# Vitamin D Serum Levels and its Relation To The Echocardiography Parameters Of Cardiac Systolic And Diastolic Functions In Patients With Systolic Heart Failure

*Thesis*

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# List of Abbreviations

| | |
|---|---|
| 95% CI | : 95% confidence interval |
| CVD | : Cardiovascular disease |
| CYP | : cytochrome P450 |
| DBP | : D-binding protein |
| EIA | : Enzyme-Immuno-Assay |
| FGF23 | : Fibroblast Growth Factor 23 |
| IHD | : Ischemic heart disease |
| ION | : Institute of Medicine |
| PI3K | : Phosphotidyl inositol 3 kinase |
| RAAS | : Renin-angiotensin-aldosterone system |
| TLRs | : Toll-like receptors |
| TNF | : Tumor necrosis factor |
| UV | : Ultraviolet |
| VDR | : vitamin D receptor |

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# Introduction

Worldwide, the prevalence of vitamin D deficiency is as high as almost 50% among the elderly. A recent meta-analysis showing that vitamin D supplementation significantly decreased all cause mortality raised the public health interest in vitamin D. the classic role of vitamin D for maintaining bone health was recently extended by reports linking vitamin D deficiency to various other diseases, including arterial hypertension and diabetes mellitus. It also turned out that the myocardium is an important target tissue for vitamin D-mediated effects on a genomic and nongenomic level 3-5. Cardiomyocytes express the vitamin D receptor, and studies in rodents have shown that vitamin D protects against cardiac hypertrophy and myocardial dysfunction **(Mosekilde, 2005).**

The association between vitamin D and cardiovascular- disease events is widely debated and analyzed in the recent literature. In a very recent cross-sectional study, Pilz et al. measured 2 5-hydroxy vitamin. D (25(OH) vitamin D) levels in 3.299 Caucasian patients who were routinely referred for coronary angiography **(Pilz et al., 2008).** They found that vitamin D deficiency is

associated with prevalent myocardial dysfunction, heart failure, and sudden cardiac death. Although the link between vitamin D deficiency and cardiovascular disease may be, in part, mediated through elevated PTH and calcium-phosphate metabolism, recent scientific evidence showed that vitamin D has 3 major potential protective mechanisms. First, experimental studies indicate phosphate metabolism, recent scientific evidence showed that vitamin D has 3 major potential protective mechanisms. First, experimental studies indicate that 1.25- (OH) Vitamin D could directly suppress rennin gene expression. Second, the presence in the cardiac muscle cells of a vitamin D receptors, a calcitriol-dependent Ca2+binding protein and a calcitriol-mediated rapid activation of voltage-dependent Ca2+ channels. Third, vitamin D deficiency triggers secondary hyperparathyroidism, which then directly promotes cardiac hypertrophy (the direct PTH toxicity hypothesis) **(Nibbelink et al., 2007)**.

However, despite the suggested relation between vitamin D Deficiency and cardiac functions in patients with heart failure, to the best of our knowledge, has not been studied yet.

# Aim of the Work

Accordingly, we aim to study the relation between serum 25-hydroxy vitamin D levels and parameters of cardiac systolic and diastolic function in patients with LV systolic heart failure.

# Physiology of Vitamin D

## Introduction

Vitamins are chemically unrelated families of organic compounds that are essential in small amounts for normal metabolism. Because vitamins (with the exception of vitamin D) cannot be synthesized by humans, they need to be ingested in the diet to prevent disorders of metabolism **(Sassan and David, 2009).**

Vitamins are divided into water-soluble and fat-soluble, vitamin D is a fat-soluble vitamin, vitamin D is unique because it can be ingested as cholecalciferol (vitamin $D_3$) or ergocalciferol (vitamin $D_2$) and also the body can also synthesize it (from cholesterol) when sun exposure is adequate (hence its nickname, the "sunshine vitamin") **(Sassan and David, 2009).**

Vitamin D works like a hormone because it is produced primarily in one organ (the kidney) before circulating through the blood stream to organs where it has wide-ranging effects **(Holick, 2007).**

Actually it's a pro hormone that is synthesized in the skin after exposure to ultraviolet radiation. Less than **10%** of vitamin D comes from dietary sources in the absence of food fortification or use of supplements. The pro hormone is then converted to the metabolically active form in the liver and kidneys **(Madhusmita, 2011).**

Vitamin D has received a great deal of attention late in the scientific literature. Scores of mostly observational studies have investigated the possible role of vitamin D in the prevention of chronic diseases ranging from cancer to cardiovascular disease to autoimmune disorders & infections. No one doubts that vitamin D is essential to the health of older adults; the abundance of vitamin D receptor binding sites throughout the human genome highlight the pleiotropic nature of vitamin D in the human body **(Ramagopalan et al., 2010).**

Deficiency of vitamin D (commonly referred to as "rickets" when it occurs in children) is of unique historical value. Rickets was first described in the mid **1600s** by Whistler and Glisson **(Fraser and Scriver 1979).**

But for decades thereafter, no progress was made in identifying the cause. In **1918**, Sir Edward Mellanby

described the deficiency of a fat-soluble nutrient as the cause for rickets **(Mellanby, 1918).**

Shortly thereafter, Goldblatt and Soames demonstrated that skin exposed to sunlight or ultraviolet light produced a substance with similar properties to this fat-soluble nutrient **(Goldblatt and Soames, 1923).**

This ultimately led to the discovery of the chemical structure of vitamin D by Windaus **(Windaus et al., 1936).**

Vitamin D and its metabolites have a significant clinical role because of their interrelationship with calcium homeostasis and bone metabolism. Rickets due to vitamin D deficiency is now rare except in populations with unusually low sun exposure and lack of vitamin D in fortified foods **(Das et al., 2006).**

Subclinical vitamin D deficiency, as measured by low levels of 25(OH)D, has been described among adolescents**,** and the elderly**,** and may contribute to the development of osteoporosis and an increased risk of fractures and falls in the elderly **(Lips et al., 2006).**

Moreover, sufficient concentrations of vitamin D may be important in reducing the occurrence of

autoimmune diseases, such as multiple sclerosis**,** rheumatoid arthritis, diabetes and some cancers **(Garland et al., 2009).**

Adequate vitamin D may also allow for a normal innate immune response to pathogens, improve cardiovascular function and mortality and increase insulin responsiveness **(Mason et al., 2011).**