Correlation between Hemodialysis and Sarcopenia in Elderly Patients with Chronic Kidney Disease

Thesis

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Shahd Helmy Aly

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List of Abbreviations

Abb.	Full term
ADL	*Activities of Daily Living*
ASL	*Activities of Daily Living*
BIA	*Bioelectrical Impedance Analysis*
BMI	*Body Mass Index*
CBC	*Complete Blood Count*
CC	*Calf Circumference*
CKD	*Chronic Kidney Disease*
CRP	*C-reactive Protein*
CSA	*Cross-Sectional Area*
CT	*Computed Tomography*
DEXA	*Dual Energy X-Ray Absorptiometry*
eGFR	*Estimated GFR*
ESKD	*End-Stage Kidney Disease*
ESRD	*End Stage Renal Disease*
EWGSOP	*European Working Group for the Study of Sarcopenia*
GDS	*Geriatric Depression Scale*
GFR	*Glomerular Filtration Rate*
GH	*Growth Hormone*
HGS	*Hand Grip Strength*
IADL	*Instrumental Activities of Daily Living*
IL-6	*Interleukin-6*
LMM	*Low Muscle Mass*
LMS	*Low Muscle Strength*
LPP	*Low Physical Performance*
M	*Mean*
MNA	*Mini-Nutritional Assessment*
MRI	*Magnetic Resonance Imaging*
NICE	*National Institute for Health and Care Excellence*

List of Abbreviations (Cont...)

Abb.	Full term

PBK .....Partial Body Potassium
PEF .....Peak Expiratory Flow
PEW .....Protein-Energy Wasting
PTH .....Parathyroid Hormone
RE .....Resistance Exercise
SD .....Standard Deviation
SPPB .....Short Physical Performance Battery
SPSS.....Statistical Package for Social Science
TBK.....Total Body Potassium
TGF .....Transforming Growth Factor
TNF-a .....Tumor Necrosis Factor Alpha
TSMMI .....Total Skeletal Muscle Mass Index
TUGT.....Timed Up & Go Test
UPS .....Ubiquitin-Proteasome Proteolysis

ABSTRACT

Background: sarcopenia is a common health problem among elderly population with chronic kidney disease. It is a syndrome characterized by progressive and generalized loss of skeletal muscle mass, strength and performance. Sarcopenia is not noticeable in earlier stages but becomes apparent as stage of kidney disease advances so it is better to prevent progressive loss of skeletal muscle mass, strength, and function rather than try to restore it at older ages.

Aim of the Work: to study the relationship between chronic kidney disease (CKD) and sarcopenia in elderly people, and to study the effect of hemo-dialysis on occurrence of sarcopenia.

Subjects and Methods: we conducted a case control study to find the relation between development of sarcopenia and chronic kidney disease in patients on conservative therapy and on regular dialysis. Our participants were older adults, both men and women, 60 years old and above, who were admitted to Ain Shams University Hospital (El-Demerdash), and were either on conservative therapy or on maintenance hemodialysis therapy.

Results: clinical findings agree with standard methods of diagnosis of sarcopenia. There was muscle weakness affecting proximal and distal muscles of upper-limb, trunk and lower-limb in this group.

Conclusion: sarcopenia is common in patients with chronic kidney disease and its prevalence increases as the disease advance and became more severe in hemodialysis patients.

Keywords: *Hemodialysis – Sarcopenia - Chronic Kidney Disease*

INTRODUCTION

Sarcopenia is considered a major health problem that is anticipated to grow with aging ***(Kalinkovich and Livshits, 2015).***

The European Working Group for the study of sarcopenia (EWGSOP) in older population defined sarcopenia as the presence of both low muscle mass and either decreased strength or performance ***(Cruz-Jentoft et al., 2010).***

According to EWGSOP, sarcopenia could be divided into: pre-sarcopenia where there is decreasing muscle mass, sarcopenia where there is decreasing of both muscle mass and strength or performance, severe sarcopenia where there is decreasing muscle mass, strength and performance ***(Cruz-Jentoft et al., 2010).***

The pathogenesis of sarcopenia is multi-factorial. It could be primary: age related due to increase apoptosis of muscle cell, mitochondrial dysfunction, or it could be secondary with advanced organ failure, deconditioning, and sedentary lifestyle. Also, it could result from inadequate intake of energy and protein, as with malabsorption or gastrointestinal disorders and use of medications that cause anorexia ***(Cruz-Jentoft et al., 2010).***

Chronic kidney disease (CKD) is a very common clinical problem in elderly patients and is associated with increased morbidity and mortality. As life expectancy continues to

improve worldwide, there is a rising prevalence of comorbidities and risk factors such as hypertension and diabetes predisposing to a high burden of CKD in older adults ***(Mallappallil et al., 2014).***

The etiology of sarcopenia in hemodialysis patients is multifactorial. Sarcopenia could be due to loss of amino acids and albumin into the dialysate, systemic inflammation induced by contact with artificial substances; such as dialysis membrane and circuits, decreased physical activity, hormonal imbalance, malnutrition, impaired oxygen transport due to anemia, metabolic acidosis, vitamin D deficiency, increase expression of myostatin, insulin resistance, change of sex hormones and the activation of ubiquitin and proteasome system ***(Cruz-Jentoft et al., 2010; Lamarca et al., 2014).***

Sarcopenia and physical inactivity synergistically progress through loss of skeletal muscle, which in turn induces loss of physical function. Several studies show that both sarcopenia and physical inactivity have an association with increase mortality in CKD patients **(*Kortebein et al., 2007; Lee et al., 2007; Pillard et al., 2011).***

Aim of the Work

To study the relationship between chronic kidney disease (CKD) and sarcopenia in elderly people, and to study the effect of hemo-dialysis on occurrence of sarcopenia.

Chapter 1

SARCOPENIA

Introduction:

The term Sarcopenia (Greek, sarx for "flesh" and penia for "loss") refers to the phenomenon of reduction of both muscular mass and function with aging ***(Rosenberg, 1997)***.

Sarcopenia starts in the 4th decade of life and accelerates at the age of 75 years ***(Baumgartner and Garry, 2000)***.

As the number and proportion of older persons continue to rise, sarcopenia-related morbidity will become an increasing area of health care resource utilization ***(Dhillon and Hasni, 2017)***.

Sarcopenia is significantly associated with physical disability in both men and women, independent of ethnicity, age, morbidity, obesity, income, or health behaviors ***(Baumgartner et al., 1998)***.

Definition of sarcopenia:

Initial descriptions of sarcopenia focused on loss of muscle mass and did not consider inclusion of muscle strength or physical impairment as part of the disease process ***(Roubenoff, 2001)***.

The 2010 European Working Group on Sarcopenia in Older People (EWGSOP) recognized that muscle strength and muscle mass are significant components of sarcopenia. The

group defined sarcopenia as "a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with increasing risk of adverse outcomes such as physical disability, poor quality of life, and death" ***(Cruz-Jentoft et al., 2010)***.

Most scientists consider sarcopenia to be an inevitable part of aging. However, the degree of sarcopenia is highly variable and is dependent upon the presence of certain risk factors, lack of exercise, malnutrition, hormonal and cytokines imbalance ***(Dhillon and Hasni, 2017)***.

Epidemiology:

There is a significant variability in the reported prevalence of sarcopenia ***(Dhillon and Hasni, 2017)***.

Although the prevalence of sarcopenia in elderly people has been broadly investigated in the Unites States, European countries and to a lesser extent in Asian countries, there are no reports on the prevalence of sarcopenia in the African countries. There is no data on the epidemiology of sarcopenia in Egypt, and no studies done on community dwelling elderly ***(Abdel Rahman et al., 2014)***.

The prevalence of sarcopenia among nursing home older residents in Cairo was 22.2% in elderly men and 22.2% and in elderly women ***(Abdel Rahman et al., 2014)***.

In the United Kingdom, the prevalence of sarcopenia among community-dwelling older adults was about 4.6% in men and 7.9% in women using the EWGSOP criteria ***(Patel et al., 2013)***.

In another study done in the United States, conducted among older adults with an average age of 70.1 years, prevalence of sarcopenia was reported as high as 36.5% ***(Brown et al., 2016)***.

While, in a Japanese study that included community-dwelling elderly adults, the prevalence of sarcopenia ranged from 2.5% to 28.0% in men and 2.3% to 11.7% in women (using dual-energy X-ray absorptiometry for measuring lean body mass ***(Kim et al., 2016).***

In a large cohort study done in Taiwan, the prevalence of sarcopenia in community-dwelling older adults (age >65 years) varied from 3.9% to 7.3% with prevalence reaching 13.6% among men aged 75 years and older ***(Wu et al., 2014)***.

Risk factors for sarcopenia

1. Lack of Exercise

Lack of exercise is believed to be the foremost risk factor for sarcopenia ***(Abate et al., 2007)***.

A gradual decline in muscle fiber numbers begins around 50 years of age. The decline in muscle fiber and strength is more pronounced in patients with sedentary lifestyle as

compared to patients who are physically more active. Even professional athletes such as marathon runners and weight lifters show a gradual, but slower, decline in their speed and strength with aging ***(Faulkner et al., 2007)***.

There is a bidirectional relationship between sarcopenia and physical inactivity. With aging there is loss of skeletal muscles which increases the risk of sarcopenia and induces physical inactivity. The latter accelerates the progression of sarcopenia ***(Pillard et al., 2011)***.

2. Hormone and Cytokine Imbalance

Age-related decrease in hormone concentrations occurs; including growth hormone, testosterone, thyroid hormone, and insulin-like growth factor, which lead to loss of muscle mass and strength. Extreme muscle loss often results from a combination of diminishing hormonal anabolic signals and promotion of catabolic signals mediated through pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-a) and interleukin-6 (IL-6) ***(Ryall et al., 2008)***.

3. Protein Synthesis and Regeneration

A decrease in the body's ability to synthesize proteins, together with inadequate calories and/or protein intake to sustain muscle mass, is common in sarcopenia. Oxidized proteins increase in skeletal muscle with aging and lead to a buildup of lipofuscin and cross-linked proteins that are