



Effects of Exercise Training on Delaying Disease Progression in Patients with Chronic Kidney Disease: a Review of the Literature

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(Citation)

Reviews on Recent Clinical Trials, 11(4):333-341

(Issue Date)

2016

(Resource Type)

journal article

(Version)

Accepted Manuscript

(Rights)

The published manuscript is available at EurekaSelect via
<https://www.eurekaselect.com/openurl/content.php?genre=article&doi=10.2174/1574887111666160724182015>

(URL)

<https://hdl.handle.net/20.500.14094/0100494160>



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3 **Effects of Exercise Training on Delaying Disease Progression in Patients with**
4 **Chronic Kidney Disease: a Review of the Literature**

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Abstract

Chronic kidney disease (CKD) is an important public health problem throughout the world. The effects of exercise training are unclear in patients with CKD. This review aimed to evaluate the effects of exercise training to delay the progression of CKD and which training style is most effective.

We developed individualized search strategies for the National Library of Medicine including the PubMed MeSH database to June 2015. We searched articles related to exercise training and kidney disease using the terms “CKD”, “renal disease”, “renal insufficiency”, “renal failure”, “end-stage renal disease (ESRD)” and “physical therapy”. We searched only for reports in English and for full free papers. We also chose papers based on the references in the papers obtained by the search.

Our search identified 6 different trials including 131 participants. Our review of these 6 studies suggests that aerobic exercise training may improve exercise capacity, and resistance training may also improve muscle function in patients with CKD. No cardiac events were reported in any of the published exercise training studies reviewed, suggesting the safety of exercise in patients with CKD.

Keywords: aerobic, chronic kidney disease, exercise, progression, renal dysfunction, resistance, training

1. INTRODUCTION

Chronic kidney disease (CKD) is an important public health problem throughout the world [1]. CKD, or chronic renal disease (CRD), is characterized by a progressive deterioration in renal function that ultimately leads to the irreversible loss of nephrons and nephron function. This decline can occur over several months or can take years to progress [1]. Sarcopenia, i.e., loss of muscle mass, is a common result of kidney disease [2]. Further, in patients with CKD, impairment of the balance between the anti- and pro-oxidant systems can cause increased oxidative stress [3].

In Japan, the guidelines formulated by the Japanese Society of Nephrology in 1997 have been used in regard to exercise in CKD patients [4]. The concept espoused in the 1997 guidelines that exercise worsens renal function led to the limitation of exercise and restriction of the activity of daily living (ADL) in these patients. The guidelines tended to consider exercise and physical activity negatively. Then, the CKD practice guidelines that were created in 2009 [5] referenced reports on exercise therapy in foreign countries in which rest or non-movement was found to lead to a poor prognosis, exercise reduced the mortality from cerebral vascular disease, and exercise inhibited the new onset of diabetes mellitus and hypertension. It was also shown that exercise therapy might be important in patients with CKD. However, there are few empirical reports on exercise therapy or of evidence as to how much exercise is safe and effective in such patients [6]. Therefore, we hypothesized that exercise intervention might delay the progression of CKD. Although the progression of CRD was studied in rats [7,8], few studies have evaluated exercise such as that of aerobic and muscle training in people with CKD not requiring dialysis. Therefore, the purpose of this review was to evaluate the effects of exercise training to delay the progression of CKD and to determine which training style is most effective.

2. METHODS

2.1 Data sources and search strategies

We developed individualized search strategies for one database, the National Library of Medicine database including the PubMed MeSH database, in which searching was completed in July 2015. We searched for articles using terms related to exercise training and kidney disease, which included “CKD”, “renal failure”, “renal disease”, “renal insufficiency”, “renal failure”, “end-stage renal disease (ESRD)” and “physical therapy”. We searched only for articles in English and for full free papers. We also checked the references of the papers that were found by our search and chose papers based on these references.

2.2 Study selection

We considered English-language studies eligible for inclusion if they reported data on exercise training in non-dialysis CKD patients with pre- and post-outcome measures. We included studies that met the following criteria: participants with CKD as classified by the Kidney Disease Outcome Quality Initiative (K/DOQI) guideline [9], use of aerobic, resistance or combined aerobic and resistance training, and outcome measures that included exercise capacity or maximal muscle strength and kidney function.

2.3 Data extraction

One author (AI) independently abstracted 3 categories of variables from each of the included studies: exercise intervention, aerobic training, and muscle training and complex training. From these categories, we extracted exercise capacity, blood pressure, muscle strength, blood lipids and kidney function.

2.4 Evaluation of renal function

One author (AI) calculated the estimated glomerular filtration rate (e-GFR) using the data reported in each of the included studies. The e-GFR was calculated using the following formulae recommended by the Japanese Society of Nephrology [10]:
$$\text{e-GFR(male)} = 194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287}, \text{e-GFR(female)} = \text{GFR(male)} \times 0.739$$

3. RESULTS

3.1 Characteristics

Our search found 84 potentially relevant papers of which 61 were excluded based their titles, which include rat model, hemodialysis, children and transplant. Next, we excluded 18 papers after reading their abstracts. We read 5 full papers and chose one additional paper from the references of these 5 papers. Finally, 6 papers were chosen for review (Fig. 1).

3.2 Exercise intervention

The patients, interventions and outcomes of the 6 papers are summarized in Table 1. Among these 6 trials, 131 patients participated, with 71 patients assigned to intervention

groups and 60 patients assigned to control groups. Patient ages ranged from 22 to 84.9 years. Three categories of exercise were performed: aerobic training, muscle training and complex training. Eidemak *et al.* [11], Leehey *et al.* [12] and Toyama *et al.* [13] studied aerobic training on land, and Pechter *et al.* [14] evaluated aerobic exercise in water. Castaneda *et al.* [15] evaluated resistance training only, and Greenwood *et al.* [16] studied combined resistance and aerobic training. The intervention period ranged from 12 weeks to 20 months, with most interventions averaging about 12-18 weeks. Intervention frequency varied from daily to once a week, and intensity was about 60-85% of maximal exercise capacity except for one low-intensity trial.

3.3 Aerobic training

The outcomes of aerobic training are shown in Table 2. The modes of exercise prescribed were bicycling or an equal amount of other physical activities [11], walking [12], in-hospital bicycle ergometer and home exercise [13]. Exercise in water comprised aquatic exercise in a pool [14].

3.4 Muscle training

Only one study was conducted using resistance training only [15], and the outcomes of this study are shown in Table 3. Castaneda *et al.* reported the initial state of peak oxygen consumption in their study subjects, but they did not investigate the final state. Thus, we could not determine the effect of resistance training on the exercise capacity of CKD patients. The blood pressure of the subjects was not stated in this paper.

The exercise intensity in these trials varied: one [15] conducted training sessions at 80% of the one-repetition maximum. Participants performed 3 sets of 8 repetitions per session on latissimus pull-down, chest and leg press, knee extension and knee flexion machines for about 45 minutes per session.

3.5 Combination aerobic and resistance training

Combined resistance and aerobic training is considered to be the most effective means to achieve improved health and fitness outcomes [17]. However, only the study reported by Greenwood *et al.* used combination training [16], the outcomes of which are shown in Tables 4 and 5. Their subjects performed aerobic exercise and muscle training. Aerobic exercise was performed predominantly on recumbent stationary exercise cycles at an intensity corresponding to 80% of heart rate reserve, with maximum heart rate as derived from incremental exercise training. Resistance training was prescribed at 80%

of 1 repetition maximum, the maximum amount of weight an individual can lift or press once but not twice, for various upper and lower body muscle groups (e.g., latissimus pull-down, bicep curl, triceps pull-down, bench press, leg press, knee extension, hamstring curl, and calf raises).

4. DISCUSSION

4.1 Aerobic training

Eidemak *et al.* [11] reported that VO₂ peak increased from 25 to 27 ml/kg/min (8% improvement) in the intervention group, whereas in the control group peak, VO₂ peak dropped from 21 to 19 ml/kg/min (10% decrease). Toyama *et al.* [13] also reported similar increases in exercise capacity in the intervention group: the anaerobic threshold (AT-VO₂) increased by 10% after training, whereas it decreased by approximately 14% in the control group. Pechter *et al.* [14] reported a slight increase in VO₂ peak from 18.8 to 19.2 ml/kg/min in the exercise group and a similar increase in the control group, from 21.0 to 21.3 ml/kg/min, thus indicating no significant difference between the two groups. Low-intensity exercise was prescribed that was performed exclusively in water. Leehey *et al.* [12] also reported no significant change in maximal oxygen uptake (VO₂ max) following exercise intervention, likely because a high number of participants dropped out of the study. Of the 20 patients recruited, one person failed prescreening laboratory tests and six were excluded because of a positive stress test (n=2), investigator's decision (n=2), patient choice (n=1) and commencement of hemodialysis (n=1). Thus, only 13 patients remained who were respectively randomized to the exercise group (n=7) and the control group (n=6). Ultimately, 4 patients remained in the control group after 2 patients were excluded (investigator's decision and patient wish, respectively).

The evaluation of blood pressure is important in the CKD population. Pechter *et al.* [14] showed that the resting blood pressure in their training group dropped from 147/87 to 139/84 mmHg, whereas that in their control group did not change. Aquatic exercise was previously reported to be effective in decreasing the blood pressure in patients with hypertension [18]. This type of exercise is useful because plasma renin activity drops, and renal sympathetic nerve activity and levels of catecholamines and prostaglandins [19], which contribute to sodium excretion and renal vascular pressure [20], are lowered. In the other studies, exercise training had no effect on blood pressure. Eidemak *et al.* [11] and Toyama *et al.* [13] both reported improvements in exercise capacity, although no improvements in blood pressure were seen. Leehey *et al.* [12] reported slight lowering of the resting systolic and diastolic blood pressure, which they thought was the result of a training effect, but they could not determine any statistical

significance of the change because their study's small sample size.

The major goal in treating kidney disease is to retard the deterioration of kidney function by controlling the blood pressure with medications such as angiotensin converting enzyme inhibitors and by aggressive management of other cardiovascular risk factors. Pechter *et al.* [14] reported encouraging results from their study of aquatic exercise, which showed improved kidney function. However, this improvement must be interpreted with caution because the number of subjects evaluated was low. Toyama *et al.* [13] also reported a significant improvement in e-GFR, but only 9 patients were studied, and the study lasted only 12 weeks. Eidemak *et al.* [11] showed that exercise intervention had no protective effect against the decline in kidney function. Results of analysis of covariance (ANCOVA) on the basis of the change in the GFR at 12 months showed that the rate at which loss of function occurred in the exercise group (median loss, -0.27; 95% confidence interval [CI], +0.57 to -1.31 ml/min/1.73 m²/month) and the control group (median loss, -0.28; 95% CI, +0.18 to -0.93 ml/min/1.73 m²/month) was similar. They suggested that the study numbers were likely too small to exclude an exercise effect on disease progression. Leehey *et al.* [12] observed reductions in renal function parameters. The Eidemak *et al.* [11] study was the only one reporting a significant change in total cholesterol in the exercise group, in which cholesterol increased from 5.0 to 5.6 mmol/l. This unusual finding is not typical of the usual changes in cholesterol seen with exercise training [21]. Toyama *et al.* reported a significant decrease in triglycerides and low-density lipoprotein cholesterol in the exercise training group but a significant increase in high-density lipoprotein cholesterol (HDL-C) [13], which was positively related with an increase in e-GFR levels.

4.2 Resistance training

With regard to resistance training, Castaneda *et al.* [15] reported that kidney function as indicated by GFR improved in the exercise group by a small but significant amount (from 24.8 to 30.0 ml/min/1.73 m²) compared with that in the control group (from 27.5 to 28.0 ml/min/1.73 m²). However, this finding must be interpreted with caution because of the small sample size and short follow-up period in this study. They also reported an 18% increase in the concentrations of insulin-like growth factor I in the subjects who ate a low-protein diet alone (P=0.125) during their resistance training program [15]. The serum prealbumin level in the resistance training group increased significantly compared with that in the low-protein diet alone group, with similar trends also reported for serum albumin and transferrin. The total body potassium following the intervention correlated significantly with the post-intervention serum albumin concentration (r=0.52; P<0.01). In those who performed resistance training, urinary creatinine excretion decreased by 8%, but it did not change in those eating the low-

protein diet alone.

Sarcopenia is a common result of kidney disease because with CKD, the body is in a catabolic state. The intervention caused significant increases in total body potassium and hypertrophy of type I and II muscle fibers, suggesting that such exercise training can counter the effects of a low-protein diet and the catabolic state caused by kidney disease. The increase in hypertrophied muscle fibers was complemented by significant increases in both upper and lower body strength, whereas strength in the low-protein diet group decreased (overall improvement in muscle strength, $32\% \pm 14\%$ vs. $-13\% \pm 20\%$; $P < 0.001$).

4.3 Aerobic and resistance training

In terms of aerobic resistance training, Greenwood *et al.* [16] reported that although peak VO_2 decreased in the control group, peak VO_2 in the intervention group increased from 20.1 to 23.0 ml/kg/min. In addition, results of ANCOVA using the amount of change in peak VO_2 between the two groups showed a significant change in the mean difference of relative peak VO_2 of 5.7 (95% CI, 1.34-10.10) ml/kg/min ($P = 0.01$). This intervention had no significant effect on blood pressure at rest, heart rate, high-sensitivity C-reactive protein level or lipid levels. The mean change in creatinine-based e-GFR (e-GFRcr) was -9.7 ± 7.2 ml/min/ 1.73 m^2 per year in the 12-month pre-intervention period and -3.8 ± 2.8 ml/min/ 1.73 m^2 per year in the 12-month intervention period in the intervention group. During the same period, the control group experienced a change from -6.6 ± 4.7 to -8.5 ± 6.4 ml/min/ 1.73 m^2 per year. Result of ANCOVA the e-GFRcr change amount of the two groups, by the end of the 12-month exercise intervention period, the mean difference in the change in e-GFRcr slopes between the intervention and control groups was statistically significant (7.8 ± 3.0 [95% CI, 1.1-13.5] ml/min/ 1.73 m^2 per year; $P = 0.02$).

The primary observations on kidney function are based on the rate of change in e-GFRcr data across a 24-month period. The secondary outcomes investigate between-group mean differences in absolute e-GFR at the end of the intervention, with the addition of cystatin C level. Although all 3 e-GFR equations (yielding e-GFRcr, creatinine and cystatin-based e-GFR, and cystatin-based e-GFR) showed an increase in e-GFR in the exercise group between 0 and 12 months of the intervention, between-group analysis did not reveal a significant mean difference in these values at the 12-month point. The inconsistency between these results is a limitation of the Greenwood *et al.* study, and as such, it is suggested that observations about kidney function and exercise therapy be interpreted with caution. This study also has limitations, such as its small sample size, small exercise dose, variability in response and the lack of data about muscular function. However, a change in mean waist circumference was observed

between the groups at 12 months. This was associated with mean rate of change in e-GFRcr. This finding is in agreement with the study by Baria *et al.* [22]. Observation of a significant inverse relationship between the rate of change in e-GFRcr and the change in waist circumference suggests that the approximately 36% improvement noted in the rate of change of the e-GFRcr could be explained by the reduction in waist circumference and perhaps associated central adiposity. These six studies have several limitations [11–16]. Common to all is their small sample size, and thus, further large trials are required. As a limitation of the present review, we developed an individualized search strategy for only one database. However, the aim of this review was to evaluate the beneficial effects of exercise on renal function, and we believe this review is valuable in that may promote further investigation.

5. CONCLUSION

The effects of exercise training on patients with CKD were reviewed in 6 different trials comprising 131 participants. The conclusions from these 6 studies suggested that aerobic exercise training may lead to improved exercise capacity and that resistance training may improve muscle function. These are beneficial effects for this particular population. Four of the studies reported an improvement in e-GFR [13–16]. Among these studies, Castaneda *et al.* [15] reported a similar increase in e-GFR between the exercise and control groups. However, the other three studies reported that the e-GFR of the control group decreased whereas that of the exercise groups increased [13, 14, 16]. Especially, the trial of Toyama *et al.* [13] revealed a significant improvement in e-GFR. The study of Pechter *et al.* [14] reported significant reductions in proteinuria and cystatin C and “ameliorating trends” in e-GFR. The interventions of Toyama *et al.* [13] and Pechter *et al.* [14] likely have one thing in common. In these studies, leaders supervised and led the exercise sessions and interventions; thus, the participants were able to exercise under appropriate guidance. There were no reports of cardiac events in any of the published exercise training studies, suggesting the safety of exercise in patients with CRD.

ACKNOWLEDGEMENTS

We appreciate the support and encouragement of Taku Shinoda (Kobe University School of Medicine Faculty of Health Sciences) and Masashi Kanai (Kobe University Graduate School of Health Sciences). We would like to express our gratitude to everyone involved in helping with our research.

CONFLICT OF INTEREST

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The authors confirm that they have no conflicts of interest to declare.

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373 **FIGURE LEGEND**

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375 Figure 1. Study flow diagram.

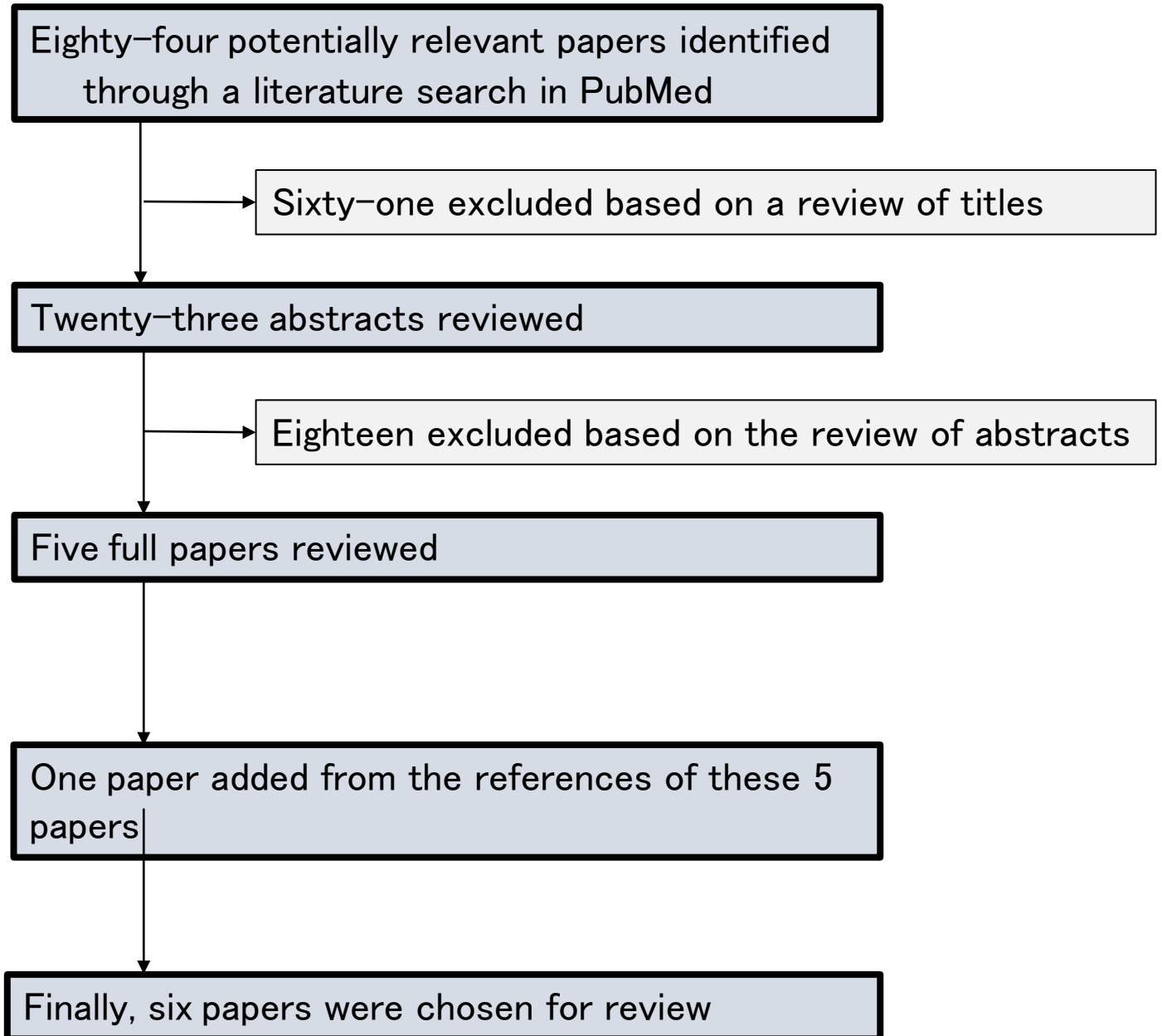


Fig. 1.

Table 1. Summary of studies, participants and interventions.

Source	Population	Duration of intervention	No. of participants (male)	Age (yrs)	Description of intervention and control	Exercise category
Eidemak et al. [11] 1997	CKD patients with median GFR of 25 (range 10-43)	20 months	16 (8)	45 (22-70)	Intervention: 30 min of bicycling daily or an equal amount of other physical activities Intensity: 60-75% of maximal exercise capacity	Aerobic
			15 (5)	44 (28-65)	Control: usual life	
Castaneda et al. [15], 2001	Older patients with moderate renal insufficiency who had achieved stabilization on a low-protein diet	12 weeks	14 (6)	65±9	Intervention: low-protein diet plus resistance training Intensity: 80% of 1 RM	Muscle training
			12 (3)	64±13	Control: low-protein diet only	
Leehey et al. [12], 2009	Patients with type 2 DM, obesity and stage 2-4 CKD (e-GFR: 15-90)	18 weeks	7 (7)	66 (55-81)	Intervention: thrice weekly aerobic training of supervised home exercise Intensity: 60-84% VO ₂ peak	Aerobic
			4 (4)	66 (55-81)	Control: educational	
Pechter et al. [14], 2003	Patients with moderate GFR	12 weeks	17 (7)	52 (31-72)	Intervention: aerobic exercise in the pool twice a week with sessions lasting 30 min Intensity: low	Aerobic in water
			9 (6)	48 (35-65)	Control: sedentary	
Toyama et al. [13], 2010	Patients with CVD and CKD (e-GFR <60)	12 weeks	9 (9)	71.1±13.8	Intervention: once a week in-hospital aerobic exercise and home exercise (30 min daily walking) Intensity: RPE at 12-13	Aerobic

			10 (8)	72.3±8.5	Control: diet therapy, mental support, counseling and education, no exercise	
Greenwood et al. [16], 2014	CKD patients whose stage is 3 to 4 (GFR: 20-60)	12 months	8 (6)	53.8±13.5	Intervention: resistance and aerobic training (3 days per week) Intensity: aerobic: 80% of heart rate reserve; RPE: 11; resistance: 80% of 1 RM	Aerobic and muscle training
			10 (9)	53.3±12.9	Control: usual care	

Abbreviations: BMI: body mass index, CKD; chronic kidney disease, DM; diabetes mellitus, e-GFR; estimated glomerular filtration rate, RM; repetition maximum, RPE; rate of perceived exertion.

Table 2. Outcomes of aerobic training.

		Eidemark et al. [11], 1997		Leehey et al. [12], 2009			Pechter et al. [14], 2003		Toyama et al. [13], 2010	
Outcome		Baseline	18 months	Baseline	6 weeks	24 weeks	Baseline	12 weeks	Baseline	12 weeks
VO ₂ peak (ml/kg/min)	Intervention	25	27	14.9 $\pm$ 1	13.8 $\pm$ 3.9	15.6 $\pm$ 2.4	18.8 $\pm$ 0.9	19.2 $\pm$ 1.1		
	Control	21	19	10.9 $\pm$ 1	11.8 $\pm$ 2.0	11.9 $\pm$ 1.3	21.0 $\pm$ 2.9	21.3 $\pm$ 3.2		
AT-VO ₂ (ml/kg/min)	Intervention	–	–	–	–	–	–	–	9.9 $\pm$ 1.9	
	Control	–	–	–	–	–	–	–	10.7 $\pm$ 0.7	
SBP (range)/DBP (range) (mmHg)	Intervention	133 (110-160)/85 (70-105)	No change	130 $\pm$ 28/71 $\pm$ 20	132 $\pm$ 13/71 $\pm$ 11	113 $\pm$ 16/65 $\pm$ 10	147 $\pm$ 4.0/87 $\pm$ 2.0	139 $\pm$ 4.0/84 $\pm$ 2.0	122.4 $\pm$ 18.9/68.8 $\pm$ 8.8	–
	Control	140 (110-170)/90 (75-100)	No change	157 $\pm$ 14/83 $\pm$ 20	156 $\pm$ 23/77 $\pm$ 12	136 $\pm$ 5/77 $\pm$ 8	148 $\pm$ 6/90 $\pm$ 3.0	147 $\pm$ 9.0/87 $\pm$ 5.0	127.7 $\pm$ 22.4/76.3 $\pm$ 9.7	–
TC (mg/dl [mmol/l])	Intervention	193.0 $\pm$ 34.4 (5.0 $\pm$ 0.9)	283.2 $\pm$ 40.6 (5.7 $\pm$ 1.1)	125 $\pm$ 25	116 $\pm$ 17	128 $\pm$ 25	247.5 $\pm$ 7.7 (6.4 $\pm$ 0.2)	235.9 $\pm$ 7.7 (6.1 $\pm$ 0.2)	–	–
	Control	206.1 $\pm$ 41.4 (5.3 $\pm$ 1.1)	209.6 $\pm$ 45.2 (5.4 $\pm$ 1.2)	152 $\pm$ 38	160 $\pm$ 53	146 $\pm$ 31	243.6 $\pm$ 23.2 (6.3 $\pm$ 0.6)	232.0 $\pm$ 19.3 (6.0 $\pm$ 0.5)	–	–
TG (mg/dl [mmol/l])	Intervention	166.5 $\pm$ 149.7 (1.9 $\pm$ 1.7)	127.6 $\pm$ 70.9 (1.4 $\pm$ 0.8)	137 $\pm$ 45	144 $\pm$ 60	179 $\pm$ 89	203.7 $\pm$ 17.7 (2.3 $\pm$ 0.2)	194.9 $\pm$ 1.8 (2.2 $\pm$ 0.2)	114.6 $\pm$ 41.4 (1.3 $\pm$ 0.5)	–
	Control	118.7 $\pm$ 52.3 (1.3 $\pm$ 0.6)	138.2 $\pm$ 110.7 (1.6 $\pm$ 1.3)	223 $\pm$ 92	245 $\pm$ 44	225 $\pm$ 104	248.0 $\pm$ 70.9 (2.8 $\pm$ 0.8)	212.6 $\pm$ 44.3 (2.4 $\pm$ 0.5)	116.1 $\pm$ 63.3 (1.3 $\pm$ 0.7)	–
LDL (mg/dl [mmol/l])	Intervention	123.0 $\pm$ 30.9 (3.2 $\pm$ 0.8)	141.9 $\pm$ 36.4 (3.7 $\pm$ 0.9)	59 $\pm$ 17	51 $\pm$ 16	54 $\pm$ 11	158.6 $\pm$ 3.9 (4.1 $\pm$ 0.1)	150.8 $\pm$ 3.9 (3.9 $\pm$ 0.1)	113.9 $\pm$ 31.6 (2.9 $\pm$ 0.8)	–
	Control	–	–	75 $\pm$ 24	80 $\pm$ 41	69 $\pm$ 22	150.8 $\pm$ 19.3 (3.9 $\pm$ 0.5)	147.0 $\pm$ 19.3 (3.8 $\pm$ 0.5)	93.2 $\pm$ 24.7 (2.4 $\pm$ 0.6)	–
HDL (mg/dl [mmol/l])	Intervention	39.4 $\pm$ 14.7 (1.0 $\pm$ 0.4)	41.4 $\pm$ 13.9 (1.1 $\pm$ 0.4)	38 $\pm$ 6	37 $\pm$ 5	39 $\pm$ 7	50.3 $\pm$ 3.9 (1.3 $\pm$ 0.1)	50.3 $\pm$ 3.9 (1.3 $\pm$ 0.1)	40.6 $\pm$ 7.4 (1.1 $\pm$ 0.2)	–

	Control	–	–	33±6	31±3	31±4	46.4±3.9 (1.2±0.1)	54.1±7.7 (1.4±0.2)	50.6±15.9 (1.3±0.4)	–
BMI	Intervention	–	–	–	–	–	29.4±1.3	29.4±1.3	24.2±4.6	–
	Control	–	–	–	–	–	28.1±1.3	28.1±1.3	26.0±2.7	–
Creatinine (mg/dl [μmol/l])	Intervention	–	–	2.9±1.5	2.7±1.3	2.8±1.2	1.6±0.1 (141.8±11.7)	1.53±0.12 (135.0±10.4)	1.2±0.5	–
	Control	–	–	2.3±0.1	2.1±0.2	2.1±0.4	1.8±0.3 (154.4±23.4)	2.0±0.4 (178.4±34.3)	1.2±0.2	–
e-GFR (ml/min/1.73 m ²)	Intervention	–	–	18.2	19.7	18.9	31.6	33.2	47.0±13.7	55.2±16.9
	Control	–	–	23.4	25.9	25.9	31.6	27.03	47.9±9.5	44.6±8.2
GFR (ml/min/1.73 m ²)	Intervention	26 (10–38)		44±36	45±31	39±22	62.9±5.9	67.1±7.0	–	–
	Control	24 (9–43)		47±9.5	36±14	41±5.3	69.8±12.3	66.3±13.2	–	–

Values are mean ± standard deviation or median.

Abbreviations: VO₂: oxygen consumption, AT: anaerobic threshold, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, LDL: low-density lipoprotein, HDL: high-density lipoprotein, BMI: body mass index, e-GFR; estimated glomerular filtration rate, GFR; glomerular filtration rate.

Table 3. Outcomes of resistance training.

		Castaneda et al. [15], 2001	
		Baseline	12 weeks
VO ₂ peak (ml/min)	Intervention	16.0±5.1	–
	Control	18.5±7.1	–
Chest press (kg)	Intervention	24.0±10.4	31.8±12.9
	Control	28.4±5.8	26.2±6.4
Pull-down (kg)	Intervention	26.4±7.5	33.9±10.0
	Control	29.5±8.0	27.6±10.0
Leg press (kg)	Intervention	167.4±102.3	210.9±129.0
	Control	135.0±26.7	134.3±36.3
Knee extension (kg)	Intervention	39.9±17.8	55.9±22.4
	Control	36.7±9.8	38.8±14.0
Knee flexion (kg)	Intervention	39.8±13.6	55.8±13.6
	Control	43.4±16.0	39.5±9.4
Hematocrit (%)	Intervention	31.6	32.8
	Control	32.1	32.7
Body weight (kg)	Intervention	84.6±15.8	84.8±16.2
	Control	76.1±13.5	72.5±9.0
Prealbumin (mg/L)	Intervention	253±46	276±46
	Control	232±60	234±50
Creatinine (mg/dl [μmol/l])	Intervention	2.12 (187.41)	1.85 (163.54)
	Control	2.29 (202.44)	2.06 (182.10)
e-GFR (ml/min/1.73 m ²)	Intervention	21.9	25.4
	Control	19.2	21.5
GFR (ml/min/1.73 m ²)	Intervention	24.8	30.0
	Control	27.5	28.0

Values are mean $\pm$ standard deviation or median.

Abbreviations: VO₂: oxygen consumption, e-GFR; estimated glomerular filtration rate.

Table 4. Outcomes of complex training.

		Greenwood et al. [16], 2014		
Outcome		Baseline	6 months	12 months
VO ₂ peak (ml/kg/min)	Intervention	20.1±5.8	20.9±5.7	23.0±5.3
	Control	18.3±4.6	16.1±4.0	16.2±5.0
SBP/DBP (mmHg)	Intervention	135.8±17.4/86.5±15.8	131.3±10.9/85.5±10.6	133.2±14.6/84.4±14.7
	Control	134.3±20.7/86.5±12.7	132.3±23.2/85.5±13.3	127.1±17.0/78.9±6.9
TC (mg/dl [mmol/l])	Intervention	193.3±19 (5.0±0.5)	185.6±19 (4.8±0.5)	193.3±34.8 (5.0±0.9)
	Control	181.7±61.9 (4.7±1.6)	185.6±61.9 (4.8±1.7)	166.3±46.4 (4.3±1.2)
LDL (mg/dl [mmol/l])*	Intervention	119.9±31.3 (3.1±0.8)	100.5±27.1 (2.6±0.7)	127.6±135.3 (3.3±3.5)
	Control	100.5±46.4 (2.6±1.2)	104.41±50.3 (2.7±1.3)	96.7±34.8 (2.5±0.9)
HDL (mg/dl [mmol/l])*	Intervention	58.0±19.3 (1.5±0.5)	54.1±19.3 (1.4±0.5)	58.0±19.3 (1.5±0.5)
	Control	58.0±19.3 (1.5±0.5)	54.1±19.3 (1.4±0.5)	42.5±23.2 (1.1±0.6)
Body weight (kg)	Intervention	76.5±15.2	75.5±16.3	72.9±16.1
	Control	83.6±12.3	84.5±12.7	85.6±12.7
BMI	Intervention	27.40±3.5		24.9±3.5
	Control	28.4±4.2	28.8±4.4	29.0±4.1
Creatinine (mg/dl [μmol/l])	Intervention	2.1±0.5 (184.3±42.9)	2.2±0.6 (191.0±56.0)	2.1±0.7 (187.3±61.6)
	Control	2.0±0.7 (175.5±58.3)	2.1±0.8 (187.3±72.4)	2.3±1.1 (203.6±100.5)
e-GFR (ml/min/1.73 m ²)	Intervention	36.6±10.1	36.9±13.8	40.3±18.7
	Control	46.5±20.6	44.5±20.9	41.7±18.2

Values are mean ± standard deviation or median.

Abbreviations: VO₂: oxygen consumption, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, LDL: low-density lipoprotein, HDL: high density lipoprotein, BMI: body mass index, e-GFR; estimated glomerular filtration rate.

* Value obtained by converting the data of the original paper.

Table 5. Outcome of complex training.

		Greenwood et al. [16], 2014		
Outcome		Pre intervention	Post intervention	Between group differences ANCOVA
Mean e-GFRcr rate-of-change slope (ml/min/1.73 m ² per year)	Intervention	-9.7±7.2	-3.8±2.8	+7.8±3.0
	Control	-6.6±4.7	-8.6±6.4	

Values: mean ± standard deviation.

Abbreviations: ANCOVA: analysis of covariance, e-GFRcr: creatinine-based estimated glomerular filtration rate.