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Effect of exercise in obese diabetic patients with chronic kidney disease

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Abstract

Introduction. Obesity is the most dangerous risk factor for kidney disease if it is coupled with diabetes mellitus and hypertension, and it has a direct impact on chronic kidney disease progression to end-stage renal disease. The present study was to document the effect of 3 months of aerobic exercises vs. resistance exercises in obese patients with diabetes and chronic kidney disease.

Methods. Overall, 84 patients (36 males and 48 females) who met the inclusion criteria were randomly assigned to 2 groups. Group 1 received aerobic exercises 3 times/week for 3 months, and group 2 was treated with resistance exercises 3 times/week for 3 months.

Results. At baseline, no significant difference was found between the groups in body mass index, waist circumference, waist-to-hip ratio, blood pressure, heart rate, or blood glucose. The difference in exercise performance between the 2 groups prior to treatment was not significant, but after 3 months of treatment, there was a significant increase in exercise performance and improvement in the parameters of body mass index, waist circumference, waist-to-hip ratio, blood pressure, heart rate, and blood glucose within group 1 and group 2, with no significant difference between the 2 groups.

Conclusions. Aerobic exercise is effective in decreasing obesity and increasing physical performance in obese diabetic chronic kidney disease patients. Resistance exercises alone can also decrease obesity and increase physical performance. So, both types of exercises can be used in the treatment of obesity.

Key words: aerobic exercise, chronic kidney disease, diabetes mellitus, obesity, resistance exercises

Introduction

About 14.8% of the population around the world are affected by chronic kidney disease (CKD) [1]. Over the last 3 decades, the number of patients with overweight or obesity (body mass index [BMI] ≥ 25 kg/m^2) has increased among adults aged more than 18 years and an estimated 600 million adults were considered obese in 2014 [2–4]. It has been found that obesity is strongly related to the development of CKD [5], and it is rapidly progressed in those with BMI above 30 kg/m^2 and previously existing CKD [6]. Some studies have argued that the waist-to-hip ratio (WHR) and waist circumference (WC) measurements are better than BMI for obesity classification and mortality prediction in CKD patients, as they are better predictors of adverse outcomes in the CKD population [7, 8]. The body delivers a special mechanism of hyperfiltration to compensate for the increased body weight to cover the increased metabolic demands, but the raised intraglomerular pressure increases the defect in the kidney tissues [9]. The liability for the occurrence of CKD is also increased by the presence of comorbid diseases such as hypertension or diabetes mellitus, in addition to obesity, which speed up the consequences of renal damage. Obesity affects kidney function directly through the endocrine hormones secreted by the adipose tissue [10].

Protein imbalance and low protein-calorie intake in CKD patients lead to changes in the capillary vascular bed associated with reduction of local blood flow and intravascular calcification. Muscle atrophy results in a change in type II muscle fibres [11]. A healthy lifestyle depends on good nutrition and adequate physical activity as studies prove that mortality is increased by physical inactivity in both CKD and non-CKD populations [12, 13], especially in obese individuals who have low functional capacity and, consequently, low cardiopulmonary fitness [14]. Greater risk of mortality, hospitalization, and morbidity in CKD patients resulted from decreased functional abilities and cardiopulmonary fitness [15].

Frailty is 2-fold higher in CKD in its early stages in comparison with healthy subjects. So, CKD patients are at a higher risk of death due to secondary sarcopenia, which elevates the fall risk and mobility limitations. For these reasons, the presence of physical therapists in the health care team is critical in treating musculoskeletal conditions and monitoring the development of sarcopenia in CKD patients. Sarcopenia affects functional performance from the early stages of the disease; patients begin to present a decrease in physical function in the pre-dialysis stage, and deterioration occurs with the progression of the disease [16]. In more advanced stages, the risk of having a frailty phenotype has been greatly observed. The phenotype is associated with a 2.5-fold increase in death and with the need to start dialysis [17, 18].

The present study sought to evaluate aerobic vs. resistance exercises effect on cardiovascular parameters, including blood pressure and heart rate, on physical performance, and on BMI, WC, and WHR in obese diabetic patients with CKD.

Subjects and methods

Study design and randomization

A 2-arm cluster randomized controlled trial was performed. Patients were given an identification number when they were admitted. Odd numbers joined group 1 and even numbers

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joined group 2. The participants' consent was obtained before starting the treatment, after full explanation of the study details.

Participants

A total of 84 obese diabetic patients with CKD (36 males and 48 females) from the Department of Internal Medicine, Cairo University Hospitals were chosen for this study in accordance with the inclusion criteria in the period from January to June 2020. They were randomly divided into 2 groups: group 1 received treatment with aerobic exercises on a stationary bicycle, group 2 was treated with resistance exercises.

The inclusion criteria were as follows: (1) CKD stages 2–4; (2) BMI ≥ 30; (3) diabetes mellitus; (4) systolic blood pressure < 180 mm Hg and diastolic blood pressure < 100 mm Hg.

The exclusion criteria involved: (1) uncontrolled hypertension or diabetes mellitus; (2) cardiac failure; (3) motor disorders; (4) dementia (Figure 1).

Intervention

Group 1: aerobic exercises

The warm-up phase and the cool-down phase each lasted for 3–5 minutes and included aerobic movement exercise for joint range of motion. Each movement was performed 20 times.

The exercise phase consisted of about 30 minutes of cycling with the rated perceived exertion of 12–13 on the Borg scale, 40–60% of maximum heart rate. The exercise was applied 3 times per week for 3 months under the supervision of the researcher, on a Wingtech ergometer (China).

Group 2: resistance exercises

The training of the lower limbs (dorsiflexion, plantar flexion, knee flexion, knee extension, hip flexion and extension) was performed 3 times per week for 3 months at 60% of 3-repetition maximum, i.e. the maximum weight lifted by the subject 3 times with a proper technique. The sessions consisted of 10 repetitions of each movement twice per session, gradually increased to 3 times as tolerated. The weight was raised when the patient could do 3 sessions successfully.

The subjects exercised 1–2 hours after a meal (breakfast) to prevent exercise-induced hypoglycaemia, as they took drugs to lower blood glucose. A finger-stick blood glucose test (On Call Plus; USA) was performed prior to exercising. The participants with blood glucose levels of more than 250 mg/dl were instructed not to exercise until their blood glucose fell below 200 mg/dl. If the blood glucose was less than 80 mg/dl, the patients were instructed to eat a snack and recheck their glucose 10–15 minutes later to ensure that it was rising before engaging in the exercise on the subsequent day or they were excluded from the study [19].

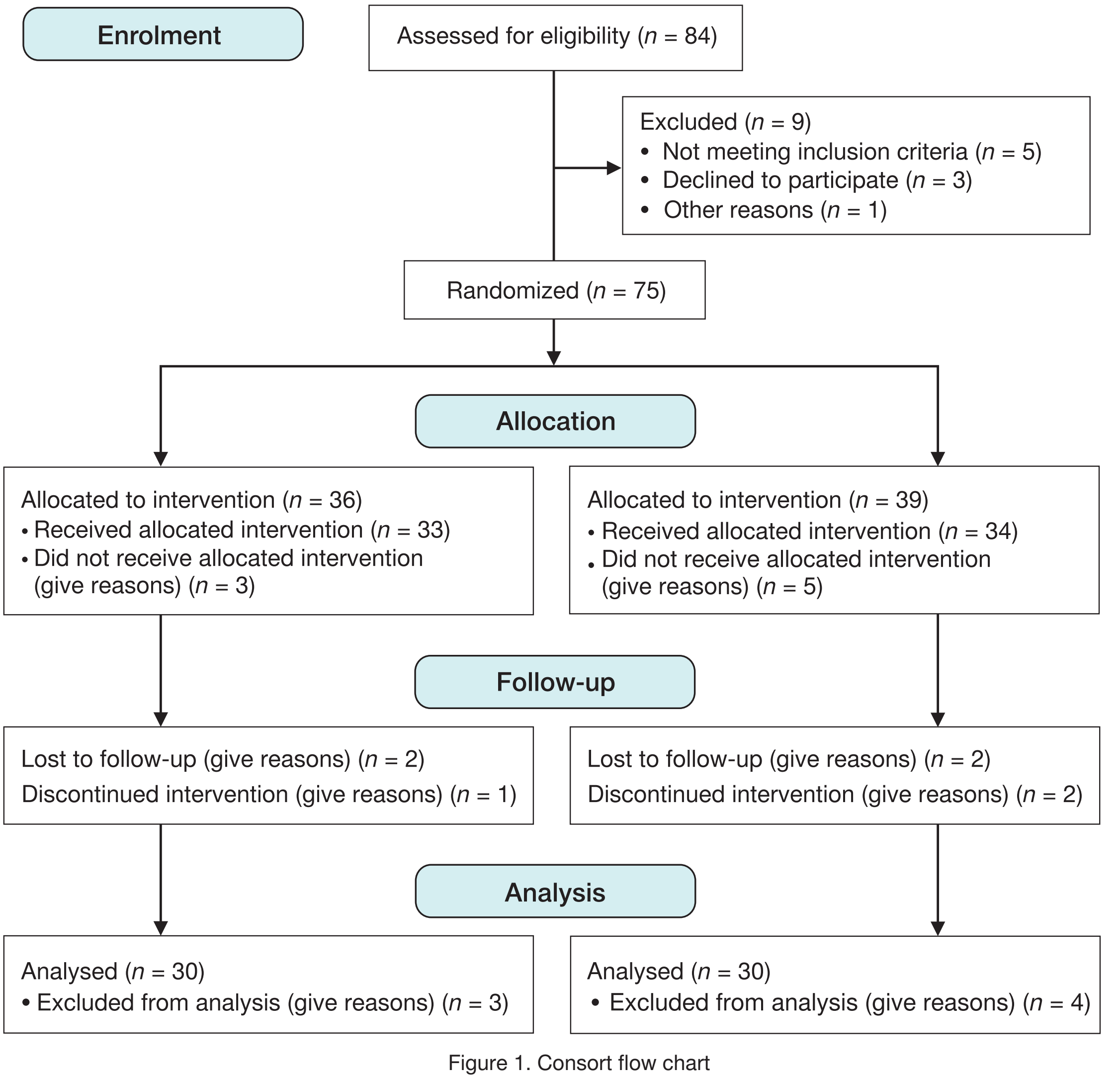

Figure 1. Consort flow chart

Measurements

The participants were then evaluated for the following:

1. BMI, calculated as the weight in kilograms divided by height in meters, squared.
2. WC, measured at the umbilicus level at the end of expiration by using a flexible plastic tape. The means of 3 measurements were used for analysis.
3. WHR.
4. Timed up and go test (TUG). The subject was to rise from a chair and walk 3 m, return to the chair, and sit down again.
5. Sit-to-stand test: STS5. The time that the patient took to finish 5 sit-to-stand-to-sit cycles was determined as a measure of muscle power.
6. Sit-to-stand test: STS60. The number of sit-to-stand-to-sit cycles that the subject could do in 1 minute was collected as a measure of muscular endurance.
7. The 6-minute walk test (6MWT), in accordance with the American Association for Thoracic Surgery. Suitable for chronic patients groups, this was used to determine aerobic fitness. It provides the maximum distance walked along an internal corridor of 30 m for 6 minutes.
8. Systolic/diastolic blood pressure. This was determined with the auscultatory technique, by using a sphygmomanometer, a pre-gauged adult cuff, and a stethoscope. The first and last Korotkoff sounds were recorded. Blood pressure was taken before exercises and after exercises, until the parameter approached the baseline values.
9. Mean blood pressure. Blood pressure was measured with the patient sitting after 10 minutes of rest. Summation and calculation of the average of 3 measurements was used to determine the mean blood pressure with the following formula

$$\text{diastolic blood pressure} + [(\text{systolic blood pressure} - \text{diastolic blood pressure}) / 3]$$

10. Heart rate, measured before and after exercises.
11. Blood glucose, measured before exercises.
12. The original Borg scale to assess the perception of exercise intensity. It is the safest scale for CKD patients. The suitable exercise intensity in this group is 12–16 on the Borg scale.

The measurements were recorded at the beginning of the study and at the end of the 3-month training.

Statistical analysis

Pre- and post-treatment measures were analysed with the Minitab software, version 18 (Minitab LLC, State College, USA). All the data were presented as mean ± standard deviation. A paired *t*-test was used to compare the pre-treatment and post-treatment values of the physical performance and obesity parameters of each group, and an independent *t*-test served to perform between-group comparisons. The significance level was set at $p \leq 0.05$ for all tests.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the ethical committee of Faculty of Physical Therapy, Cairo University, Egypt (approval No.: P.T. REC/012/002608). ClinicalTrials (www.clinicaltrials.gov) registration number: NCT04522115.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

Overall, 84 patients were chosen for this study; 9 were excluded for different reasons. The remaining 75 patients were divided into 2 groups. Then, 15 patients dropped out for several reasons. A total of 60 patients, 26 males (43.3%) and 34 females (56.7%), completed the programme. Their

Table 1. Pre- and post-treatment measures of both groups

Item	Group	Pre-treatment	Post-treatment
BMI (kg/m²)	Group1	36.3 ± 1.6	34.7 ± 1.6
	Group2	36.3 ± 1.7	35.2 ± 1.7
p-value		0.943	0.296
Waist circumference (WC) (cm)	Group1	157.07 ± 6.6	151.6 ± 6.4
	Group2	159.73 ± 7.2	154.9 ± 7.3
p-value		0.109	0.088
Waist to hip (WHR)	Group1	1.4 ± 0.2	1.2 ± 0.1
	Group2	1.6 ± 0.2	1.3 ± 0.1
p-value		0.007	0.142
Time up and go (TUG) (s)	Group1	25.8 ± 1.5	22.4 ± 1.2
	Group2	25.6 ± 1.5	21.1 ± 2.2
p-value		0.660	0.450
Sit to stand test (STS5) (s)	Group1	35.1 ± 1.8	26.3 ± 1.6
	Group2	36.3 ± 1.7	25.4 ± 2.1
p-value		0.007	0.054
STS60 (cycle/min)	Group1	8.3 ± 0.8	14 ± 2.2
	Group2	8.2 ± 0.7	14.7 ± 1.4
p-value		0.763	0.092
6minutes walk distance (6MWD) (m)	Group1	237.3 ± 4.1	265.1 ± 6
	Group2	235.9 ± 3.4	264.2 ± 4.6
p-value		0.158	0.515
Systolic blood pressure (mm Hg)	Group1	158.5 ± 8.1	145.8 ± 7
	Group2	156 ± 6.5	141 ± 20.7
p-value		0.215	0.215
Diastolic blood pressure (mm Hg)	Group1	93.3 ± 5	81.8 ± 2.8
	Group2	94.8 ± 5.2	84.7 ± 4.5
p-value		0.213	0.002
Mean blood pressure (mm Hg)	Group1	125.8 ± 3.6	112.6 ± 1.7
	Group2	126.7 ± 2.3	113.5 ± 1.9
p-value		0.230	0.055
Heart rate (beat/min)	Group1	77.4 ± 1.4	71.9 ± 2.1
	Group2	78.4 ± 1.1	72.1 ± 1.1
p-value		0.006	0.578
Blood glucose (mg/dl)	Group1	197.6 ± 3.4	179.3 ± 6.3
	Group2	198.4 ± 1.9	183.8 ± 4.6
p-value		0.191	0.009

highly significant ≤ 0.001, significant ≤ 0.05

age ranged 35–60 years. The value of p = 0.708 indicates that there was no significant difference in age between the 2 groups. Also, there was no significant difference in the groups for BMI (p = 0.943), WC (p = 0.109), WHR (p = 0.007), TUG (p = 0.660), STS5 (p = 0.007), STS60 (p = 763), 6MWT (p = 0.159). No significant difference was observed in the baseline data of systolic blood pressure (p = 215), diastolic blood pressure (p = 213), mean blood pressure (p = 0.230), heart rate (p = 0.006), or blood glucose (p = 0.191). After 3 months of exercises, there were highly significant differences between pre-treatment and post-treatment results in both groups (p = 0.000) for BMI, WC, WHR, TUG, STS5, STS60, 6MWT. The same results were found for systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, and blood glucose. The p-value for the comparison between pre-treatment and post-treatment values equalled 0.000. However, no significant difference was revealed between the 2 groups when comparing BMI (p = 0.296), WC (p = 0.088), WHR (p = 0.142), TUG (p = 0.450), STS5 (p = 0.054), STS60 (p = 0.092), 6MWT (p = 0.515). The same results were observed for systolic blood pressure (p = 0.215), diastolic blood pressure (p = 0.002), mean blood pressure (p = 0.055), heart rate (p = 0.578), and blood glucose (p = 0.009) (Table 1, 2; Figure 2–6).

Table 2. Percent of improvement of post treatment measures of both groups

Item	Group	Percent of improvement
BMI (kg/m^2)	Group1	4.41
	Group2	3.03
Waist circumference (WC) (cm)	Group1	3.48
	Group2	3.02
Waist to hip (WHR)	Group1	14.28
	Group2	18.74
Time up and go (TUG) (s)	Group1	13.18
	Group2	17.57
Sit to stand test (STS5) (s)	Group1	25.07
	Group2	30.02
STS60 (cycle/min)	Group1	68.7
	Group2	79.3
6minutes walk distance (6MWD) (m)	Group1	11.7
	Group2	12
Systolic blood pressure (mm Hg)	Group1	8.01
	Group2	9.6
Diastolic blood pressure (mm Hg)	Group1	12.3
	Group2	10.7
Mean blood pressure (mm Hg)	Group1	10.5
	Group2	10.4
Heart rate (beat/min)	Group1	7.1
	Group2	8.03
Blood glucose (mg/dl)	Group1	9.3
	Group2	7.4

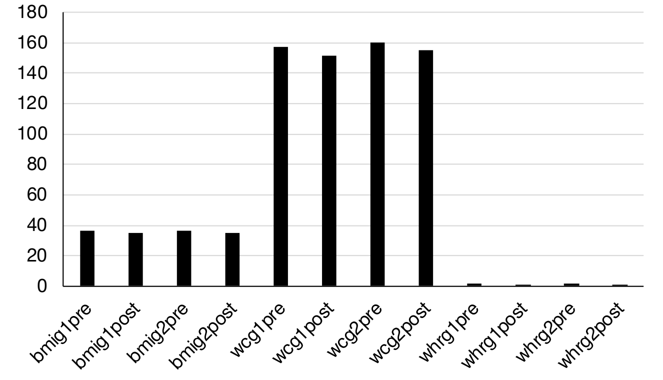

Figure 2. Pre- and post-treatment of body mass index (bmi), waist circumference (wc), waist to hip ratio (whr) of both groups (g1, g2)

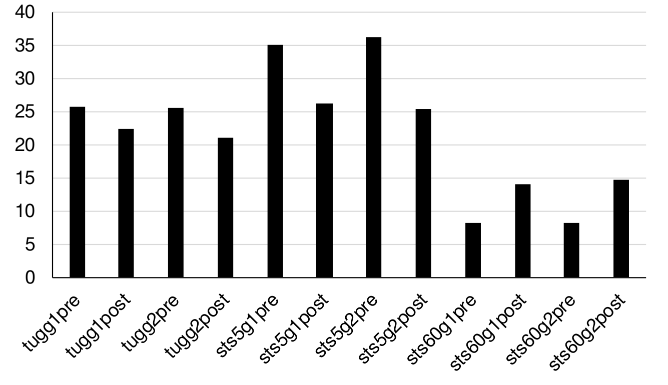

Figure 3. Pre- and post-treatment of time up and go (tug), 5 sit to stand test (sts5), sit to stand 60 (sts60) of both groups (g1, g2)

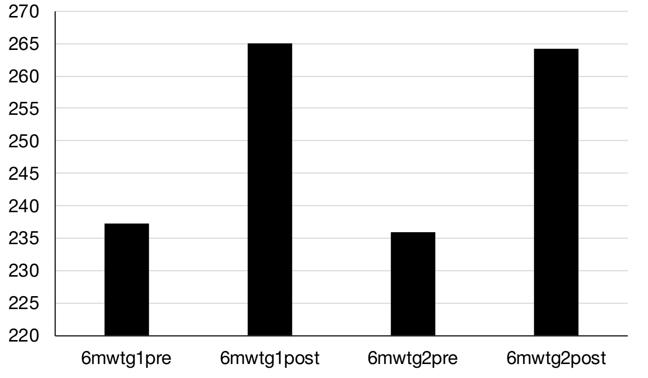

Figure 4. pre and post treatment 6 minute walk distance (6mwt) of both groups (g1, g2)

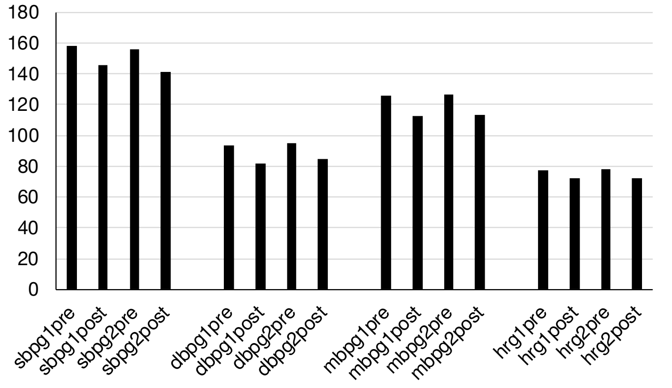

Figure 5. Pre- and-post treatment of systolic blood pressure (sbp), diastolic blood pressure (dbp), mean blood pressure (mbp), heart rate (hr) of both groups (g1, g2)

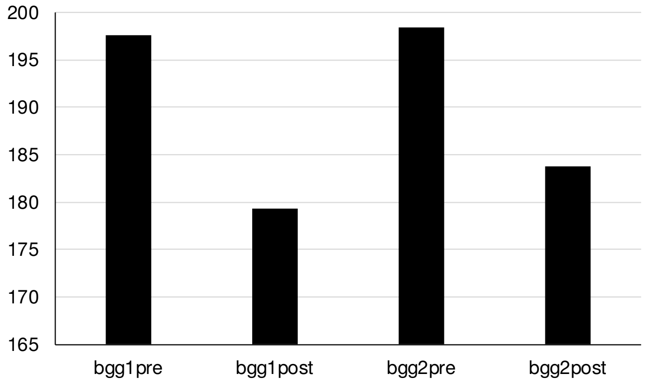

Figure 6. Pre- and post-treatment of blood glucose (bg) of both groups (g1, g2)

Discussion

According to the Kidney Disease: Improving Global Outcomes guidelines, at least 30 minutes of low/moderate-intensity physical activity 4–5 times per week are necessary for individuals with CKD. Exercise and physical activity are the cornerstone and the routine care of CKD patients [20].

It is well known that renal disease in its end stage is characterized by low physical activity and decreased exercise capacity when compared with healthy individuals and this is due to sedentary lifestyle and insufficient counselling in nephrology care [21].

In the present study, all patients exhibited reduced physical activity and exercise capacity. Cheema and Fiatarone Singh [22] found that aerobic training improved exercise capacity significantly, especially after 12 weeks of moderate-intensity exercise, but these values are still below the levels expected for sedentary healthy subjects. Aerobic capacity can be measured by 6MWT and the 2-minute step test [23]. In the current study, both groups had decreased aerobic capacity prior to treatment, but after treatment, 6MWT scores improved to (↑) 11.7% in the aerobic group and (↑) 12% in the resistance group. There were highly significant differences in both groups between pre- and post-treatment results, but no significant difference between the groups after treatment ($p = 0.515$).

Roshanravan et al. [24] observed that patients with CKD had decreased lower limb physical performance, and this indicates a strong relation with all-cause mortality. TUG, 6MWT, and gait speed are more accurate predictors of kidney function and 3-year mortality than serum biomarkers. For these reasons, we chose aerobic and resistance exercises for the lower limbs, as lower limbs have large groups of muscles which allow being an active person, as well as preventing frailty, sarcopenia and its consequences, and restless leg syndrome [25]. In this study, TUG improved in the aerobic group by 13.8%, STS5 improved by (↓) 25.07%, and STS60 improved by (↓) 68.7%. In the resistance group, TUG improved by 17.57%, STS5 improved by 30.02%, STS60 improved by 79.3%. There was a highly significant difference in both groups between pre- and post-treatment scores, although no significant difference between the groups was revealed after treatment (*p*-value of 0.450, 0.054, 0.092, respectively).

Studies have shown that improvement in muscle mass and muscle function is a reflection of improved STS10, especially in diabetic kidney disease patients who received aerobic exercises [26]. Dong et al. [27] stated the same for resistance training: after 3 months, there was an increase in maximal walking speed and a decrease in the time to perform STS10, which is considered a measure of muscle power. This can explain the results of the current study, although we did not conduct STS10 but, instead, STS5 as a measure of muscle power and STS60 as a measure of muscle endurance. This proves the importance of exercise in increasing strength and improving physical capacity. In the resistance exercise group in this study, TUG improved from 25.6 ± 1.5 to 21.1 ± 2.2 s ($p = 0.000$, a highly significant difference), STS5 improved from 36.3 ± 1.7 to 25.4 ± 2.1 s ($p = 0.000$, a highly significant difference), and STS60 improved from 8.2 ± 0.7 to 14.7 ± 1.4 cycles/min ($p = 0.000$, a highly significant difference).

Nybo et al. [28] implied that blood pressure was decreased by aerobic exercises as a result of a decreased resistance of peripheral vessels and enhancement of endothelium-mediated vasodilatation, in addition to physical capacity improvement. Neither weight loss nor a change in antihypertensive medication was noted.

In this study, exercises applied for 12 weeks improved systolic blood pressure from 158.58 to 145.87 mm Hg (by 8.01%) and diastolic blood pressure from 93.35 to 81.8 mm Hg (by 12.3%) in the aerobic group vs. from 156.65 to 141.20 mm Hg (by 9.6%) and from 94.85 to 84.74 mm Hg (by 10.7%), respectively, in the resistance group. In addition, mean blood pressure decreased from 125.8 ± 3.6 to 112.6 ± 1.7 mm Hg (by 10.5%) in the aerobic group vs. from 126.7 ± 2.3 to 113.5 ± 1.9 mm Hg (by 10.4%) in the resistance group. Heart rate decreased from 77.4 ± 1.4 to 71.9 ± 2.1 beats/min (by 7.1%) in the aerobic group vs. from 78.4 ± 1.1 to 72.1 ± 1.1 beats/min (by 8.03%) in the resistance group. There were highly significant differences in both groups after treatment, without any significant post-treatment difference between the groups (the respective *p*-values of 0.215, 0.002, 0.055, 0.578).

It is widely accepted that walking decreases blood pressure and blood sugar, but its effect on estimated glomerular filtration rate is unknown. Robinson-Cohen et al. [29] compared individuals who practised walking or any other type of exercise with those who did not undertake any exercise activity. They revealed that patients who engaged in more physical activity had a lower estimated glomerular filtration rate decline. Greenwood et al. [30] reported improvements in estimated glomerular filtration rate after exercise therapy in a group of pre-dialysis CKD patients.

The current study demonstrated a decrease in BMI from 36.3 ± 1.6 to 34.7 ± 1.6 kg/m^2 (by 4.41%), in WC from 157.07 ± 6.6 to 151.6 ± 6.4 cm (by 3.48%), and in WHR from 1.4 ± 0.2 to 1.2 ± 0.1 (by 14.28%) in the aerobic group. In the resistance group, BMI decreased from 36.3 ± 1.7 to 35.2 ± 1.7 kg/m^2 (by 3.03%), WC from 159.73 ± 7.2 to 154.9 ± 7.3 cm (by 3.02%), and WHR from 1.6 ± 0.2 to 1.3 ± 0.1 (by 18.75%). This is in agreement with the results obtained by Cook et al. [31], who found a reduction in body weight, BMI, WC ($p < 0.005$), TUG, 6MWT ($p < 0.001$), and STS60 ($p < 0.001$) after 12 months of exercise.

Exercises are known to help reduce haemoglobin A1c levels in diabetes mellitus type 2 patients, improve their lipid profile, lower the blood pressure, as well as raise cardiovascular fitness and quality of life, as evidenced by Hiraki et al. [32].

The recent instruction regarding type 2 diabetes mellitus and exercises states that the patients should perform 150 minutes of brisk walking or any other moderate-intensity exercise for 5 days weekly or 60 minutes of vigorous exercise 3 days weekly. The patient must not spend more than 2 consecutive days without practising exercise because the insulin-sensitizing effects of an acute bout of exercise only maintain for 48 hours, not more. The individuals can also benefit from

2–3 days of resistance exercise per week [33]. Structural adaptation after resistance training includes hypertrophy (increase in contractile protein content), resulting in a higher basal metabolic rate and greater absolute glucose uptake. Biochemical adaptations include an up-regulation of mitochondrial proteins involved in respiration (citrate synthase), increased glycogen synthase activity, and raised glucose transporter 4-protein content [34]. The best results are therefore gained when both types of exercises are applied together.

In this study, blood glucose decreased from 197.6 ± 3.4 to 179.3 ± 6.3 mg/dl (by 9.3%) in the aerobic group and from 198.4 ± 1.9 to 183.8 ± 4.6 mg/dl (by 7.4%) in the resistance group. This remains in line with observations by Heiwe et al. [35], who discovered that moderate-intensity aerobic or resistance exercises applied for 20–30 minutes 3–4 times per week were effective in increasing insulin sensitivity and enhancing glucose uptake by providing a repeated stimulus; 4-month aerobic walking and cycling exercises raised muscular strength, leading to an increase in glucose uptake. Similar results were obtained by Orcy et al. [36]. They indicated improved muscle strength after 12 weeks of resistance exercise performed 3 times weekly, which led to significant increases in walking capacity and functional mobility. Aerobic training accompanied by resistance training in haemodialysis patients was preferred to resistance exercises only in terms of improving functional capacity. When aerobic exercises are combined with resistance exercises, the maximum benefit is gained. Aerobic capacity can be improved by 30–90 minutes of aerobic exercises coupled with resistance training, applied 3 times every week for at least 4–6 months, at high intensity. Headley et al. [37] found that after a 48-week exercise intervention in patients with CKD stage 3–4, there were significant improvements in exercise capacity and functional ability (the intervention consisted of aerobic exercises, balance training, and resistance exercises). This supports the results of the present study.

Limitations

The study needs to be applied to large groups of patients to generalize the effect of exercises. Follow-up is needed to see if the effect of exercises continues or disappears.

Conclusions

Regular exercises, either aerobic or resistance exercises alone, have a significant effect in obese diabetic patients with CKD. They can reduce obesity, as well as increase aerobic capacity, muscle power, and endurance. They also help to decrease blood pressure and blood glucose. So, both aerobic or resistance exercises can be used in the rehabilitation of CKD patients.

Disclosure statement

The author does not have any financial interest and did not receive any financial benefit from this research.

Conflict of interest

The author states no conflict of interest.

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