



KASR ALAINY

25-Hydroxy Vitamin D, Arterial calcification and Cardiovascular risk marker in haemodialysis patients Thesis

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Abstract

(Key Words): 25OH vitamin D3 – left ventricular mass index(LVMI)
– intimal media thickness (IMT)

Vascular calcification is frequent in patients with chronic kidney disease (CKD). The presence and extent of vascular calcifications are predictors of cardiovascular and all-cause mortality in stable end-stage renal disease patients on hemodialysis. **Accordingly, the present study was designed to examine the possible relation between** vascular calcifications, 25-hydroxyvitamin D3 [25(OH)D3] serum level and the cardiovascular risk factors associated. In this study, the significant increase in LVMI in the Dialysis group is inversely correlated to the vitamin D level ; patients with low levels of vitamin D have a high Left ventricular mass index. A significant negative correlation was observed also between plasma levels of vitamin D and intimal media thickness.



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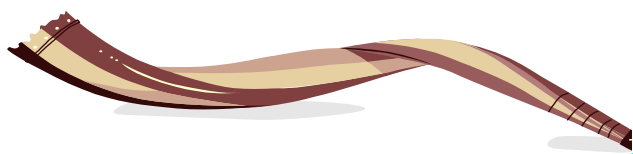
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Sameh M. Helmy

List of Abbreviations

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%	Percentage
Δ	Delta
25OH VIT D	25 hydroxy vitamin D3
4D	Deutsche Diabetes Dialyse Studie
ABD	Adynamic bone disease
AC	Arterial calcifications
ACE-I	Angiotensin converting enzyme inhibitor
ADPN	Adiponectin
ANP	Atrial natriuretic peptide
APOL-1	Apolipoprotein-1
ARBS	Angiotensin receptor blockers
ARIC	Atherosclerosis risk in community study
AUC	Area under curve
BMI	Body mass index
BMP-2	Bone morphogenetic protein 2
BNP	Brain natriuretic peptide
BP	Blood pressure
Ca	Calcium
cGMP	Cyclic guanosine monophosphate
CHD	Coronary heart disease
CHF	Congestive heart failure
CHS	Cardiovascular health study
CKD	Chronic kidney disease
CNH	Cardiac natriuretic hormone
CRP	C-reactive protein
cTNT	Cardiac troponin T
CVD	Cardiovascular disease
DEXA	Dual energy x-ray absorptiometry
EDD	End diastolic diameter
EF	Ejection fraction
eGFR	Estimated glomerular filtration rate

List of Abbreviations

ERA-	European renal association registry
EDTA	
ESD	End systolic diameter
ESRD	End stage renal disease
Fmol	Femto mole
FGF-23	Fibroblast growth factor
FS	Fractional shortening
GFR	Glomerular filtration rate
gm	gram
Hb	Hemoglobin
HD	Hemodialysis
HDL	High density lipoprotein
HS	Highly significant
HS-CRP	High sensitivity C-reactive protein
HUNT	The Norg-Trondelag health study
IL-18	Interleuken-18
IGF-1	Insulin growth factor-1
IMT	Intimal media thinkness
IVS	Interventricular septum
KD	Kilo Dalton
Kg	Kilogram
La	Left atrium
LDL	Low density lipoprotein
LVH	Left ventricular Hypertrophy
LVM	Left ventricular mass
LVMi	Left ventricular mass index
MBD	Mineral bone density
ml	milliliter
mm-Hg	Millimeter mercury
NF-Kβ	Nuclear factor K β
NKF	National kidney foundation
NPR	Natriuretic peptide receptor
NS	Non Significant
NT-	N terminal pro brain natriuretic peptide

List of Abbreviations

proBNP	
O PG	osteoprotegerin
P	Phosphorus
PTH	Parathormone
PTHrP	PTH-related peptide
pQCT	peripheral quantitative computed tomography
PWT	Posterior wall thickness
PWTS	Posterior wall thickness during systole
PWTD	Posterior wall thickness during diastole
RANKL	Receptor activator of NF- κ B ligand
RRF	Residual renal function
S	Significant
SHPT	Secondary hyperparathyroidism
STD	Standard
TREAT	Trial to reduce cardiovascular events with Aranesp therapy
USRDS	United States renal data system
VDR	Vitamin D receptor
VSMCs	Vascular smooth muscle cells

List of figures

<u>Figure</u> <u>1:</u>	Pathophysiology of bone mineral disease	57
<u>Figure</u> <u>2:</u>	Mean age value among the studied groups	99
<u>Figure</u> <u>3:</u>	Comparison between heights of studied groups	103
<u>Figure</u> <u>4:</u>	Comparison between urea of studied groups	105
<u>Figure</u> <u>5:</u>	Comparison between creatinine of studied groups	106
<u>Figure</u> <u>6:</u>	Comparison between calcium of studied groups	108
<u>Figure</u> <u>7:</u>	Comparison between phosphorus of studied groups	108
<u>Figure</u> <u>8:</u>	Comparison between SGpT of studied groups	109
<u>Figure</u> <u>9:</u>	Comparison between OH vit D3 of studied groups	110
<u>Figure</u> <u>10:</u>	Comparison between serum PTH of studied groups	111
<u>Figure</u> <u>11:</u>	Comparison between EF of studied groups	114
<u>Figure</u>	Comparison between PWT of studied groups	116

12:
Figure**13:**

Comparison between IVS of studied groups

117

Figure**14:**

Comparison between LVMI of studied groups

118

Figure**15:**

Comparison between IMT of studied groups

119

Figure**16:**

Correlation between height and 25 HOVD of patients included in the study

119

Figure**17:**

Correlation between PTH and 25 OHVD of patients included in the study

121

Figure**18:**

Correlation between LVMI and 25 OHVD of patients included in the study

122

Figure**19:**

Correlation between EDD and 25 OHVD of patients included in the study

123

Figure**20:**

Correlation between EDD and 25 OHVD of patients included in the study

124

Figure**21:**

Correlation between IMT and 25 OHVD of patients included in the study

125

Figure**22:**

Comparison between SGpT of in relation to sex

128

Figure**23:**

Comparison between 25OH VIT D in relation to sex

129

Figure**24:**

Comparison between EF in relation to sex

130

Figure**25:**

Comparison between IVS in relation to sex

131

<u>Figure</u> <u>26:</u>	Correlation between FS of patients in relation to 25 OH VIT D	132
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<u>Figure</u> <u>27:</u>	Correlation between weight of patients in relation to 25 OH VIT D	134
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List of Tables

Table	Title	Page
1	Classification and definitions of cardiorenal syndromes	20
2	Procalcificant and anticalcificant factors of vascular calcification	69
3	Comparison between demographic and laboratory data of patients in relation to sex	98
4	Comparison between echocardiographic data of patients in relation to sex	99
5	Descriptive statistics of demographic and laboratory data of patients included in the study	100
6	Descriptive statistics of demographic and laboratory data of controls included in the study	101
7	Comparison between demographic and laboratory data of patients and controls included in the study	102
8	Descriptive statistics of echocardiographic data of patients included in the study	112
9	Descriptive statistics of echocardiographic data of controls included in the study	113
10	Comparison between echocardiographic data of patients and controls included in the study	113
11	Correlation between echocardiographic data of patients with calcium, phosphorus and PTH	131
12	Comparison between demographic and laboratory data of patients in relation to 25 OHVD	137
13	Correlation between demographic and laboratory data of patients with calcium, phosphorus and PTH	133
14	Comparison between echocardiographic data of patients in relation to 25 OHVD	135

Contents

Introduction	1
Aim of work	4
Review of literature	5
<u>Chapter I:</u> Chronic Kidney disease and end stage renal disease	5-16
<u>Chapter II:</u> Cardiovascular disease and the kidney	17-51
<u>Chapter III:</u> vitamin D	52-91
Patients and methods	92
Results	98
Discussion	132
Summary and Conclusion	141
Recommendations	145
References	146
Arabic summary	\

Introduction

Cardiovascular disease is the most common cause of death in dialysis patients. Increasing evidence shows that abnormalities in mineral metabolism may play an important role in cardiovascular disease in patients with chronic kidney disease (CKD), as hyperphosphatemia, hypercalcemia, high calcium-phosphorus product and secondary hyperparathyroidism have all been associated with increase mortality in dialysis patients.(*Kalantar-Zadeh K, 2006 et al.*)

Advanced CKD leads to divalent cation exchange and metabolic derangements as well as decreased production of 1, 25-dihydroxyvitamin D₃ [1, 25 (OH)₂ D₃] (Calcitriol) all of which can cause parathyroid gland hyperplasia and development of bone disease. One of the main functions of vitamin D is to maintain calcium and phosphate serum concentrations in the normal range and to allow for mineralization of newly synthesized bone. Its main sites of actions are the small intestine, bone and kidney. (*Hendy GN, 2006 et al.*)

Vitamin D has also been recognized to have numerous non-calcaemic function, probably associated with wide distribution of Vitamin D receptor (VDR), namely in the brain ,heart skeletal muscle, smooth muscle, pancreas, activated T and B lymphocytes and monocytes. CKD also interferes

With the interaction of the VDR with DNA, the nuclear uptake of the Calcitriol-receptor complex and the synthesis and expression of the receptor (*Andress DL, 2006*)

Vascular calcifications are highly prevalent in dialysis patients and have been associated with an increased risk of total mortality and cardiovascular mortality. Recent studies have demonstrated that vascular calcification is an active cellular process, similar to bone formation (*Moe SM, 2002 et al.*) Vascular smooth muscle cells (VSMCs) can differentiate into osteoblasts due to different stimuli, like hyperphosphatemia and hypercalcemia (*Giachelli CM, 2004*). Reduction of calcification inhibitors, such as fetuinA or matrix-Gla protein, may be another factor associated with the development of calcification. The presence of (Vitamin D-receptor) VDR in VSMCs has been recently described and may explain a possible mechanism of the action of vitamin D in vascular calcifications. (*Andress DL, 2006*)

Patients with renal failure frequently have low serum 25-hydroxyvitamin D [25(OH) D₃] (the substrate of [1, 25(OH) ₂]. There are several reasons for this [25(OH) D₃] deficiency or insufficiency in these patients; they are inactive and have decreased exposure to sunlight, have reduced ingestion of foods that are natural sources of vitamin D, the endogenous synthesis of vitamin D in the skin is also compromised in uremic patients. (*LaClair RE, et al. 2005*)

Some mechanisms linking vascular calcifications with cardiovascular risk, such as the association between vascular calcifications and arterial stiffness, have also been recognized. The loss of arterial distensibility is associated with increased pulse