EXTRA SKELETAL CALCIFICATION AND CARDIOVASCULAR MORBIDITY AND MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS

Essay

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Master Degree in Nephrology

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Noha Khalifa

Dedication

To my Great Parents,

the two true gems in my life and
to my mentor sister and gorgeous friend,
Heba.

God bless you

Noha Khalifa

LIST OF ABBREVIATIONS

Abbrev.	Meaning
AHSG	Alpha-٢-Heremann Schmitt Glycoprotein
AS	Aortic Stenosis
BCP	Basic Calcium Phosphate
Ca	Calcium
CAC	Coronary Artery Calcification
CAD	Coronary Artery Disease
CaxP	Calcium x Phosphorous Product
CCA	Common Carotid Artery
CCA Einc	Common Carotid Artery Incremental Elastic Modulus
CHD	Conventional Haemodialysis
CKD	Chronic Kidney Disease
CRF	Chronic Renal Failure
CRP	C-Reactive Protein
CVC	Cardiovascular Calcification
CVD	Cardiovascular Disease
DN	Diabetic Nephropathy
EBCT	Electron Beam Computed Tomography
ECF	Extracellular Fluid

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Meaning
EPC	Epithelial Progenitor Cells
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
HD	Haemodialysis
HSMC	Human Smooth Muscle Cells
IDNT	Irbersartan Diabetic Nephropathy Trial
LDL	Low Density Lipoprotein
Lp(a)	Lipoprotein (a)
LVEF	Left Ventricualr Ejection Fraction
MAC	Mitral Annular Calcification
MGP	Matrix G\a protein
MRI	Magnetic Resonance Imaging
NHD	Nocturnal Home Haemodialysis
OPG	Osteoprotegerin
OPN	Osteopontin
PFA	Polyunsaturated fatty acids
PO_4	Phosphate
PTH	Parathyroid Hormone
TGF-β	Transforming Growth Factor-β
TNF	Tumour Necrosis Factor
VSMCs	Vasomotor Smooth Muscle Cells

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I. INTRODUCTION

Over the last few years, a number of studies have focused on the clinical significance of vascular calcification in chronic kidney disease (CKD). Nearly half the deaths in dialysis patients are due to cardiovascular disease ***(USRDS, ٢٠٠٠)***. In CKD patients, vascular calcification is significantly associated with coronary ischemic disease ***(Raggi et al., ٢٠٠٢)***. In addition, increased vascular calcification in CKD patients leads to increased arterial wall stiffness and increased pulse pressure both correlating with enhanced cardiovascular mortality in CKD patients ***(Blacher et al., ١٩٩٨; Blaches et al., ٢٠٠١; Klasser et al., ٢٠٠٢).*** Furthermore, cardiac valve and myocardial calcification are also increased and probably contribute to morbidity and mortality in dialysis patients ***(Levin and Hoenich, ٢٠٠١).***

The most important evolution in the understanding of the clinical significance of disordered bone and mineral metabolism in CKD is the recognition that it is a systemic disorder affecting soft tissues, particularly vessels, heart valves, and skin. Cardiovascular disease accounts for approximately half of all deaths of dialysis patients. Coronary artery and vascular calcifications occur frequently in stage ٥ CKD and increase as a function of the number of years on dialysis. Gaining a better understanding of the aetiology for this increased vascular calcification

seen in patients with CKD and of how it may influence clinical cardiovascular events is of crucial importance ***(Tanenbaum and Quarles, ٢٠٠٥).***

Kidney disease increases the risk of coronary mortality ***(Mann et al., ٢٠٠١)*** and all cause mortality ***(Culleton et al., ١٩٩٩).*** Among patients with end stage renal disease (ESRD), the risk of cardiovascular disease is ١٠ to ٢٠ times higher than in the general population ***(Foley et al., ١٩٩٨)***, and cardiovascular disease accounts for ٥٠% of all deaths in this population ***(USRDS, ٢٠٠٢)***. However, this increased risk occurs even at moderate reductions in kidney function, independently of cardiovascular risk factors ***(Manjunath and Ibrahim et al., ٢٠٠٣; Manjunath and Coresh et al., ٢٠٠١).***

Finally, severe medial calcification of small arterioles leads to calciphylaxis, a rare but often fatal syndrome of ischemic necrosis of the skin and adjacent tissues seen almost exclusively in uremic patients ***(Coates et al., ١٩٩٨).*** Thus, understanding regulation and potentially controlling vascular calcification in CKD patients is a high priority ***(Yang et al., ٢٠٠٣).***

The contribution of accelerated atherosclerosis and disordered mineral metabolism to the high vascular calcification burden among individuals with CKD has not been previously evaluated ***(Mehrotro et al., ٢٠٠٤).***