Myostatin Level in CRF Patients With And Without HCV +ve And Its Correlation With BMI

Thesis

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By

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List of Abbreviations

Abbrev.	Full term
CKD	Chronic kidney disease
NDD-CKD	Non-Dialysis Dependent
GFR	Glomerular filtration rate
ESKD	End stage Kidney disease
ROD	Renal Osteodystrophy
HD	Hemodialysis
DHCC	Dihydroxycholecalciferol
HCV	Hepatitis C virus
HOMA-IR	Homeostasis model assessment of insulin resistance
GN	Glomerulonephritis
MPGN	Membranoproliferative glomerulonephritis
MGN	Membranous nephropathy
DOPPS	Dialysis Outcomes and Practice Patterns Study
KDQOL	The Kidney Disease Quality of Life
HO	Hepatic osteodystrophy
IGF-1	Insulin-like growth factor 1
mTOR	Mammalian target of rapamycin
UPP	Ubiquitin–proteasome pathway
GI	Gastrointestinal
BCAAs	Branched chain amino acids
DXA	dual-energy X-ray absorptiometry
CT	Computerized tomography
BMD	Bone mineral density
PTH	Parathyroid hormone
RAAS	Renin angiotensin aldosterone system
LBM	Lean muscle mass
ADL	Activities of daily living
SPPB	Short physical performance battery

MRI	Magnetic resonance imaging
APLM	Appendicular lean mass
CSA	Cross-sectional area
GDF-8	Growth/differentiation factor-8
ALK	Activin-like kinase
mTOR	Mammalian target of rapamycin
GASP-1	GDF-associated serum protein-1
FLRG	Follistatin-related gene

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Abstract

Background: Chronic kidney disease (CKD) is a progressive condition that may negatively affect musculoskeletal health. Secondary sarcopenia due to CKD may be associated with mobility limitations and elevated fall risk. Myostatin is a member of transforming growth factor β family, which regulates synthesis and degradation of skeletal muscle proteins and is associated with the development of sarcopenia.

Objective: To evaluate myostatin level in HCV +ve and HCV-ve hemodialysis patients and to study its correlation with body mass index in chronic renal failure patients as compared to matched control group.

Patients and methods: All the studied cases were subjected to the following: careful medical history taking, full physical examination, abdominal ultrasonography and laboratory investigations including CBC, liver function tests, renal function tests, Na, K, PO4 and serum myostatin level.

Results: Our results revealed; there is a highly significant increase in the level of myostatin in case of HCV +ve hemodialysis patients; with highly significant statistical difference ($p<0.001$).

Conclusion: Our results revealed; Serum myostatin level is a predictor for the presence of sarcopenia.

Keywords:

Chronic renal faluire, sarcopenia, myostatin.

Introduction

Chronic kidney disease (CKD) is a progressive condition that may negatively affect musculoskeletal health. These comorbidities may include malnutrition, osteoporosis and decreased lean body mass. Secondary sarcopenia due to CKD may be associated with mobility limitations and elevated fall risk **(Hernandez et al., 2018)**.

Loop diuretic use was associated with increased risk of sarcopenia in patients with NDD-CKD (Non-Dialysis Dependent) **(Ishikawa et al., 2018)**.

The classification and staging of sarcopenia includes not only the loss of muscle mass, but also the impact of poor body composition on muscle strength and mobility status **(Cruz-Jentoft et al., 2010)**.

Patients with chronic kidney disease are subjected to muscle wasting. Therefore, it is important to investigate surrogate methods that enable the assessment of muscle mass loss in the clinical setting **(Giglio et al., 2018).**

The hemodialysis procedure stimulated protein degradation and reduced protein synthesis. These responses persisted for 2 h following dialysis, suggesting that a process causing protein loss was initiated by the therapy and persisted. Although increasing the intake of protein and calories improved protein turnover, it did not fully correct the responses to hemodialysis **(Carrero et al., 2013).**

Mid-arm circumference is a simple anthropometric method that reflects the amount of muscle mass by deducting the amount of measured fat in the triceps and bone width. The diagnosis of sarcopenia can be established when this value is below the 10^{th} percent mometer and predicts the muscle function **(Duarte-Rojo et al., 2017)**

Myostatin is a member of transforming growth factor β family, which regulates synthesis and degradation of skeletal muscle proteins and is associated with the development of sarcopenia. It is up regulated in the skeletal muscle of chronic kidney disease patients and considered to be involved in the development of uremic sarcopenia. However, serum myostatin levels have rarely been determined and the relationship between myostatin levels with clinical and metabolic factors remain unknown **(Yamada et al., 2016).**

Myostatin regulates the proliferation and differentiation of myoblasts **(Langley et al., 2002).** Moreover, it also controls the activation and proliferation of satellite cells, the stem cells of skeletal muscle **(McCroskery et al., 2003)**.

Aim of the Work

Assessment of myostatin level in HCV +ve and HCV -ve hemodialysis patients and to study its correlation with body mass index in chronic renal failure patients as compared to matched control group.

Chapter I
Chronic Renal Disease

Anatomy and physiology of the kidney:-

In humans, the kidneys are located high in the abdominal cavity, one on each side of the spine, and lie in a retroperitoneal position at a slightly oblique angle **(*Kumar et al., 2014*).**

The substance, or parenchyma, of the kidney is divided into two major structures: the outer renal cortex and the inner renal medulla. Grossly, these structures take the shape of eight to 18 cone-shaped renal lobes, each containing renal cortex surrounding a portion of medulla called a renal pyramid ***(Walter, 2004).***

The nephron is the microscopic structural and functional unit of the kidney. It is composed of a renal_corpuscle and a renal tubule. The renal corpuscle consists of a tuft of capillaries called a glomerulus and an encompassing Bowman's capsule. The renal tubule extends from the capsule. The capsule and tubule are connected and are composed of epithelial cells with a lumen. A healthy adult has 0.8 to 1.5 million nephrons in each kidney **(*Bard et al., 2003*).**

The renal circulation supplies the blood to the kidneys via the renal arteries, left and right, which branch directly from the abdominal aorta. Despite their relatively small size, the kidneys receive approximately 20% of the cardiac output **(*Walter, 2004)***

The kidneys are central to homeostasis ***(Hoenig, and Zeidel, 2014)***. Through exquisite sensory mechanisms they regulate blood pressure, water, sodium, potassium, acidity, bone minerals and hemoglobin **(Blaine et al., 2015)**, but their core function is the excretion of the waste products of metabolism in urine **(Rayner et al., 2016)**

About 22 % of cardiac output goes to the kidneys and about 20 % of the plasma is filtered, producing about 170 L of glomerular filtrate per day. Ninety-nine percent of this is reabsorbed as it flows along the nephrons so only about 1.5 L of urine is produced per day **(Rayner et al., 2016).**

Filtration occurs through the glomerular filtration barrier **(Pollak et al., 2014)**. This is made up of five layers

- The glycocalyx covering the surface of the endothelial cells.
- Holes (fenestrations) in the glomerular endothelial cells.
- The glomerular basement membrane.
- The slit diaphragm between the foot-processes of the podocytes.
- The sub-podocyte space between the slit diaphragm and the podocyte cell body (**Arkill et al., 2014)**

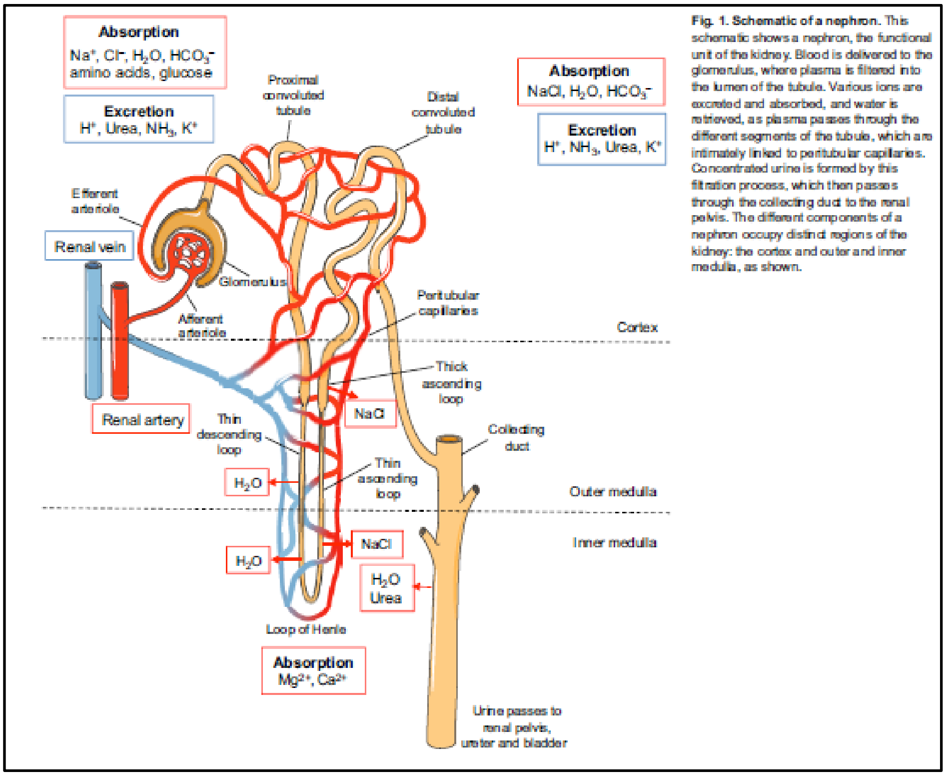

Figure (1): Schematic of a nephron ***(Linda et al., 2016)***

Chronic kidney disease:

CKD is defined as:

- Abnormalities of kidney structure or function, present for more than 3 months, with implications for health **(NCGC 2014)**.

Criteria for CKD (any of the following present for more than 3 months):

- Markers of kidney damage (one or more):
- Albuminuria (ACR ³ 3 mg/mmol).