Fibroblast Gross Factor-23 and Arterial Stiffness in Hemodialysis Patient

Thesis

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Internal Medicine

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Salwa Yasser Mohammed Ali

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List of Abbreviations

ABI	**:**	Ankle - brachial index
AC	**:**	Arterial compliance
ACEIs	**:**	Angiotensin Converting Enzyme Inhibitors
AD	**:**	Aortic distensibility
ADHR	**:**	Autosomal dominant hypophosphatemic rickets
AIx	**:**	Augmentation index
ARBs	**:**	Angiotensin 2 Receptor Antagonists
ARHR	**:**	Autosomal recessive hypophosphatemic rickets
CaSRs	**:**	Calcium-sensing receptors
CAD		Coronary artery disease
CCIMT	**:**	Common carotid intima media thickness
Chr 12p13	**:**	Chromosome 12p13
CKD	**:**	Chronic Kidney Disease
CKD-MBD	**:**	Chronic Kidney disease – mineral bone disorder
CTA	**:**	Computed tomographic angiography
CVD	**:**	Cardiovascular Disease
CYP24A1	**:**	Cytochrome p450 subfamily A member 1 (Protein coding)
CYP27B1	**:**	Cytochrome p450 subfamily B member 1 (Protein coding)

DMP-1	**:**	Dentin matrixprotein-1
eGFR	**:**	Estimated glomerular filtration rate
ELISA	**:**	Enzyme-Linked Immunosorbent Assay
ESRD	**:**	End-stage Renal Disease
FD	**:**	Fibrous dysplasia
FGF	**:**	Fibroblast growthfactor
FGF-23	**:**	Fibroblast growth factor 23
FGF23-R		Fibroblast growth factor 23-receptor
GFR	**:**	Glomerular Filtration Rate
HRP	**:**	Horseradish Peroxidase
IMT	**:**	Intima media thickness
iPTH	**:**	Intact Parathyroid Hormone Serum Levels
KD	**:**	Kilo Dalton
LL37	**:**	The only human member of cathelicidin family of antimicrobial peptides
LRNc	**:**	Lipid rich necrotic core
MEPE	**:**	Matrix Extracellular Phosphoglycoprotein
MRI	**:**	Magnetic resonance imaging
mRNA	**:**	Messenger Ribonucleic Acid
PCR	**:**	Polymerase chain reaction
PET	**:**	Positron emission tomography
PP	**:**	Pulse pressure
PWV	**:**	pulse wave velocity
S.Ca	**:**	Corrected Serum Calcium

S.Creat.	**:**	Serum Creatinine
S.Po4	**:**	Serum Phosphorous
SAC	**:**	Systemic arterial compliance
TCD	**:**	Trans cranial Doppler
TIO	**:**	Tumor induced osteomalacia
URR	**:**	Urea Reduction Rate
VC	**:**	Vascular calcification
VDRs	**:**	Vitamin D receptors
XLH	**:**	X -linked hypophosphatemia

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Introduction

Fibroblast growth factor 23 (FGF-23) is a circulating osteocyte derived hormone that is often seen in elevated serum concentrations in patients with advanced chronic kidney disease (CKD) ***(Gutierrez et al., 2005).***

Fibroblast growth factor 23 (FGF-23) plays a key role in regulating serum phosphorous concentration by promoting phosphorous excretion and inhibiting 1 alpha hydroxylase in the renal proximal tubule ***(Burnett et al., 2006).***

FGF-23 requires its co-receptor which is a Klotho-receptor to bind to target tissue and exert its biological effects and most studies have showed that there is no expression of Klotho-receptor in human vascular cells as the one done by ***(Scialla et al., 2013 and Lindberg et al., 2013).***

However, there is a study suggested that, the expression of Fibroblast growth factor-23 (FGF-23) may be induced by vitamin D.receptor activator in human aortic smooth muscle cells as demonstrated by ***(Lim et al., 2012).***

Elevated serum Fibroblast growth factor-23 (FGF-23) is associated with cardiovascular disease (CVD), yet the mechanism remain uncertain Since, FGF-23 is integral in regulating phosphorous and vitamin D. metabolism, not only it responds to increased serum phosphorous, but it may also induce arterial calcification and stiffness as demonstrated by several studies like the one done by ***(Jeffry et al., 2014)*** and also there are many previous studies like those done by ***(Nasrallah et al., 2010 and Desfardins et al., 2012)*** that, have observed associations of elevated serum Fibroblast growth factor 23 (FGF-23) with arterial calcification and stiffness.

However the study done by ***(Scialla et al., 2013)*** revealed that Fibroblast growth factor-23 FGF23 is not associated with and does not induce arterial calcification.

Multiple community- based studies have demonstrated associations between measures of increased arterial stiffness ***(Peralta et al., 2012)*** and high ankle - brachial index (ABI) ***(OH et al., 2006)*** with increased cardiovascular morbidity and mortality, as well as incident hypertension, coronary heart disease, stroke, heart failure and kidney function decline.

Aim of the Study

Aim of study is to verify the usefulness of FGF23 as a marker for diagnosis of arterial stiffness in CKD patients on regular hemodialysis (3 sessions per week, 4 hours each).