted for age, gender, past history of AMI/angina, hypertension, diabetes, hypercholesterolaemia, ECG ST change, Killip class, eGFR, smoking, plasma NTproBNP), showed 25-(OH)D₃ quartile as an independent predictor of MACE (P<0.001) and non-fatal MACE (P<0.01), but not death. Using the lowest 25-(OH)D₃ quartile (<7.3 ng/ml) as reference for MACE prediction, the 2nd, 3rd and 4th quartiles showed significantly lower hazard ratios (HR 0.59 (P<0.002), 0.58 (P<0.001), and 0.59 (P<0.003) respectively). For non-fatal MACE prediction, the 2nd, 3rd and 4th 25-(OH)D₃ quartiles were all significantly different from the lowest reference quartile (HR 0.69 (P<0.05), 0.54 (P<0.003) and 0.59 (P<0.014) respectively). **CONCLUSIONS: VDS is prognostic for MACE (predominantly non-fatal MACE) post-AMI, with approximate 40% risk reduction for 25-(OH)D₃ levels above 7.3 ng/ml.**

[J Appl Physiol \(1985\)](#). 2013 Apr;114(8):979-87.

Vitamin D signaling pathway plays an important role in the development of heart failure after myocardial infarction.

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Accumulating evidence suggests that vitamin D deficiency plays a crucial role in heart failure.

However, whether vitamin D signaling itself plays an important role in cardioprotection is poorly understood. In this study, we examined the mechanism of modulating vitamin D signaling on progression to heart failure after myocardial infarction (MI) in mice. Vitamin D signaling was activated by administration of paricalcitol (PC), an activated vitamin D analog. Wild-type (WT) mice underwent sham or MI surgery and then were treated with either vehicle or PC. Compared with vehicle group, PC attenuated development of heart failure after MI associated with decreases in biomarkers, apoptosis, inflammation, and fibrosis. There was also improvement of cardiac function with PC treatment after MI. Furthermore, vitamin D receptor (VDR) mRNA and protein levels were restored by PC treatment. Next, to explore whether defective vitamin D signaling exhibited deleterious responses after MI, WT and VDR knockout (KO) mice underwent sham or MI surgery and were analyzed 4 wk after MI. VDR KO mice displayed a significant decline in survival rate and cardiac function compared with WT mice after MI. VDR KO mice also demonstrated a significant increase in heart failure biomarkers, apoptosis, inflammation, and fibrosis. **Vitamin D signaling promotes cardioprotection after MI through anti-inflammatory, antifibrotic and antiapoptotic mechanisms.**

[Curr Opin Cardiol](#). 2013 Mar;28(2):216-22.

The role of vitamin D in chronic heart failure.

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PURPOSE OF REVIEW: Despite advanced medical and device-based therapies, congestive heart failure (CHF) remains a major medical problem, associated with significant morbidity and mortality. Vitamin D deficiency is prevalent in CHF and is associated with poor outcomes. In this manuscript we review the evidence linking vitamin D deficiency and CHF and discuss potential mechanisms involved, as well the clinical data on vitamin D supplementation in CHF patients.

RECENT FINDINGS: A clear relationship has been established between Vitamin D deficiency and increased mortality and morbidity in CHF. However, the mechanism involved is not clearly understood.

Recent clinical and experimental evidence have identified the renin-angiotensin-aldosterone system and inflammatory cytokines as likely mediators that can lead to poor clinical outcomes via the cardiorenal syndrome. Clinical data on vitamin D supplementation also remain unestablished, with potential clinical benefits recently reported in patients with vitamin D deficiency. Nonetheless, large-scale randomized clinical trials are lacking. **SUMMARY: Vitamin D is an emerging agent with tremendous potential and may represent a novel target for therapy in CHF. Further studies are needed to identify the mechanism(s) involved in the pathophysiology as well as to adequately examine the role of Vitamin D measurement and supplementation in patients with CHF.**

[Am J Physiol Cell Physiol.](#) 2013 Jun 1;304(11):C1027-39.

The world pandemic of vitamin D deficiency could possibly be explained by cellular inflammatory response activity induced by the renin-angiotensin system.

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This review attempts to show that there may be a relationship between inflammatory processes induced by chronic overstimulation of the renin-angiotensin system (RAS) and the worldwide deficiency of vitamin D (VitD) and that both disorders are probably associated with environmental factors. **Low VitD levels represent a risk factor for several apparently different diseases, such as infectious, autoimmune, neurodegenerative, and cardiovascular diseases, as well as diabetes, osteoporosis, and cancer. Moreover, VitD insufficiency seems to predispose to hypertension, metabolic syndrome, left ventricular hypertrophy, heart failure, and chronic vascular inflammation.** On the other hand, inappropriate stimulation of the RAS has also been associated with the pathogenesis of hypertension, heart attack, stroke, and hypertrophy of the left ventricle and vascular smooth muscle cells. Because VitD receptors (VDRs) and RAS receptors are almost distributed in the same tissues, a possible link between VitD and the RAS is even more plausible. Furthermore, from an evolutionary point of view, both systems were developed simultaneously, actively participating in the regulation of inflammatory and immunological mechanisms. Changes in RAS activity and activation of the VDR seem to be inversely related; thus any changes in one of these systems would have a completely opposite effect on the other, making it possible to speculate that the two systems could have a feedback relationship. In fact, the pandemic of VitD deficiency could be the other face of increased RAS activity, which probably causes lower activity or lower levels of VitD. **Finally, from a therapeutic point of view, the combination of RAS blockade and VDR stimulation appears to be more effective than either RAS blockade or VDR stimulation individually**

[Clin Interv Aging.](#) 2013;8:149-56.

The influence of selective vitamin D receptor activator paricalcitol on cardiovascular system and cardiorenal protection.

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The ubiquitous distribution of vitamin D receptors in the human body is responsible for the pleiotropic effects of vitamin D-receptor activation. We discuss the possible beneficial effects of a selective activator of vitamin D receptor, paricalcitol, on the cardiovascular system in chronic heart failure patients and chronic kidney patients, in light of new trials. Paricalcitol should provide additional clinical benefits over the standard treatment for chronic kidney and heart failure, especially in cases of cardiorenal syndrome.

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Reprint of: Vitamin D receptor activation and prevention of arterial ageing.

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In chronic kidney disease (CKD) patients, cardiovascular (CV) morbidity and mortality rate is higher than in the general population, because of frequently concomitant hypertension, peripheral vascular disease, heart failure, vascular calcification (VC), diabetes and mineral bone disease. **Recently, another important factor associated to CV risk in CKD has been deeply investigated: vitamin D deficiency.** Vitamin D Receptors (VDRs) are present in several systems and tissues and VDR activation is associated to positive effects, resulting in better blood pressure control and prevention of diabetic nephropathy. Unfortunately, the natural, non-selective vitamin D receptor activator (VDRA), calcitriol, is associated to higher serum calcium and phosphate levels, thus worsening CV risk in CKD. **Recent data showed that the selective VDRA paricalcitol might have ameliorative CV effects. The potential positive impact of the use of paricalcitol on diabetic nephropathy, cardiac disease, hypertension, and VC may open new paths in the fight against CV disease in CKD patients.**

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Prevalence of vitamin D deficiency during the summer and its relationship with sun exposure and skin phototype in elderly men living in the tropics.

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OBJECTIVE: The aim of the study reported here was to determine the prevalence of vitamin D deficiency among elderly men and its association with sun exposure and skin phototypes.

SUBJECTS AND METHODS: This was an analytical cross-sectional study, which involved 284 men aged 60 years or over, randomly recruited from a basic care unit in the city of Recife (Brazil).

MEASUREMENTS: Serum levels of 25 hydroxyvitamin D (25(OH)D), sun index, and skin phototypes were evaluated.

RESULTS: The prevalence of vitamin D deficiency was 31.5% and 66.7% when cut points of less than 20 and 30 ng/mL, respectively, were used. Mean serum 25(OH)D was 27.86 ± 13.52 standard deviation (SD) ng/mL. There was no difference ($P = 0.113$) in 25(OH) D (23.98 ± 14.66 SD vs 29.88 ± 13.78 SD) between individuals in the lowest quartile (Q) of the sun index (Q1: 1.96) compared with those in the highest (Q4: 7.86). When considering a cutoff of 20 ng/mL, the sun index was different in the two groups ($P = 0.006$), but there was no difference when cutoffs of 25 and 30 ng/mL were used. After adjustment, sun index and body mass index were associated positively and negatively, respectively with serum 25(OH)D independently. Most subjects (66.7%) had Fitzpatrick's skin phototypes IV, V, and VI. Low calcium intake was observed in 72%. There was no difference in serum 25(OH)D levels between patients with low intake and those with intermediate and high intakes. Only 2.5% were taking a vitamin supplement.

CONCLUSION: We found a high prevalence of vitamin D deficiency among elderly men despite their high sun exposure during the summer months.