Sarcopenia in Chronic Kidney Disease and the Effectiveness of Physical Activity

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Abstract

Chronic kidney disease is a problem of enormous relevance and recognized as a complex disease, requiring multiple approaches to its treatment. A high percentage of sarcopenia in CKD has been reported and its cause is multifactorial. This literature review was perform to present the current evidence on etiology of sarcopenia, adverse outcomes and effectiveness of physical activity in sarcopenic CKD individuals. According to national and international researchers, the practice of aerobic training and combination with resistance exercises generated significant effects in the functional capacity, muscle function, physical performance and quality of life of patients with CKD.

Keywords: sarcopenia; physical performances; chronic kidney disease.

Introduction

It is well documented that chronic kidney patients, especially those on dialysis, have significantly less physical capacity than healthy individuals. The worsening of physical capacity occurs in parallel with the evolution of the disease.1 Prevalence of sarcopenia has been suggested in advanced and growing countries, and this disease impacts each healthful people and people with continual diseases, which includes hypertension, diabetes and continual kidney disease. The cause of sarcopenia is multifactorial and usually associated with environmental factors, chronic diseases, activation of inflammatory mediators, physical inactivity, mitochondrial abnormalities, loss of neuromuscular junctions, a decrease in the number of satellite cells and hormonal changes.2

In this review, we focus on definitions of sarcopenia in CKD, a concise review of the cause of skeletal muscle changes in CKD and the benefits of exercises to prevent and treat sarcopenia.

Chronic Kidney Disease Definitions and Considerations

Chronic kidney disease (CKD) is described as kidney harm or an envisioned glomerular filtration rate (eGFR) beneath 60 ml/min/1.73m2 persisting for three months or extra of the cause. In this important document, a new conceptual framework of diagnosis of CKD was proposed which was worldwide accepted in the following years. Is primarily based totally on three components: (1) an anatomical or structural component (markers of kidney damage), (2) a purposeful component (primarily based totally on GFR), and (three) a temporal component.3 In 2012, in the last classification, the Kidney Disease Outcomes Quality Initiative (KDOQI) recommended detailing the cause of CKD, classifying it into six categories related to GFR (G1 to G5, being G3 in 3a and 3b), and also based on the three levels of albuminuria (A1, A2 and A3), evaluated by the urinary albumin/creatinine ratio. The True prevalence and occurrence of CKD inside a network are tough to examine due to the fact slight to slight CKD is typically asymptomatic. However, epidemiological studies suggest a prevalence between 10-14% in the general population, albuminuria 7% and GFR less than 60ml/min/1.73 m2 around 3-5%.5

CKD is a problem of enormous relevance and recognized as a complex disease, requiring multiple approaches to its treatment. Although the implementation of evidence-based medicine has resulted in advances in treatment, there is still a need for better preparation of patients who start renal replacement therapy (RRT), as well as a reduction in mortality and hospitalization rates.6
Currently, in addition to traditional conservative treatment, where the nephrologist assesses blood pressure control, anemia control, restriction of excessive sodium use, use of medications that control albuminuria, diet with or without protein restriction, delay the onset of bone mineral disorder, early referral to the vascular surgeon for definitive access, guide patients regarding kidney transplantation or peritoneal dialysis, optimization of glycemic control, maintenance of oral health is also guided the initiation of physical rehabilitation programs. There is a wide range of research in the field of physical activity for adults with chronic kidney disease showing significant beneficial effects on physical fitness, cardiovascular parameters, well-being and nutritional markers.7

**Related Pathophysiology of Sarcopenia in CKD**

In continual kidney disease, sarcopenia might also additionally have an effect on about 37% of dialysis patients. However, its incidence in in advance tiers of CKD is poorly understood and levels among 5% to 9%. The lack of muscle tissue on this populace is correlated with more morbidity and mortality, mainly because of a boom in cardiovascular complications.8 Therefore, the early identification os sarcopenia and evaluation of the modifiable factors associated with it are essential. Data from literature show that some inflammatory markers such as IL6, C-GRP and tumor necrosis factor (TNF) alpha were associated with sarcopenia, and in patients with CKD, these markers were higher than compared with patients who had normal renal function, in addition to being associated with a worse outcome.9

Muscle atrophy, kind I and II, specifically kind IIB, is an vital element that, collectively with histochemical adjustments at low awareness of cardio enzymes, low oxidative capacity, lack of capillarity and occasional degrees of contractile proteins make a contribution to the muscle dysfunction.10

Muscle losing etiology in renal sufferers is multifactorial and just like that of sarcopenia in general, regarding hormonal and immunological causes; myocardial changes; inflammation; metabolic acidosis; protein consumption reduction; bodily inactivity; extra angiotensin II; abnormalities in insulin/IGF-1 signaling and in myostatin expression; and decreased characteristic of satellite tv for pc cells. Most of those mechanisms stimulate the ATP-established SUP pathway, that is diagnosed as one of the maximum vital sorts of muscle loss.11

It is crucial to emphasise that each sarcopenia and uremia are modern diseases, which make a contribution to maximizing morbidity and lift healthcare costs. The time period uremic sarcopenia suitable to explain the method of revolutionary and cumulative lack of muscle tissue that takes place in CKD, as a consequence turning into a concern healing goal closer to prevention and remedy as muscle losing in those patients. Muscle weak spot and fatigue are regularly stated with the aid of using sufferers with CKD and there are numerous mechanisms chargeable for those symptoms, inclusive of hormonal imbalance, malnutrition, ATP and glycogen depletion, insufficient oxygen delivery due to anemia, metabolic acidosis and electrolyte disorder, way of life changes, muscle losing and weak spot because of muscle fiber atrophy.2

The maximum not unusualplace abnormality in muscle biopsies of uremic sufferers is kind II muscle fiber atrophy, that have a smaller pass sectional area, and muscle fiber grouping.12 After muscle injury, satellite tv for pc cells are activated and specific MyoD and myogenin transcription elements on their surface, which ends up in myoblast formation and proliferation, and that they differentiate to shape new muscle fibers to restore the muscle damage. In CKD, the function of satellite cells is impaired, producing low levels of myogenic and MyoD proteins, hampering muscle regeneration.13

Proteolysis via the ATP-dependent ubiquitin system stands out as the main cause of muscle wasting degradation in CKD. The pathway is primarily activated by inflammation and metabolic acidosis. Inflammation activates the ubiquitin-proteasome system, leading to the cleavage of a fragment of 14-kD actin, which is the hallmark of muscle proteolysis. Metabolic acidosis, on the other hand, stimulates ubiquitin-proteasome system via amino acid oxidation in skeletal muscle, resulting in muscle protein loss and protein caloric loss.2

**Progressive Muscle Degradation**

Anorexia, described because the lack of choice for food, is not unusualplace and complicated in CKD. Disturbances in appetite-regulating hormones, reduced cappotential to differentiate flavours, altered taste, uraemia associated gastrointestinal symptoms, depression, haemodynamic instability due to publicity to antihypertensive medicinal drugs or haemodilysis, and a sensation of fullness for the duration of peritoneal dialysis are most of the reasons cited within the literature.8

In sufferers with CKD and obesity, the manufacturing of inflammatory mediators with the aid of using adipose tissue is related to an improved incidence of cardiovascular headaches and improved mortality.14 Thus, the affiliation among sarcopenia and obesity, additionally referred to as sarcopenic obesity, appears to make a contribution considerably to the incidence of damaging consequences on this population, together with reduced bodily function.15,16

The renin-angiotensin machine is activated in numerous catabolic conditions, which includes CKD, which ends up in activation of caspase three in skeletal muscles, ensuing in actin cleavage.17 Angiotensin II can growth muscle proteolysis through decreasing circulating stages of IGF-1 and activating the TGF-β pathway, that’s essential mechanism of muscle groups loss.18
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Diagnosis of Sarcopenia

Sarcopenia has been defined as an age-related loss of skeletal muscle mass. Four presently used diagnostic criteria [European Working Group on Sarcopenia in Older People (EWGSOP), Foundation for the National Institutes of Health (FNIH), International Working Group on Sarcopenia (IWGS), and Society on Sarcopenia Cachexia and (SCWD) criteria] had been applied.19

The European definition was recently updated and recommends low muscle strength as the primary diagnostic parameter of sarcopenia. Once low muscle strength is detected, low appendicular skeletal muscle mass poses the definitive diagnosis of sarcopenia. Then, low physical performance indicates the severity of the disease.20

To pick out people at hazard for sarcopenia, the EWGSOP2 recommends the usage of the Strength, Assistance with walking, Rise from a chair, climb stairs and Falls (SARC-F) questionnaire (Annex 1) or medical studies to locate signs and symptoms related to sarcopenia.21 The EWGSOP2's modern-day definition of probably sarcopenia is low muscle strength. If, in addition, the affected person has low muscle extent or low muscle quality, his prognosis of sarcopenia could be confirmed. The aggregate of the 3 elements will result in the prognosis of extreme sarcopenia.20

Annex 1: SARC-F questionnaire (based on Barbosa-Silva et al).21 Abbreviations: CC (calf circumference); SARC-F (Strength, Assistance with walking, Rise from a chair, Climb stairs and falls).

<table>
<thead>
<tr>
<th>SARC-F (Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls) Questionnaire</th>
</tr>
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<tbody>
<tr>
<td>How much difficulty do you have lifting and carrying 10 pounds?</td>
</tr>
<tr>
<td>None = 0</td>
</tr>
<tr>
<td>How much difficulty do you have walking across a room?</td>
</tr>
<tr>
<td>None = 0</td>
</tr>
<tr>
<td>How much difficulty do you have transferring from a chair or bed?</td>
</tr>
<tr>
<td>None = 0</td>
</tr>
<tr>
<td>How much difficulty do you have climbed a flight of 10 stairs?</td>
</tr>
<tr>
<td>None = 0</td>
</tr>
<tr>
<td>How many times have you fallen in the past year?</td>
</tr>
<tr>
<td>None = 0</td>
</tr>
<tr>
<td>CC Measure (the patient’s exposed right CC with the legs relaxed and feet 20 cm apart from each other)</td>
</tr>
<tr>
<td>Females &gt;33 cm = 0</td>
</tr>
<tr>
<td>Males &gt; 34 cm = 0</td>
</tr>
<tr>
<td>Sum (0-20 points)</td>
</tr>
<tr>
<td>0-10: no suggestive signs of sarcopenia at the time (consider periodical re-evaluation)</td>
</tr>
<tr>
<td>11-20: suggestive of sarcopenia (proceed with further diagnostic examinations)</td>
</tr>
</tbody>
</table>

Physical Activity in Sarcopenia and CKD

The lack of muscle tissues in persistent kidney disease (CKD) is taken into consideration an critical complicating factor, contributing to a sedentary life-style and compromising cardiovascular fitness because of elevated morbimortality.22 The musculature atrophies and, as a consequence, there is a generalized weakness in the body, caused by the loss of strength, which, compared to that of normal individuals, is 30 to 40% smaller, leading the patient to physical deconditioning.

Physical schooling is an vital thing within the manipulate and reversal of the loss.23 Public health recommendations are aimed at increasing guidance for regular physical activity in order to reduce premature death from cardiovascular disease, improve quality of life, and increase productivity in daily activities.24

Resistance training (RT) is a fairly powerful approach to make amends for sarcopenia and has severa useful effects. The fundamental applicable consequences for this evaluate are apparent will increase in muscle mass, electricity and purposeful overall performance in older individuals.25 Resistance workout stimulates the synthesis of new muscle protein via the movement of the mTORC1 (mechanistic aim of rapamycin complex 1) protein.26
Wang et al., in an experimental model with rats and CKD, showed that muscle growth can be improved with resistance exercise. Mechanisms for this response include improvement in protein synthesis, protein breakdown and the function of progenitor muscle cells. In contrast, the group in which physical exercise was performed by treadmill running, showed partial suppression of protein degradation but did not stimulate protein synthesis or improvement in the functions of the progenitor cells. There was an attempt to increase the running time on the treadmill, but an increase in rat mortality was seen. Admittedly, the two types of exercises cannot be rigorously compared because of the difference in the design of the experiment. CKD patients may respond differently to the two exercise models. The results provide experimental information that can be used in further work on physical activity in this group of patients.  

To verify the effects of exercise on the alterations present in patients with renal failure in HD muscle, Sakkas et al. examined the morphology of the twin muscle in 12 patients before and after an aerobic exercise program performed three times a week for 6 months. The results showed that the proposed training improved muscle tropism, increased the cross-sectional area by 46% and reduced the atrophy of muscle fibers type I (51% to 15%), type IIA (58% to 21%) and type IIB (62% to 32%). Furthermore, significant differences were found regarding the increase in muscle capillarization.  

Exercise has favorable effects on several parameters, including physical function and muscle function/atrophy. Physical capacity has been shown to be increased in CKD patients after exercise programs. Physical work capacity is generally decreased in HD patients due to myopathies, neuropathies, peripheral vascular pathology, or anemia. As these pathologies are associated with uremic toxins, it was hypothesized that increased toxin clearance with intradialytic exercise would minimize their effect on various physiological systems, thereby enhancing cardiovascular and skeletal muscle performance. With to muscle wasting, it was shown that both high-intensity training programs improved the muscle strength in HD patient. Storer et al. demonstrated that after 8.6 ± 2.3 weeks of endurance exercise performed three times a week, it significantly increases muscle strength and fatigue. Thus, resistance exercise training, even at lower intensities, can provide adequate resistance to improve muscle function in patients with CKD.  

Resistance training greatly increases the metabolism of protein synthesis, leading to an increase in the transversal volume of muscle fibers. Exercise can increase levels of growth factors, such as insulin-like growth factor I receptor, and decrease muscle hypertrophy inhibitors in HD patients. Thus, these factors may be responsible for the beneficial effects on physical function and muscle atrophy.  

A systematic evaluation of RCT in 2015 hooked up that the most powerful proof in dialysis sufferers had been the outcomes of cardio workout on bodily fitness, muscular strength, and pleasant of life. More recently, in 2018, a meta-analysis of 11 RCT (362 patients) in CKD stages 3–4 reported an increased exercise tolerance with an average of a 35-week aerobic training program as compared to standard care. The prescription of exercise in CKD patients is still the most corroborated intervention and could be effective in preventing and reversing sarcopenia, thus it should be a considered for all patients.  

Last year, in 2020, another systematic review evidence that exercise has significant benefits in elderly patients with sarcopenia. Aerobic (walking) exercises routinely prescribed in clinical practice do not achieve significant benefits. Current evidence shows that training based on strength resistance and its combination in multimodal programs with aerobic and balance exercise have significantly beneficial effects on anthropometric and muscle function parameters, and that exercises should be adapted to the characteristics of each subject.  

**Conclusion**  

This review highlights and reinforces that sarcopenia is prevalent in a significant proportion of individuals with CKD and increases with the severity of the disease. In view of the negative impact of sarcopenia upon important health outcomes in CKD population, mostly the high expenses of the Public Health System, is essential to find preventive and therapeutic strategies. Especially, determined whether specific exercise are effective to decelerate sarcopenia in CKD.  

Present evidence shows that resistance training and its combination with aerobic exercise show crucially beneficial effects on anthropometric and muscle function parameters, confirming that aerobic exercises should be avoided alone, which do not generate muscle strengthening.  

Actually, diagnosis and clinical approach are the focus of most research about sarcopenia in CKD, and is fundamental remain that a part of treatment is largely based on resistance exercises.  

This paper is expected to provide great information for future studies, given the importance of promoting strength exercise, an active and healthy lifestyle.  

In conclusion, all suggests that patients with CKD should be guided to include resistance training in exercise programs to prevent and treat sarcopenia. However, future studies need to effectively investigate incorporating resistance exercise in all levels of CKD.
Conflict of Interest

The authors declare no conflict of interest.

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