

Cardiac Structure and Function in Predialysis Chronic Kidney Disease Patients

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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 **Ahmed Mosleh Monir**

Dedication

*I dedicate this work with sincere love
and appreciation to my **Father**, for his great
support and assistance.*

✍ Ahmed Mosleh

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List of Abbreviations

Abbr.	Full-term
ACE	Angio-tensin enzyme
Alb/Cr	Albumin/creatinine
ALK	Alkalinephosphatase
ApoB	Apolipoprotein B
ApoC	Apolipoprotein C
ARBs	Angiotensin receptor blocker
ARIC	Atherosclerosis Risk in Communities
AVF	Arterio-venous fistula
BMI	Body mass index
BP	Blood pressure
Ca	Calcium
CARE	Combined analysis of the cholesterol and recurrent events
CERA	Continous erythropiosis receptor activator
CKD	Chronic kidney disease
CRP	C reactive protein
CRS	Cardio renal syndrome
CV	Cardiovascular
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DC	Dentritic cells
DKD	Diabetic kidney disease
DM	Diabetis mellitus
DN	Diabetic nephropathy
ECHO	Echocardiograthy
EDV	End diastolic volume
EF	Ejection fraction
eGFR	Estimated glomerular filtration rate
EPO	Erythropiotin
ESRD	End stage renal disease
FBG	Fasting blood glucose

FDA	Food and Drug Administration
FGF 23	Fibroblast growth factor 23
GMB	Glomerular basement membrane
HB	Hemoglobin
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Hemodialysis
HDL	High density lipoprotein
HF	Heart failure
HF-REF	Heart failure reduced left ventricle ejection fraction
HIF	Hypoxia inducible factor
HPS	Heart protection study
HTN	Hypertension
IDL	Intermediate density lipoprotein
KDIGO	Kidney disease improving global outcomes
LDL	Low density lipoprotein
Lp(a)	Lipoprotein a
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVM	Left ventricle mass
MC	Mast cell
MDRD	Modification of diet in renal disease study
mPAP	Mean pulmonary arterial pressure
NO	Nitric oxide
PAH	Pulmonary arterial hypertension
PCWP	Pulmonary capillary wedge pressure
PH	Pulmonary hypertension
PLT	Platelets
Po4	Phosphorus
PTH	Parathyroid hormone
RAS	Renin angiotensin system
RCT	Randomized control trial
SBP	Systolic blood pressure
SD	Standard deviation
T1DM	Type 1 diabetes mellitus
TC	Total cholesterol

TG	Triglyceride
TNT	Treatment to new targets
UAE	Urinary albumin excretion
US	Ultrasound
VDR	Vitamin D receptor
VLDL	Very low density lipoprotein
VSMC	Vascular smooth muscle cell
WBC	White blood cell

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Introduction

Chronic kidney disease (CKD) is a global public health problem and is associated with increased cardiovascular risk and mortality and increased incidence of heart failure (HF) (*Park et al, 2012, Cai et al., 2014*).

Cardiovascular mortality is estimated to be at least 10- to 100- fold higher in patients with end stage renal disease (ESRD) than in the age-, race-, and sex-matched general population (*Go et al., 2004*).

This higher mortality is attributed to an increased risk of developing accelerated atherosclerosis, inflammation, vascular calcification, heart failure, and sudden cardiac death (*Herzog et al., 2011*).

Cardiac structural and functional changes are important subclinical measures that have been associated with adverse clinical outcomes among patients with CKD and ESRD and a key factor in accelerating heart failure risk in these patients (*Otsuka et al., 2009, Park et al., 2012, Bansal et al., 2013, Cai et al., 2014*).

A better understanding of changes in left ventricular structure and function during the transition from CKD to ESRD may provide important insights to opportunities to improve cardiovascular outcomes.

Aim of the Work

The aim of the present study is to evaluate changes in cardiac structure and function among pre-dialysis CKD patients without heart failure and to assess the possible relationship between these changes and clinical and laboratory data.

Chapter 1

Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on cause, GFR category (G1–G5), and albuminuria category (A1–A3), abbreviated as CGA (*Wheeler et al., 2017*).

Prognosis of CKD by GFR and albuminuria category						
Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories, description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m ²), description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

Figure (1): Stages of chronic kidney disease (*KDIGO, 2012*)

The *eGFR* is primarily determined by serum creatinine (SCr), and the preferred method for estimating GFR is the body surface area-normalized, 4-variable, Modification of