

Influences of high vs. low-intensity exercises on muscle strength, function, and quality of life in post-COVID-19 patients with sarcopenia: a randomized controlled trial

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Abstract. – OBJECTIVE: The aim of this study was to compare the effectiveness of high vs. low-intensity exercise training on muscle strength, physical function, and quality of life in post-COVID-19 patients with sarcopenia secondary to chronic kidney disease (CKD).

PATIENTS AND METHODS: 82 subjects were randomized into 2 groups: high intensity (HIG, n=42), which received high-intensity resistance training, and low intensity (LIG, n=40), which conducted low-intensity aerobic activities. Exercises were performed for 30 min, 3 times per week for 6 weeks. A handheld dynamometer, pinch press, and 1 min sit-to-stand (STS) test were used to assess muscle strength. Modified physical performance test and sarcopenia Quality of Life questionnaire (SAR-QoL) were used to assess function and quality of life, respectively. Measures were collected before and at the end of the treatment program.

RESULTS: Participants were similar at baseline. The within-group comparisons demonstrated statistically significant improvement in both HIG and LIG groups in all outcome measures ($p < 0.001$). Between groups, comparisons revealed statistically significant better achievements with high effect size in Modified Physical Performance Test (MMPT) ($p < 0.001$, $d = 1.28$), handgrip ($p < 0.001$, $d = 3.6$), STS ($p < 0.001$, $d = 2.38$), and SAR-QoL ($p < 0.001$, $d = 3.24$) in favor of the HIG. On the other hand, pinch press strength was equally improved in both groups ($p = 0.09$, $d = 0.36$).

CONCLUSIONS: High-intensity exercise is better than low-intensity exercises in post-COVID-19 patients with sarcopenia secondary to chronic kidney disease regarding muscle strength, physical function, and quality of life.

Key Words:

Resistance, Performance, Function, Kidney.

Introduction

Sarcopenia is a prevalent chronic disease caused by aging and is characterized by a reduction in muscle strength and mass¹. Consequently, deterioration in physical function and quality of life² usually takes place. Sarcopenia is associated with a higher risk for stroke, frailty³, and mortality⁴. Generally, there are different causes of sarcopenia, including chronic kidney diseases (CKD)⁵, lack of physical activity, inflammatory mediator activation, mitochondrial dysfunction, hormonal changes, environmental factors, and loss of neural junctions⁶.

Patients with CKD already suffer from decreased functional reserve due to increased catabolism, higher protein wasting, and other metabolic disorders^{7,8}. Additionally, the decline in physical function due to the deterioration of muscle mass, power, and strength could significantly decrease balance and increase the risk of falling in these populations⁹.

After the pandemic of COVID-19 and the mandatory quarantine of patients during the recovery period, CKD patients with sarcopenia who were infected with COVID-19 were deprived of regular physical rehabilitation activities and forced

to assume a more sedentary lifestyle which consequently magnifies all health risks¹⁰ and jeopardized the subject's vitality¹¹.

Exercise has been proposed as one of the solutions for sarcopenia-associated symptoms¹, so they were studied in previous literature¹²⁻¹⁸. Muscle strength, physical function, balance, and quality of life were the outcomes of interest in the majority of these studies. Additionally, variations of sarcopenia patients were investigated; for example, obese patients with sarcopenia were the sample in one study¹⁶, sarcopenia secondary to COVID-19¹² or associated with CKD¹⁷ was studied in a single study, while sarcopenia secondary to aging was the concern in another study¹⁴.

Moreover, variation in the mode of exercise delivery was observed when group therapy¹⁴, fun type of exercises¹⁵, home-based^{13,14}, resistance¹⁶⁻¹⁸, and aerobic activities¹² were conducted by different researchers. Unfortunately, no studies compared patients to resistance training with high-intensity vs. low-intensity aerobic exercises, especially in chronic kidney patients with sarcopenia who had recently recovered from COVID-19 infection.

After COVID-19 infection, both lung function and peripheral muscle integrity might be affected, and so it might have a negative effect on physical performance and quality of life (QoL). Additionally, some patients may suffer from post-intensive care syndrome that affects their mental health and magnify the effect of sarcopenia in this group of patients¹⁹.

This study aimed to compare the effectiveness of high vs. low-intensity exercises on muscle strength, physical function, and quality of life in post-COVID-19 patients with sarcopenia secondary to CKD. The research hypothesis is that both high and low-intensity exercises will be equally effective for post-COVID-19 patients with sarcopenia secondary to CKD.

Patients and Methods

The study followed the declaration of Helsinki and was reported as per the CONSORT statement for reporting randomized controlled trials. Ethical approval was granted by the University of Ha'il Ethical Committee Board (No.: H-2022-342) and was registered at clinicaltrials.gov (No.: NCT05593471). A consent form was signed by all participants before joining the study.

Design

This study was designed as a double-blind, randomized, controlled trial. This study was conducted between January 15th and March 20th, 2023, in the Ha'il Region Hospitals, Saudi Arabia.

Participants

Ninety-one chronic kidney patients who recently (within 1-2 months) recovered from COVID-19 infection were screened; of them, 82 met the inclusion criteria and signed the consent to participate in the study. The inclusion criteria were: to be diagnosed with sarcopenia secondary to CKD, to have been infected by COVID-19 and recovered 1-2 months ago, a score of 4 or more on SAR-QoL questionnaire, and to have no severe comorbidities hindering their participation.

The exclusion criteria were medications affecting cognitive functions, balance abilities, or muscle performance, current COVID-19 infection, inflammatory, neurological, or cardiovascular diseases, chronic chest disease, and mental impairments.

Interventions

For both groups, each session started with 5 minutes of passive stretching exercises that were performed as a warmup. Another 5 minutes of pace walk in place was performed as a cooling down after finishing the exercise intervention.

High-Intensity Exercise

This type of exercise was performed by the participants in the high-intensity exercise group (HIG). 30 min of progressive resistance training were performed where theraband with different colors, dumbbells, and sandbags were used to apply the resistance. For using theraband, at the beginning of the exercise program, the patients were trained to wrap the bands around their hands to make sure the bands do not slip during exercise; patients were instructed to use the elastic bands of different tensile strengths by pulling on the band in the same position. While, for using sandbags, the patients were asked to wear sandbags weighing 1-3 kg around each of their ankles then, they were asked to wear sandbags that were one kg heavier than the ones they were wearing previously. Finally, for using dumbbells, patients were asked to carry on their hand with the appropriate weight according to the 10-repetition maximum and start the exercise session. The exercised muscles were (knee extensors, elbow flexors, chest muscles, hip adductors and abductors, abdominal

muscles, back muscles, and hand grip muscles)²⁰. The intensity of exercise was determined by the load, which was kept at 65% of the 10-repetition maximum throughout the program duration²¹. The repetitions of each exercise were kept at a fixed value of 2 sets of 10-12 repetitions per session (exercises stopped if the patient reached fatigue level). A 2-minute rest interval was allowed between each set of exercises. For progression, the 10-repetition maximum (10 RM) test was performed on a weekly schedule, and the amount of resistance was adjusted accordingly to keep the resistance at 65% of the new value of the 10 RM.

Low-Intensity Exercise

30 minutes of the aerobic exercise program was conducted by the participants in the low-intensity exercise group (LIG). Arm and leg ergometer (Arm Crank, Panatta Sport, Apiro, Italy) was used to train both upper and lower body muscles. The intensity of the exercises was fixed at a 3-4 level on the Rate of Perceived Exertion (RPE) scale. This scale is a valid and reliable tool for assessing exercise intensity²². Sessions were performed 3 times per week for 6 weeks^{12,23}.

Outcomes

All outcomes were collected before and after the end of the intervention period. A therapist with 15 years of experience was responsible for the initial screening of the subjects and data collection.

Muscle Strength

Isometric hand-grip strength of the dominant hand was assessed using the procedures performed in a recent study²⁴, while a Lafayette push hand-held dynamometer (model 01163, Lafayette Instrument Co., Lafayette, IN, USA) was used to collect data. This dynamometer has a dual-pointer system to record the maximum effort in Kg. The device is a valid and reliable tool for assessing isometric hand muscle strength²⁵. The participants were asked to sit on a chair with armrests. The tested arm was slightly abducted at the shoulder, and the elbow was at 90° of flexion. Participants were asked to squeeze the handle of the device as hard as possible and then relax. This procedure was repeated three times with 1-minute rest intervals. The average of the three readings was used for the analysis.

Pinch press strength was assessed for the thumb adductors in the dominant hand. The strength of such muscles is important to maintain the grasp pattern during regular hand activities. Lack of

muscular strength and coordination might lead to difficulty with daily activities that require fine motor strength²⁶. The purpose and procedures of testing were described to the participants. Each participant was tested in a quiet room in an upright seated position. The upper limbs were kept adducted against the body with elbows at 90° of flexion. Participants were asked to press the device between the thumb and index fingers as hard as possible for 3 trials, to minimize the effect of fatigue, three-minute resting periods were allowed between tests. The average of the 3 trials was calculated and used for analysis²⁷.

Sit to stand in 30 seconds (STS- 30) is a well-known test that can be used to identify the strength and power of the lower quadrant in older individuals²⁸. The validity and reliability of this test have been assessed previously. To perform this test, participants were asked to sit on a chair, then stand up and sit down again as fast as they could within 30 seconds, keeping their arms folded across the chest²⁹⁻³¹. The maximal number of chair stands completed for 30 seconds was recorded and used for analysis.

Physical Function

The basic and complex Activities of Daily Living (ADL) were assessed by the Modified Physical Performance Test (MPPT). This test consists of nine standardized tasks: walking 15.2 meters, doing a 360° turn, putting on a coat, picking up a coin, rising from a chair, lifting a book, and climbing stairs in 2 variations. The maximum score that can be achieved in the MPPT test is 36 with the following cut-off points: from 32-36 means no physical disabilities, 25-31 indicates mild physical disability and 17-24 indicates moderate physical disability³².

Quality of Life

To assess the quality of life, participants were asked to fill out a validated Arabic Sar-QoL questionnaire³³. This questionnaire consists of 22 questions, each of which has 4-point answers options. These questions cover seven domains assessing the health of patients with sarcopenia¹². The total scoring ranged between 0, which indicated the worst health status, to 100, which indicated the best health status³⁴.

Sample Size

The sample size calculations were based on the outcomes of the Sar-QoL scores. According to the guidelines described by Witham et al³⁵, to obtain

a minimal clinically important difference of 17 points, with 80% power (adjusted), 2 equal groups of 34 subjects should be included per group. The number was raised to 40 per group to compensate for withdrawal.

Randomization, Concealment, and Blinding

Immediately after the initial assessment, participants were randomly assigned to either the HG or LG groups. Randomization was conducted using a computer-generated randomized sequence. Randomization data were concealed from all researchers and kept safe with a coworker who was involved neither in assessment nor treatment. To conceal the randomization sequence, a specific identification number was assigned for each participant. The participants and the assessor were kept blindfolded throughout the study.

Statistical Analysis

Version 23 of the Statistical Package of Social Science (SPSS, IBM Corp., Armonk, NY, USA) was used for analysis. Intention-to-treat analysis was adopted. Descriptive statistics (mean \pm SD) were calculated for all variables. When data were normally distributed, paired and Unpaired *t*-tests were used to assess the within and between groups changes. When data were not normally distributed, Wilcoxon signed-rank and Mann-Whitney U tests were used to conduct the within and between-group comparisons, respectively. The level was set at $p < .05$. Cohen's *d* formula was used to calculate the clinical effect size (ES) between groups.

Results

This study included 82 participants, 42 in the HG aged 60.45 \pm 4.73 years and 40 in the LG aged 59.15 \pm 4.3. Most of the participants were males

whereas 3 and 2 female participants were allocated to the HG and LG, respectively. Participants were similar regarding demographic characteristics (Table I) as well as comorbidities such as diabetes mellitus, hypertension, atherosclerosis, and body composition (Figure 1). Furthermore, participants underwent tailored nutritional support as described by their physicians according to each case¹.

No significant adverse effects were reported throughout the study. Additionally, all participants were committed to the treatment sessions, and no dropout was reported (Figure 2).

The within-group comparisons demonstrated statistically significant improvement in both HG and LG groups ($p < 0.001$) in favor of all outcome measures (Tables II and III). The highest mean difference (MD) was observed in the handgrip strength demonstrated by HG (MD=24.12). The lowest MD was the value of the STS in the 60-second test demonstrated by the LG (MD=3.25).

Between groups, comparisons revealed statistically significant better achievements in MPPT, handgrip, STS in 60 seconds, and Sar-QoL ($p < 0.001$) in favor of the HG. High effect size, as represented by Cohen's *d* formula, was evident in the MPPT, STS in 60 mins, and Sar-QoL. On the other hand, pinch press strength was equally improved in both groups at the end of the treatment ($p = 0.09$, $d = .36$). These findings were presented in Tables III and IV.

Discussion

This study compared the effects of high and low-intensity exercises on muscle strength, physical function, and quality of life in post-COVID-19 patients with sarcopenia secondary to CKD. This trial found that while all outcomes were better af-

Table I. Demographic data of the participants.

Variable	HIG (n = 42)		LIG (n = 40)		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Age	60.45	4.73	59.15	4.31	1.31	.194
Height	158.80	4.87	156.25	5.49	2.23	.028
Weight	79.14	9.27	80.95	10.79	-.814	.418
BMI	27.04	5.13	29.12	4.98	1.86	.066

N, number; HIG, high-intensity group; LIG, low-intensity group; SD, standard deviation; BMI, body mass index; *t*, t-value; *p*, significant level.

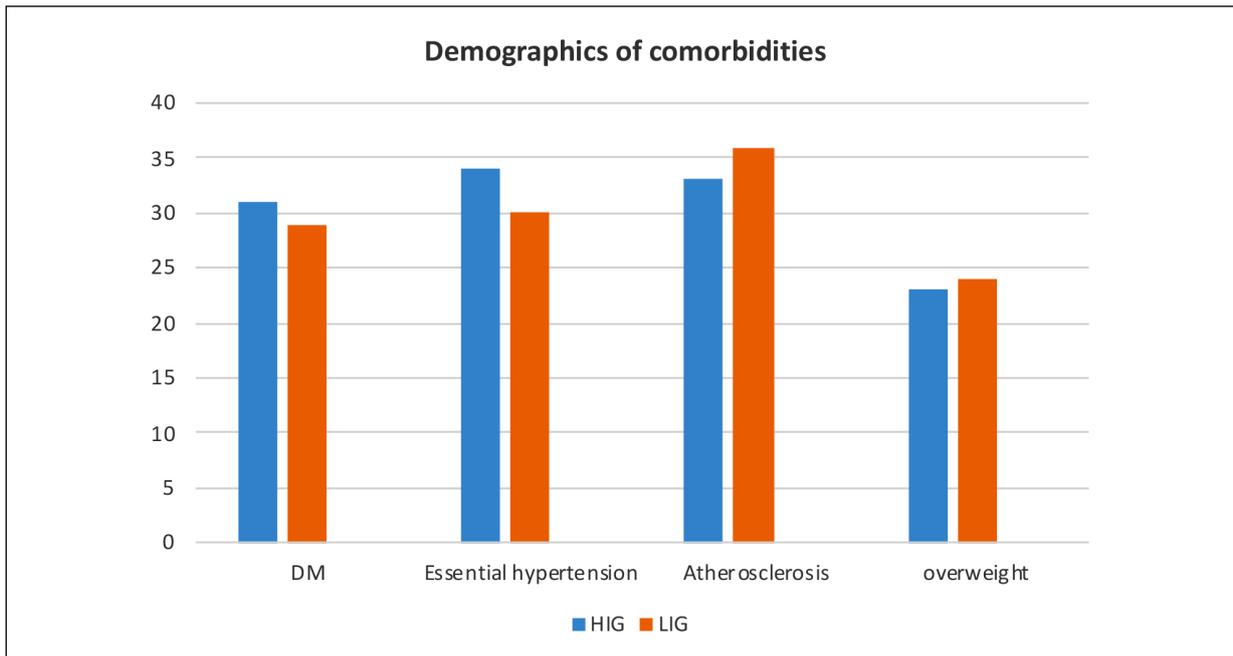


Figure 1. Distribution of comorbidities among groups.

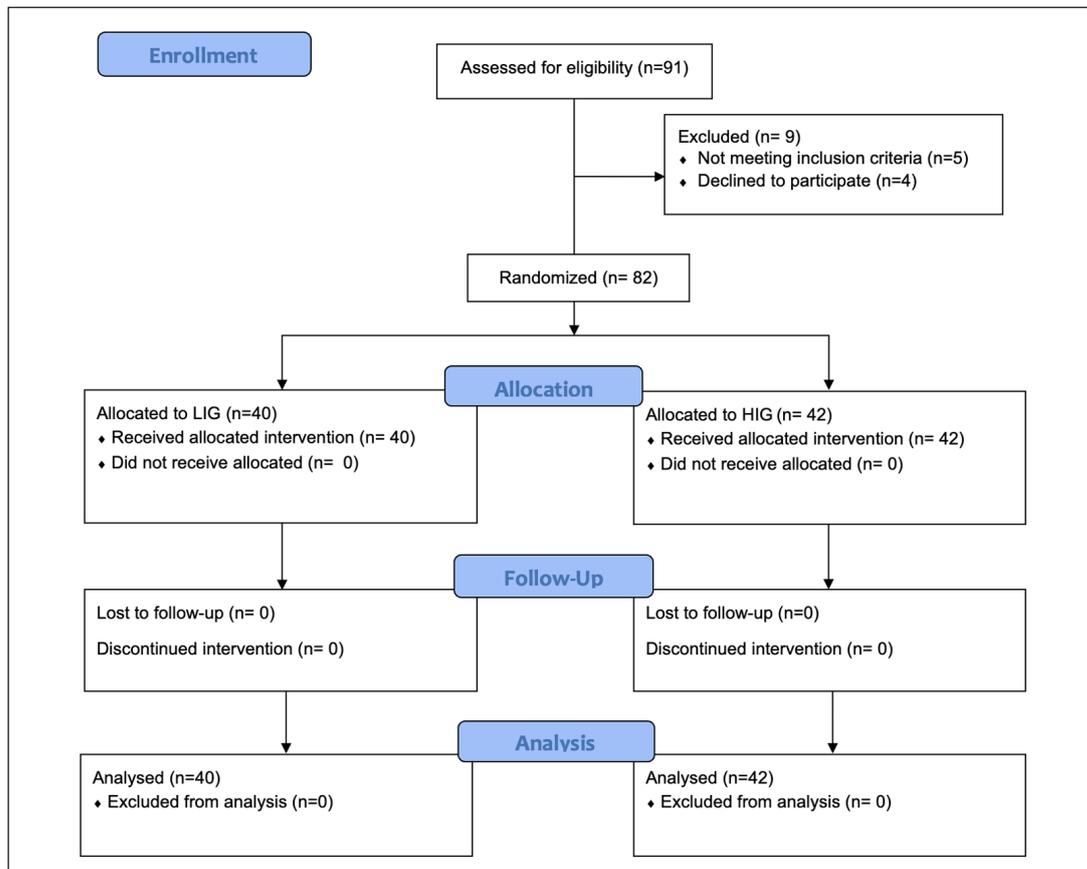


Figure 2. Flow diagram.

Table II. Within-group comparisons.

Group	Pre-treatment		Post treatment		MD	t	p	95% CI	
	Mean	SD	Mean	SD				Lower	Upper
HIG									
- Hand grip	18.48	3.57	42.60	7.01	24.12	-20.43	<.001	-26.50	-21.73
- Pinch press	6.65	0.78	10.11	0.87	3.46	-16.65	<.001	-3.88	-3.04
- STS in 60 mins	20.11	1.72	24.78	2.37	4.67	-6.14	<.001	-7.37	-6.33
- QoL	66.45	4.57	73.30	4.39	6.58	-9.33	<.001	-5.30	-4.02
LIG									
- Hand grip	17.48	2.96	23.72	2.42	6.24	-10.70	<.001	-7.42	-5.06
- Pinch press	5.9	0.59	9.48	2.27	3.58	-7.25	<.001	-3.46	-1.95
- STS in 60 mins	18.30	2.67	21.55	1.35	3.25	-5.36	<.001	-6.33	-2.86
- QoL	63.20	6.69	67.80	5.84	4.6	-7.13	<.001	-4.17	-2.32

HIG, high intensity exercises group; LIG, low intensity exercises group; STS, sit-to-stand in 60 minutes; QoL, Quality of Life.

Table III. Within and between groups comparisons using Wilcoxon and Mann-Whitney tests respectively.

Variable	Time	HIG		LIG		U	p	d
		M	SD	M	SD			
MPPT	Pre	18.97	1.90	19.10	1.90	803	.728	.068
	Post	27.85	2.45	24.60	2.61	319.5	<.001	1.283
MD		8.88		5.5				
Z		-5.652		-5.527				
p		<.001		<.001				

HIG, high intensity exercises group; LIG, low intensity exercises group; U, Mann-Whitney value; Z, Z statistics of Wilcoxon test; M, mean; SD, standard deviation; MPPT, modified physical performance test; d, Cohen’s d value of effect size.

Table IV. Between group comparisons.

Group	Time	HIG		LIG		t	d	p	95% CI	
		Mean	SD	Mean	SD				Lower	Higher
Hand grip	Pre-treatment	18.48	3.57	17.48	2.96	1.38	.304	.169	-4.38	2.45
	Post treatment	42.60	7.01	23.72	2.42	16.11	3.60	<.001	16.54	21.21
Pinch press	Pre-treatment	6.65	0.78	7.18	0.54	-820	.790	.415	-0.437	0.182
	Post treatment	10.11	0.87	9.48	2.27	1.68	.366	.097	-0.11	1.38
STS in 60 mins	Pre-treatment	20.11	1.72	18.30	2.67	1.96	.805	.053	-0.013	2.03
	Post treatment	24.78	2.37	21.55	1.35	7.52	1.67	<.001	2.38	4.09
QoL	Pre-treatment	66.45	4.57	63.20	6.69	2.91	.567	.005	1.11	5.91
	Post treatment	73.30	4.39	67.80	5.84	4.84	1.06	<.001	3.24	7.77

HIG, high intensity exercises group; LIG, low intensity exercises group; QoL, Quality of Life.

ter interventions in both groups, participants who received high-intensity exercises demonstrated higher achievements in 3 (MPPT, handgrip, STS in 30 seconds, and QoL) out of the 4 outcomes assessed in this study.

Up to the authors’ knowledge, comparisons between low and high-intensity exercises have not been extensively studied in previous literature. Additionally, the response of the current study population to these exercises was not clear. Re-

cently, Nambi et al¹² compared the effect of high vs. low-intensity exercises on a sample of patients having post-COVID-19 sarcopenia. Two groups each consisted of 38 participants included in the Nambi study, one of them received high-intensity aerobic training, while the other group received low-intensity aerobic exercises.

Contrary to the current findings, Nambi et al¹² reported that low-intensity aerobic exercises were more effective than high-intensity exercises at 4 and 8 weeks as well as at 6 months follow-up in favor of hand grip, strength, and quality of life. Yet, muscle mass did not show any significant difference. However, differences such as the nature of the study population, the type of exercises used, especially in the high-intensity exercises group, and the method of assessing exercise intensity could be potential reasons for these differences¹².

In another study, Stoever et al¹⁶ compared the response of elderly obese persons with sarcopenia to those with no sarcopenia to a program of resistance training. This program, which used between 80 to 85% of maximum strength and continued for 16 weeks, resulted in significant improvements in hand grip strength (9% improvement) and MPPT (11% improvement) when compared to the baseline. Interestingly, Stoever's study found that the value of the physical function measured by the MPPT and Short Physical Performance Battery reached a level equal to the baseline values of those with no sarcopenia.

Additional support for the benefits of high-intensity resistance exercises was reported in a study conducted by Dong et al¹⁷, a group of patients having CKD. Resistance exercises were performed in parallel with the kidney dialysis routine using the weight of the lower limbs as well as an elastic ball. After 12 weeks of training, significant improvements were observed in the maximum grip strength and physical function in favor of the high-intensity exercise group.

On the other hand, Zhou et al³⁶ study found that strength or balance training combined with endurance training for 12 months did not decrease sarcopenia prevalence in CKD patients³⁶. In this study, the strength exercises improved overall lean body mass. Yet, it did not affect the prevalence rate of sarcopenia. It is worth noting that the outcomes of interest (plasma statin level and body fat) were quite different from those adopted in the current study.

The mechanisms by which exercise can slow down sarcopenia are complex³⁷. It is well

known that resistance training increases muscle mass and strength by promoting satellite cell activation and proliferation, enhancing the synthesis of muscle protein, and inhibiting muscle breakdown³⁸. Sarcopenia is usually associated with a significant loss of muscle mass, which may lead to weakness and an increased risk of falls, physical disability, and poor quality of life³⁹. Exercise has positive effects on muscle strength, physical function, and quality of life in people with sarcopenia¹⁴. Hence, it can improve the feeling of well-being and improve the patient's confidence regarding walking without fear of falling⁴⁰ which in turn reflects on improving the quality of life.

Another explanation has been introduced by Dong et al¹⁷, which proposed that high-intensity exercises could efficiently control the status of the low-level systemic inflammation associated with CKD through the release of anti-inflammatory substances such as interleukin-6 (IL-6) and IL-10. This inflammatory condition has been linked to multiple complications usually seen in CKD, such as cardiovascular problems, protein energy expenditure, and mortality.

As presented in the current study, high-intensity resistance training should be incorporated as a part of the rehabilitation programs in populations having CKD with sarcopenia, especially those who recently recovered from COVID-19. Such exercises can reduce multiple risks, such as falling and reduced balance, and consequently improve physical functions and quality of life.

Limitations

The period of intervention, which was relatively short, represents the main limitation of the current study. Yet, this short period could be more realistic due to the nature of the participants, who usually tend to have less commitment to long-duration exercise programs in real life. Due to the low number of female participants in both groups, the sex-related variation in exercise response could not be investigated. So, the authors recommend addressing this variable in future studies.

Conclusions

High-intensity resistance exercises were superior to low-intensity aerobic training on strength, function, and quality of life in post-COVID-19 patients with sarcopenia secondary to kidney diseases.

Conflict of Interest

The authors declare that they have no conflict of interests.

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Ethics Approval

This study was conducted following the guidelines of the Helsinki Declaration from the Research Ethical Committee of the University of Hail dated 14/10/2022 (H-2022-342). Trial registration: www.clinicaltrial.gov number: NCT05593471.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Authors' Contribution

Ahmed Abdelmoniem Ibrahim, Hisham M. Hussein, and Ibrahim Metwally Dewir contributed substantially to the concept and design of the study. Shima T. Abu El Kasem, Mohamed Marzouk Mohamed Ragab, and Mostafa S. Abdel-fattah performed data collection. Ahmed Abdelmoniem Ibrahim and Hisham M. Hussein were responsible for the interpretation, drafting, and validation of the article. All authors gave their final approval of the version of the article to be published.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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