



# Systematic review and meta-analysis of the efficacy of exercise intervention in kidney transplant recipients

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## Abstract

**Background and objective** There is uncertainty about the beneficial effects of exercise intervention for kidney transplant recipients. The purpose of our meta-analysis is to estimate the efficacy of exercise intervention in kidney transplant recipients.

**Methods** A database search according to the PICOS framework was performed for all published randomized, double-blind, placebo-controlled trials (RCTs) about exercise intervention for kidney transplant recipients. The databases involved include PubMed, Embase, and Cochrane Library.

**Results** A total of 16 RCTs (involving 827 patients) in compliance with inclusion criteria were included in our study. The results demonstrated that adequate exercise intervention improved statistically in creatinine clearance [mean difference (MD) = -0.29, 95% confidence interval (CI) -0.46 to -0.11,  $p = 0.001$ ], serum urea (MD = -21.57, 95% CI -35.84 to -7.29,  $p = 0.003$ ),  $VO_2$  peak (MD = 3.20, 95% CI 1.97–4.43,  $p < 0.00001$ ), high-density lipoprotein-cholesterol (HDL-C) (MD = 0.21, 95% CI 0.04–0.37,  $p = 0.01$ ), 60-s sit to stand test (60-STs) (MD = 14.47, 95% CI 8.89–20.04,  $p < 0.00001$ ), 6-min walk distance (6-MWD) (MD = 91.87, 95% CI 38.34–145.39,  $p = 0.0008$ ), and 6-min walk test (6-MWT) (MD = 44.08, 95% CI 20.30–67.87,  $p = 0.0003$ ) of patients after kidney transplantation. No between-groups differences ( $p > 0.05$ ) were observed for anthropometric characteristics, body composition, serum cytokine levels, and quality of life short form-36 questionnaire (SF-36).

**Conclusions** In kidney transplant recipients, appropriate exercise intervention improved renal function, cardiopulmonary function, physical performance.

**Trial registration** The PROSPERO registration number is CRD42022357574.

**Keywords** Meta-analysis · Exercise intervention · Kidney transplant · Renal function · Randomized controlled trial (RCT)

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## Abbreviations

ESRD	End-stage renal disease
ERAS	Enhanced recovery after surgery
RCTs	Randomized controlled trials
PICOS	Populations, interventions, comparators, outcomes, and study designs
SF-36	Short form-36 questionnaire
MD	Mean difference
ORs	Odds ratios
CIs	Confidence intervals
BMI	Body mass index
BMD	Bone mineral density
LBM	Lean body mass
eGFR	Estimated glomerular filtration rate
HDL-C	High-density lipoprotein-cholesterol
TNF- $\alpha$	Tumor necrosis factor- $\alpha$
IL-6	Interleukin-6
60-STs	60-Second sit-to-stand test

6-MWD	6-Minute walk distance
6-MWT	6-Minute walk test
CVDS	Cardiovascular disease

## Introduction

Kidney transplantation is currently the most desired treatment option for patients suffering from end-stage renal disease (ESRD). Compared with other treatments, kidney transplantation has some advantages in improving survival and quality of life [1, 2]. Despite this, patients generally experience multiorgan dysfunction following the procedure, after allograft transplantation. In addition, patients after kidney transplantation often require lifelong immunosuppressants to prevent graft rejection. These immunosuppressive drugs often result in adverse events such as muscle weakness, osteoporosis, and cardiovascular disease [3, 4]. Therefore, postoperative management of kidney transplantation plays a crucial role after renal transplantation.

In recent years, with the promotion of the enhanced recovery after surgery (ERAS) concept, the effect of appropriate exercise intervention for postoperative patients has gradually begun to receive attention. Exercise is recognized as an effective non-pharmacological intervention that is generally categorized as aerobic, anaerobic, and flexibility exercises. The health benefits of exercise have been demonstrated in healthy people and people with chronic diseases [5]. Related studies have also shown that exercise interventions are effective in patients with solid

organ transplants, including heart, kidney, lung, and liver transplants [6]. Although exercise interventions are considered beneficial, routine exercise intervention programs for renal transplant recipients are not used as part of standard clinical care. Besides, the evidence on the impact of exercise intervention on kidney transplant recipients is limited. The few available studies have only focused on the effects of exercise intervention on several aspects of exercise tolerance, cardiorespiratory fitness, and quality of life in kidney transplant recipients [7–9].

This systematic review and meta-analysis aimed to compare the changes of the exercise intervention group and control group, to fully assess the effects of an exercise intervention on kidney transplant recipients.

## Methods

### Search strategy

We searched the PubMed, Embase, and Cochrane Library databases using kidney transplantation, exercise training, and randomized controlled trials as keywords. Depending on PICOS (populations, interventions, comparators, outcomes, and study designs) strategy, four authors independently conducted the searches. Table 1 shows the search strategy. This meta-analysis has been registered on PROSPERO with the number CRD42022357574. PRISMA 2020 checklist is shown in the supplementary material.

**Table 1** Search strategy according to populations, interventions, comparators, outcomes, and study designs (PICOS)

	Population	Intervention	Comparator	Outcomes	Study design
Inclusion criteria	Patients with living donor kidney transplantation	Exercise training	Standard care	Anthropometry Body composition Renal function Cardiorespiratory function Blood parameters Serum cytokine levels Physical performance 36-Item Short Form Survey	Randomized controlled trials
Exclusion criteria	Patients with any other organ transplant besides kidney Patients with any cardiac/pulmonary disease that contraindicated physical activity Patients with transplant rejection and lack of availability for regular follow-up	Not performed	Not performed	PROMIS Global Health short form Physical composite scale Mental composite scale	Letters, comments, reviews, qualitative studies

## Inclusion criteria

The RCTs included in this study were required to fulfill all of the following inclusion criteria: (1) the study analyzed the effect of exercise intervention for kidney transplant recipients was analyzed; (2) the study contained valued data that could be analyzed and related outcome index; (3) full-text content was accessible; (4) the study was an RCT. The population inclusion criteria for RCTs were more stringent than other prospective and retrospective studies.

## Quality assessment

Studies were categorized according to the Cochrane Risk of Bias Tool for Randomized Trials [10], version 2 (RoB2), recommended by the Cochrane Handbook for the Systematic Evaluation of Interventions [11], version 6.2. According to RoB2, we categorized studies into three levels: low risk of bias, moderate risk of bias, and high risk of bias.

## Data extraction

From each included RCT, the following information was extracted: (I) the name of the first author; (II) the time of publication and the type of design; (III) the sample size of each group; (IV) the methods of exercise intervention; (V) the time of intervention; (VI) the outcomes of study: anthropometric characteristics, body composition, renal function, cardiorespiratory function, blood parameters, serum cytokine levels, physical performance and quality of life.

## Statistical and meta-analysis

Data were analyzed using Review Manager software (RevMan, version 5.3.0, Cochrane Collaboration) [12]. This study adopted mean difference (MD) for assessing continuous data and adopted odds ratios (ORs) with 95% confidence intervals (CIs) for assessing dichotomous data. We considered studies with  $p$  values  $> 0.05$  as homogeneous and conducted the analysis using a fixed-effects model. Conversely, we employed a random-effects for analyzing heterogeneous studies. The present study checked for inconsistency through  $I^2$  statistics. The value of  $p < 0.05$  was deemed to be statistically significant.

## Results

### Characteristics of eligible studies

195 articles met the above inclusion criteria and were retrieved from the database. After screening the titles and abstracts, 163 articles were excluded. We reviewed the

remaining articles. Among them, 12 studies were removed due to they were not RCTs. Then, 4 studies were eliminated because they missed key information. In the end, 16 RCTs [7–9, 13–25] were included in the final analyses. The flow-chart of the selection process is shown in Fig. 1. The details of the included studies are given in Table 2.

### Quality of eligible studies

The studies included in our meta-analysis were all RCTs. All studies performed a sample size calculation. Eleven of these RCTs were graded A for quality. Only one study reported an intention-to-treat analysis [13]. No patients were lost during follow-up in the ten studies [7, 8, 13, 15–17, 19, 21, 22, 24]. The quality of included studies is shown in Table 3.

### Efficacy

We studied the effects of exercise intervention on measurement parameters in kidney transplant patients. Patients in the control group received standard treatment for the same length of time.

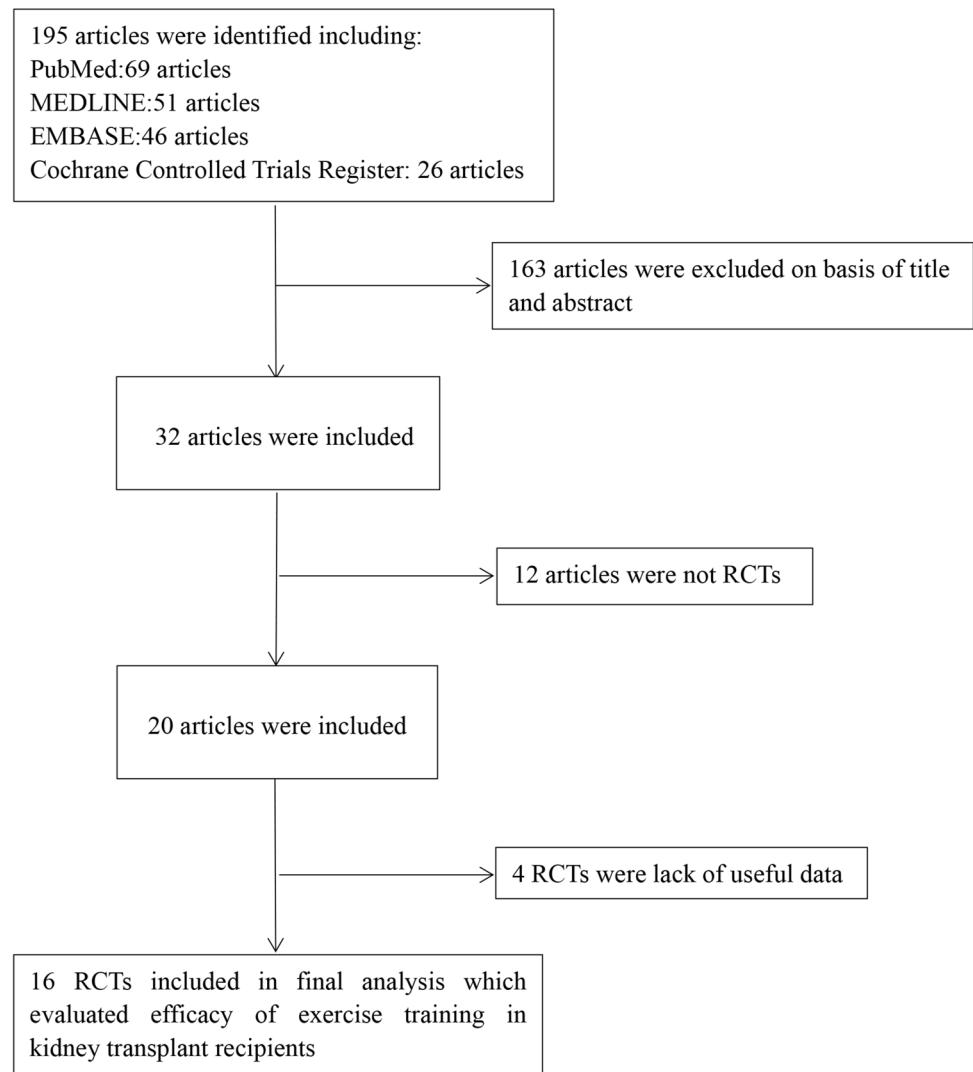
### Anthropometric characteristics

**Body mass index (BMI)** Seven RCTs involving 393 patients compared the differences between the two groups after the intervention in terms of BMI (Supplementary Fig. 1A). Because of  $p > 0.05$ , we conducted a fixed-effects model for the study. The results showed no statistical difference in BMI between the two groups after the intervention treatment (MD: 0.12, 95% CI  $-0.72$  to  $0.96$ ,  $\text{Chi}^2 = 3.40$ ,  $p = 0.78$ ).

**Waist circumference** Three RCTs reported the changes between the two groups of patients after the intervention in terms of waist circumference (Supplementary Fig. 1B). Since  $p > 0.05$ , a fixed-effects model was used to analyze group differences. The model indicated that the MD was 1.50, the 95% CI was  $-3.74$  to  $6.74$ , the  $I^2$  was 25%, and the  $\text{Chi}^2$  value was 2.67 ( $p = 0.58$ ). We suggested that the exercise intervention and control groups were similar in terms of the waist circumference of patients.

**Hip circumference** Two RCTs analyzed the changes in the hip circumference of 32 patients after the intervention (Supplementary Fig. 1C). A fixed-effects model was used to assess changes between the two groups, which showed an MD of  $-1.19$  (95% CI  $-6.10$ – $3.72$ ,  $p = 0.63$ ). There was no significant difference between the two groups concerning hip circumference.

**Fig. 1** Flowchart of the study selection process. RCT, randomized controlled trials



### Body composition

**Bone mineral density (BMD)** Because of  $p > 0.05$ , we employed a fixed-effects model to compare the BMD between the exercise intervention and control groups from two RCTs (Supplementary Fig. 2A). The pooled estimate of MD was  $-0.02$ , 95% CI was  $-0.07$  to  $0.03$ ,  $I^2$  was 45%, and  $\text{Chi}^2$  was 1.80 ( $p = 0.45$ ). The results showed that the exercise intervention and control groups were similar regarding BMD.

**Lean body mass (LBM)** Three RCTs analyzed the differences between the two groups after the intervention in terms of LBM (Supplementary Fig. 2B). Due to  $p > 0.05$ , we conducted a fixed-effects model for the study. The results showed no statistical difference in LBM between the two groups after the intervention treatment (MD: 1.21, 95% CI  $-2.35$  to  $4.78$ ,  $\text{Chi}^2 = 5.45$ ,  $p = 0.50$ ).

### Renal function

**Creatinine** Six RCTs involving 317 patients reported the changes between the two groups of patients after the intervention in terms of creatinine (Fig. 2A). Since  $p = 0.05$ , a fixed-effects model was used to analyze group differences. The model revealed that the MD was  $-0.29$ , the 95% CI was  $-0.46$  to  $-0.11$ , the  $I^2$  was 54%, and the  $\text{Chi}^2$  value was 10.90 ( $p = 0.001$ ). We concluded that creatinine was greatly improved in the exercise intervention group than in the control group.

**Urea** Two RCTs analyzed the changes in the area of 28 patients after the intervention (15 in the exercise intervention group and 13 in the control group) (Fig. 2B). We performed a fixed-effects model to analyze differences between groups, due to  $p > 0.05$ . The model revealed that the MD was  $-21.57$ , the 95% CI was  $-35.84$  to  $-7.29$ , the  $I^2$  was

**Table 2** Study and patient characteristics

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Onofre et al. [13]	Brazil	RCT	Ex: 30; Con: 33	Ex: 37.0 (9.2); Con: 35.6 (10.4)	Patients (1) performed three sets of 10 repetitions of breathing exercises associated with elevation of the upper limbs in a seated position, (2) walked in a 30-m corridor (four laps) assisted by a physiotherapist who encouraged an increase in intensity and speed according to the patient's tolerance and (3) performed five repetitions of step exercises using a 25 cm step	6–7 days	Adult patients (> 18 years old) admitted for living donor kidney transplantation in a tertiary hospital were included in this study. Patients were excluded using the following criteria: longer than 24 h spent in mechanical ventilation and the intensive care unit, reoperation, intraoperative death, or any contraindications to performing the proposed measurements and/or treatment
Karelis et al. [14]	Canada	RCT	Ex: 10; Con: 10	Ex: 45.3 (14); Con: 39.4 (8)	Patients assigned to the E group trained for 16 weeks, 3 times a week. The 45- to 60-min in-hospital RT program started each training session with a warm-up of low-intensity walking on a treadmill for 10 min. Each exercise session was individually monitored for optimal progression. The RT program consisted of the following exercises: (1) leg press; (2) chest press; (3) lateral pull downs; (4) shoulder press; (5) arm curls; (6) triceps extensions and (7) sit-ups	16 weeks	The study recruited a total of 24 patients during the follow-up appointments at the transplant clinic of Notre Dame's hospital in Montreal. Patients were included in the study if they met the following criteria: ambulatory outpatients; women and men of at least 18 years of age (no upper age limit); cadaveric, living related or living unrelated donor KT 6 to 8 weeks before the inclusion in the study; nonsmokers, low to moderate alcohol consumers (<2 drinks per day) and sedentary (<2 h of structured exercise per week)

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Hernández Sánchez et al. [15]	Spain	RCT	Ex: 8; Con: 8	Ex: 49.7 (9.6); Con: 48.6 (10.6)	The exercise program lasted 10 weeks and included 2 sessions/week on non-consecutive weekdays. Each exercise session lasted around 60 min and included a warm-up section consisting of walking gently for 7 min, 2 sets of 10 repetitions with 30-s rest within repetitions of squats with hand support on the wall, and 2 series of 10 repetitions with 30-s rest within repetitions of squats carrying their own body weight	10 weeks	The study conducted this RCT between January 2012 and December 2013, and the recruitment ended in December 2012. Participants were eligible for inclusion in the study if they met the following criteria: (i) + 1 year since the kidney transplant; (ii) aged > 18 years; (iii) no experience in resistance training. Subjects were excluded if they presented one or more of the following conditions: (i) severe cardiovascular disease; (ii) uncontrolled hypertension; (iii) or skeletal muscle problems that hinder the performance of the tests and exercise

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Kenneth James Riess et al. [7]	Canada	RCT	Ex: 16; Con: 15	Ex: 56.9 (12.2); Con: 52.4 (14.3)	The 12-week EST program consisted of endurance training (2 days/week). Endurance training was performed on a cycle ergometer and treadmill at 60–80% $VO_{2peak}$ for 30–60 min/session. The endurance exercise intensity was increased when the subjects reported a Borg scale score of < 11 (6–20 scale) or if their HR was $\leq 60\%$ of $VO_{2peak}$ . This progression ensured that the exercise intensity was between a range of 11–13 on the Borg 6–20 scale throughout the study period. Lower extremity strength training was performed at 50% 1RM for 2 sets of 10–15 repetitions	12 weeks	Subjects recruited from the University of Alberta Renal Transplant Clinic between June 2006 and October 2008 were $\geq 18$ years of age and > 6 months post-surgery with no biopsy or clinical evidence of rejection. Exclusion criteria were uncontrolled hypertension (systolic blood pressure > 180 mm Hg and (or) diastolic blood pressure > 110 mm Hg), type 1 diabetes mellitus, or any other condition that would limit exercise testing or training
Kouidi et al. [16]	Greece	RCT	Ex: 11; Con: 12	Ex: 52.1 (5.6); Con: 52.6 (5.4)	The patients of the exercise group followed a 6-month exercise training program in a municipal gym consisting of four 60–90 min weekly sessions. Each exercise session started with a 10-min warm-up and finished with a 10-min cool-down period with breathing and relaxation exercises. Each main training routine consisted of a 30–40 min aerobic exercise program followed by 10–30 min of strengthening exercises for upper and lower extremity and abdominal muscles	6 months	Patients were included if they were aged between 18 and 60 years, were sedentary and non-smokers, had received their transplant at least a year previously and their transplant function was stable with serum creatinine level < 1.8 mg/dL and moreover, they were not using drugs that were known to modify autonomic nervous system

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Greenwood et al. [17]	United Kingdom	RCT	Ex: 26; Con: 20	Ex: 53.9 (10.7); Con: 49.5 (10.6)	Participants in the aerobic training and resistance training groups were inducted into a gym setting in a hospital. Patients attended free supervised structured exercise classes twice per week for 12 weeks	12 weeks	Participants were approached during routine transplantation clinics at King's College Hospital and Guy's and St Thomas Hospital. They were included if they were adults (aged 18 years or older), less than 12 months post-transplantation, and able to give written consent. Patients were excluded if they were pregnant, required support for ambulation for a distance, 50 m, had unstable medical conditions, had participated in structured exercise within the previous 6 months, or had a psychiatric illness
Hemmati et al. [18]	Iran	RCT	Ex: 13; Con: 10	Ex: 32.9 (9.81); Con: 37.8 (8.48)	The exercise group participated in a 12-week exercise training program consisting of three days per week in 60–90-min exercise sessions. Each training session (60–90 min) started with a 10-min warm-up period consisting of stretching exercise, jogging, and aerobic movements, followed by a 60–90-min exercise session, and finally ended with a 10-min cool-down period consisting of breathing and relaxation	12 weeks	Potential participants were eligible for the study if they met the following inclusion criteria: kidney transplantation for at least one year without experiencing graft failure and no concomitant diseases including diabetes, hypertension, and respiratory or autoimmune diseases



Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Lima et al. [19]	Brazil	RCT	Ex: 7; Con: 5	Ex: 54(3); Con: 43 (18)	The subjects performed one free-weight exercise for each muscle group in the following order: dumbbell bent row, dumbbell bench press, dumbbell overhead press, dumbbell squat, and standing knee flexion	12 weeks	Potential subjects were recruited at the Center for Prevention of Renal Diseases at the local University Hospital. The initial recruitment list consisted of 300 subjects, 150 did not meet the inclusion criteria, and 50 did not attend their respective scheduled appointment. With that, 100 subjects were invited to continue the study
Painter et al. [20]	United States of America	RCT	Ex: 54; Con: 43	Ex: 39.7(12.6); Con: 43.7(10.7)	Individualized prescriptions were developed for each subject randomized into the EX on the basis of their treadmill test results. The prescription was for independent home-based exercise and included cardiovascular exercise (primarily walking or cycling); frequency of at least four times per week; duration that worked up to at least 30 min per session; and an intensity that was initially 60–65% of maximal heart rate, which was gradually (every 2 weeks) increased to 75–80% of maximal heart rate. Patients kept exercise logs, which were returned to the study staff every 2 weeks	12 months	Patients were recruited within 2 months after kidney transplantation at the University of California at San Francisco. Recruitment took place from January 1994 through November 1995. Patients were excluded from entry into the study if they had transplant rejection or psychiatric or neurologic disorder that would preclude participation; had orthopedic limitations that precluded exercise testing or training; were unavailable for regular follow-up; had any absolute contraindications to exercise testing as established by the American Heart Association or the American College of Sports Medicine; or had any medical complications that would prevent regular participation

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Painter et al. [21]	United States of America	RCT	Ex: 51; Con: 45	–	Individualized prescriptions were developed for each subject randomly assigned to the EX group based on their treadmill test results. The prescription was for independent home-based exercise and included cardiovascular exercise (primarily walking or cycling) with a frequency of at least 4 times per week, a duration that worked up to at least 30 min/session, and intensity that was initially 60% to 65% of maximum heart rate and gradually (every 2 weeks) increased to 75% to 80% of maximum heart rate	12 months	Patients were recruited within 1 month of kidney transplantation at the University of California at San Francisco. Recruitment took place from January 1994 through November 1995
Tzvetanov et al. [22]	United States of America	RCT	Ex: 9; Con: 8	Ex: 46(6.9); Con: 45(19)	This method was named after its founder Greg Hachaj and incorporates multiple disciplines, including physical fitness, psychology, and nutrition. The multidisciplinary rehabilitation program is built around the application of a standardized process and curriculum customized to each individual patients' energy level, medical wellness, physical status/limitations, and emotional life. The rehabilitation program was conducted for 12 months	12 months	The study conducted an internal review board-approved randomized prospective study involving a 12-month supervised multidisciplinary rehabilitation program (GH method) initiated after kidney transplantation in obese recipients (body mass index > 30)

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Juskowa et al. [23]	Poland	RCT	Ex: 32; Con: 37	Ex: 43.75 (12.2); Con: 46.11 (12.3)	The participating patients trained every other day for 30 min/per session assisted by a physiotherapist. On alternate days the patients repeated the exercise program on their own	6 months	A total of 69 renal transplant recipients participated in the study: 32 women and 37 men with mean age of $45.5 \pm 9.0$ years. The patients were recruited by the study staff within 2 or 3 days after renal transplantation and the study continued for 4 or 5 weeks posttrans-plantation during hospitalization and subsequently for a period of 6 months or 1 year
Pooranfar et al. [8]	Iran	RCT	Ex: 29; Con: 15	–	Patients who received transplants 2–3 years before, had no history of consumption of alcohol and caffeine, and had no regular exercise activities were included in this study	10 weeks	The subjects in exercise group participated in the designed exercises for three 60–90-min sessions per week for 10 weeks. The sessions were divided to three stages of pre-warming, main step, and rest
O'Connor et al. [24]	United Kingdom	RCT	Ex: 22; Con: 20	Ex: 53.9 (10.7); Con: 49.5 (10.6)	Participants were randomized after baseline assessment to either 12 weeks of supervised aerobic training, resistance training, or usual care by computer randomization. Once a week, 30-min, physiotherapist-led patient education was also provided	9 months	Participants were included if they were 18 years of age or older, able to provide written consent, and if they had received a kidney transplant in the preceding 12 months. They were excluded if they were unable to walk 50 metres independently, were pregnant, had participated in a structured exercise program in the past six months, or if they had any medical condition that would preclude participation

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Senthil Kumar et al. [9]	India	RCT	Ex: 61; Con: 61	Ex: 36.24 (8.66); Con: 35.08 (8.78)	The patients got trained in three phases. The phase I training included graded ambulation, strength training with the use of gravity and own body weight. The study group was assessed for 10 repetitions maximum of the muscle quadriceps, a key muscle for ambulation. Phases II and III had exercises involving resistance training (50–80% of 10 RM), flexibility exercises and aerobic conditioning (walking/bicycle pedalling) as per rating of perceived exertion on the Borg scale in graded manner	12 weeks	This randomized controlled trial was conducted in 104 subjects after renal transplantation in January 2012 and December 2016 under the approval of the National Ethics Committee (IEC-NI/11/DEC26/83) and CTRI retrospective registration (CTRI/2017/11/010601), and the results were measured. Patients with unstable vital signs, surgical complications, acute renal rejection, and preexisting neuromuscular deficits were excluded from the study

Table 2 (continued)

Study	Country	Design	Sample size	Mean age (SD), years	Exercise intervention	Time of intervention	Inclusion population
Zhang et al. [25]	China	RCT	Ex: 53; Con: 53	Ex: 43.16 (10.76); Con: 42.06 (9.51)	The physical exercise program was divided into two stages: the post-discharge stage and the pre-discharge stage. The non-ambulatory stage included [from day 3 to passing the Timed Up and Go Test] and the ambulatory stage (from passing the TUG test to discharge). The exercise training intervention changed from the non-ambulatory stage to the ambulatory stage if the participants passed the Timed Up and Go test on postoperative day 7. If not, the participants continued the non-ambulatory exercise until they passed the Timed Up and Go test (the test was conducted every day after day 7). During the ambulatory stage, the physical exercise program included the traditional Chinese exercise Baduanjin and anti-resistance training. The post-discharge stage included doing the same exercises as in the ambulatory stage at home. All patients in the intervention group recorded a daily exercise rehabilitation video and sent the video to the nurses by smartphone. The whole exercise rehabilitation process was led by nurses and a group supervised by the rehabilitation specialist	6 months	Age > 18 years, were undergoing their first kidney transplant, could use a smartphone, had no experience in resistance training before the kidney transplant, were not participating in other research projects and agreed to participate in the study and sign the informed consent form

RCT randomized controlled trials, Ex exercise group, Con control group, KT kidney transplant, EST endurance and strength training

**Table 3** Quality assessment of individual study

Study	Allocation sequence generation	Allocation concealment	Blinding	Loss to follow-up	Calculation of sample size	Statistical analysis	Level of quality	ITT analysis
Onofre et al. [13]	A	A	B	0	Yes	ANCOVA	A	Yes
Karelis et al. [14]	A	A	B	Unmentioned	Yes	ANCOVA	B	No
Hernández Sánchez et al. [15]	A	A	B	0	Yes	ANCOVA	A	No
Riess et al. [7]	A	A	A	0	Yes	ANCOVA	A	No
Kouidi et al. [16]	A	A	A	0	Yes	ANCOVA	A	No
Greenwood et al. [17]	A	A	A	0	Yes	ANCOVA	A	No
Hemmati et al. [18]	A	A	B	Unmentioned	Yes	Independent T-test	B	No
Lima et al. [19]	A	A	B	0	Yes	ANCOVA	A	No
Painter et al. [20]	A	A	B	30	Yes	ANCOVA	B	No
Painter et al. [21]	A	A	B	0	Yes	ANCOVA	A	No
Tzvetanov et al. [22]	A	A	B	0	Yes	2-tailed Student T-test	A	No
Juskowa et al. [23]	A	A	B	Unmentioned	Yes	ANCOVA	B	No
Pooranfar et al. [8]	A	A	B	0	Yes	Student's T test	A	No
O'Connor et al. [24]	A	A	A	0	Yes	ANCOVA	A	No
Senthil Kumar et al. [9]	A	A	B	Unmentioned	Yes	ANCOVA	B	No
Zhang et al. [25]	A	A	B	2	Yes	ANCOVA	A	No

A all quality criteria met (adequate): low risk of bias, B most quality criteria met (adequate): moderate risk of bias, ITT intention-to-treat, ANCOVA analysis of covariance

0%, and the  $\text{Chi}^2$  value was 0.62 ( $p=0.003$ ). Significant improvements in urea were found in the exercise intervention group.

**Estimated glomerular filtration rate (eGFR)** Three RCTs were included in our study. A random-effects model showed that there was no difference between the exercise intervention group and the control group in eGFR (MD: 16.16, 95% CI  $-3.98$  to  $36.29$ ,  $\text{Chi}^2=9.33$ ,  $p=0.12$ , Fig. 2C).

### Cardiorespiratory function

**Systolic blood pressure** Because of  $p<0.05$ , we employed a random-effects model to compare the systolic blood pressure between the exercise intervention group and control group from six RCTs (Supplementary Fig. 3A). The pooled estimate of MD was  $-1.53$ , 95% CI was  $-4.70$  to  $1.64$ ,  $I^2$  was 0%, and  $\text{Chi}^2$  was 3.34 ( $p=0.34$ ). The results showed that the exercise intervention and control groups were similar regarding systolic blood pressure.

**Diastolic blood pressure** Six RCTs involving 258 patients analyzed the differences between the two groups after the intervention in terms of diastolic blood pressure (Supplementary Fig. 3B). Due to  $p>0.05$ , a fixed-effects model

was utilized for analyzing data. The results showed no statistical difference in diastolic blood pressure between the two groups after the intervention treatment (MD:  $-0.03$ , 95% CI  $-2.25$  to  $2.19$ ,  $\text{Chi}^2=4.52$ ,  $p=0.98$ ).

**Heart rate** Because of  $p<0.05$ , we compared the heart rate between the exercise intervention and control groups from four RCTs by a random-effects model (Supplementary Fig. 3C). The pooled estimate of MD was  $-2.32$ , 95% CI was  $-9.26$  to  $4.62$ ,  $I^2$  was 79%, and  $\text{Chi}^2$  was 14.12 ( $p=0.51$ ). The results showed that the exercise intervention and control groups were similar in heart rate.

**Peak oxygen uptake ( $\text{VO}_{2\text{peak}}$ )** Six RCTs involving 251 patients (136 patients in the exercise intervention group, and 115 patients in the control group) reported the changes between the two patients after the intervention regarding  $\text{VO}_{2\text{peak}}$  (Supplementary Fig. 3D). Since  $p>0.05$ , a fixed-effects model was used to analyze group differences. The model revealed that the MD was 3.20, the 95% CI was 1.97–4.43, the  $I^2$  was 6%, and the  $\text{Chi}^2$  value was 5.34 ( $p<0.00001$ ). We concluded that the exercise intervention group recorded a statistically significant improvement regarding the  $\text{VO}_{2\text{peak}}$ .

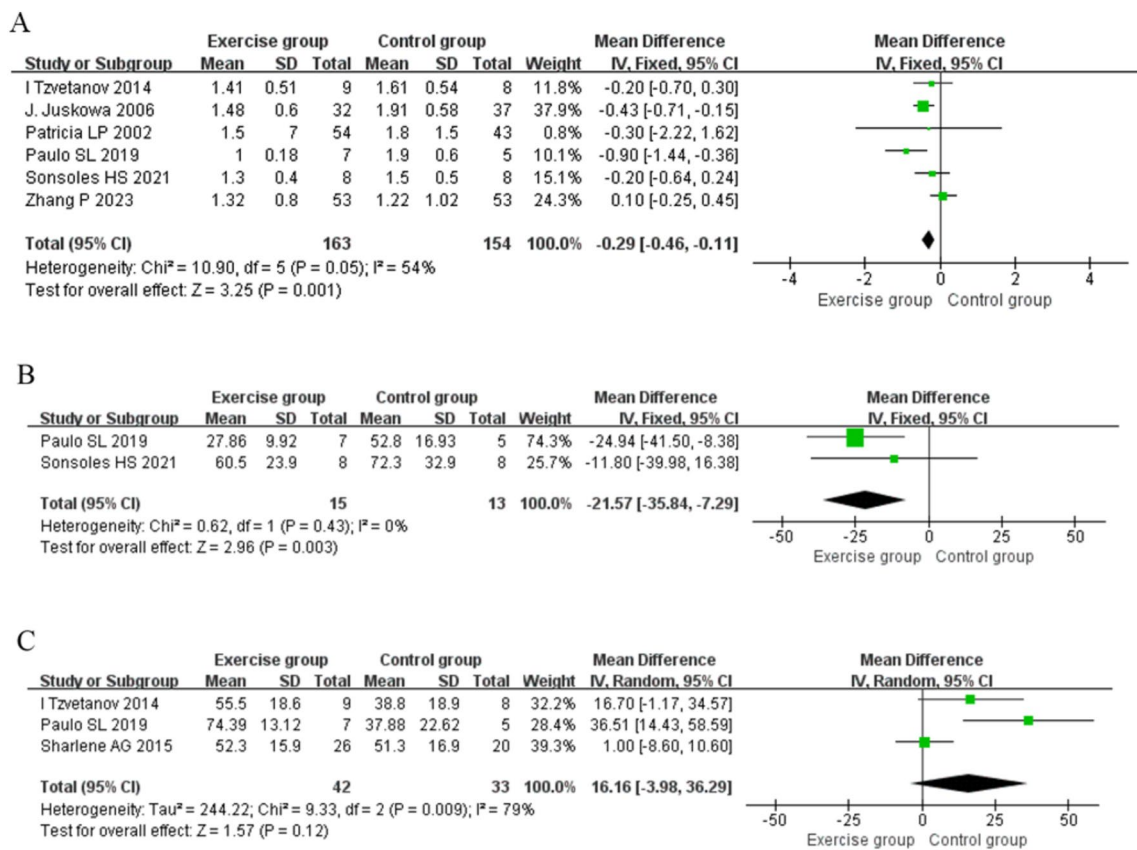


Fig. 2 Forest plots showing changes in **A** creatinine; **B** urea; **C** estimated glomerular filtration rate (eGFR)

**Blood parameters**

**Total cholesterol** Five RCTs analyzed the changes in total cholesterol of 335 patients after the intervention (Supplementary Fig. 4A). A fixed-effects model was utilized to evaluate differences between the two groups, which showed an MD of  $-0.06$  (95% CI  $-0.33$  to  $0.21$ ,  $p = 0.65$ ). These results reflect no significant effect on kidney transplant recipients of total cholesterol with exercise intervention.

**High-density lipoprotein-cholesterol (HDL-C)** Four RCTs reported differences in HDL-C of 229 patients after the intervention (Supplementary Fig. 4B). A fixed-effects model was used to conduct the analysis, due to  $p > 0.05$ . The model revealed that the MD was  $0.21$ , the 95% CI was  $0.04$ – $0.37$ , the  $I^2$  was  $0\%$ , and the  $\text{Chi}^2$  value was  $0.62$  ( $p = 0.01$ ), confirming greater improvements in HDL-C in the exercise intervention group.

**Hemoglobin** Because of  $p > 0.05$ , we analyzed the hemoglobin between the exercise intervention and control groups from three RCTs using a fixed-effects model (Supplementary Fig. 4C). The pooled estimate of MD was  $0.23$ , 95% CI was  $-0.10$  to  $0.56$ ,  $I^2$  was  $0\%$ , and  $\text{Chi}^2$  was  $0.88$  ( $p = 0.18$ ).

The exercise intervention group had a similar hemoglobin compared to the control group.

**Serum cytokine levels**

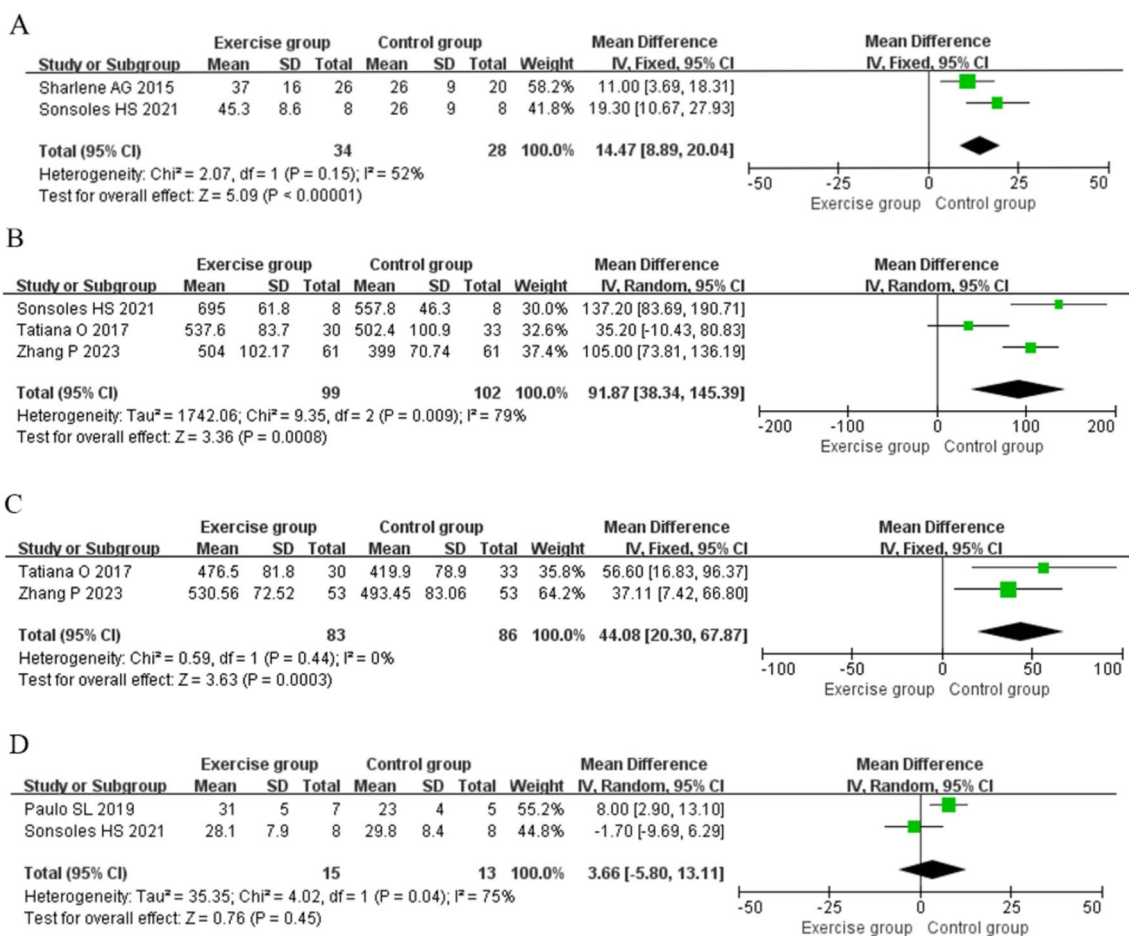
**Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )** Two RCTs were included in our study. A random-effects model suggested that there was no difference between the exercise intervention group and the control group in TNF- $\alpha$  (MD:  $-1.44$ , 95% CI  $-4.39$  to  $1.51$ ,  $\text{Chi}^2 = 8.17$ ,  $p = 0.34$ , Supplementary Fig. 5A).

**Interleukin-6 (IL-6)** Two RCTs analyzed levels of IL-6 (Supplementary Fig. 5B). Pooled results from a fixed-effects model suggested that the exercise intervention group did not differ significantly from that of the control group regarding levels of IL-6 (MD =  $-0.70$ , 95% CI  $-1.56$  to  $0.17$ ,  $p = 0.11$ ).

**Physical performance**

**60-s sit-to-stand test (60-STST)** Two RCTs recorded the differences in 60-STST of 62 patients after the intervention (Fig. 3A). We employed a fixed-effects model to compare differences between groups, due to  $p > 0.05$ . The model





**Fig. 3** Forest plots showing changes in **A** 60-s sit-to-stand test (60-STs); **B** 6-min walk distance (6-MWD); **C** 6-min walk test (6-MWT); **D** handgrip strength

revealed that the MD was 14.47, the 95% CI was 8.89–20.04, the  $I^2$  was 52%, and the  $\text{Chi}^2$  value was 2.07 ( $p < 0.00001$ ). The exercise-trained patients had obvious improvement in the 60-STs.

**6-Minute walk distance (6-MWD)** Three RCTs analyzed the changes in 6-MWD of 201 patients after the intervention (Fig. 3B). A random-effects model was utilized to evaluate differences between the two groups, which showed an MD of 91.87 (95% CI 38.34–145.39,  $p = 0.0008$ ). The results suggested a statistically significant improvement in the exercise intervention group regarding the 6-MWD.

**6-Minute walk test (6-MWT)** Two RCTs analyzed the changes in 6-MWT of 169 patients after the intervention (Fig. 3C). A fixed-effects model was utilized to evaluate differences between the two groups, which showed an MD of 44.08 (95% CI 20.30–67.87,  $p = 0.0003$ ). The results suggested that the exercise intervention group was significantly superior to the control group in 6-MWT.

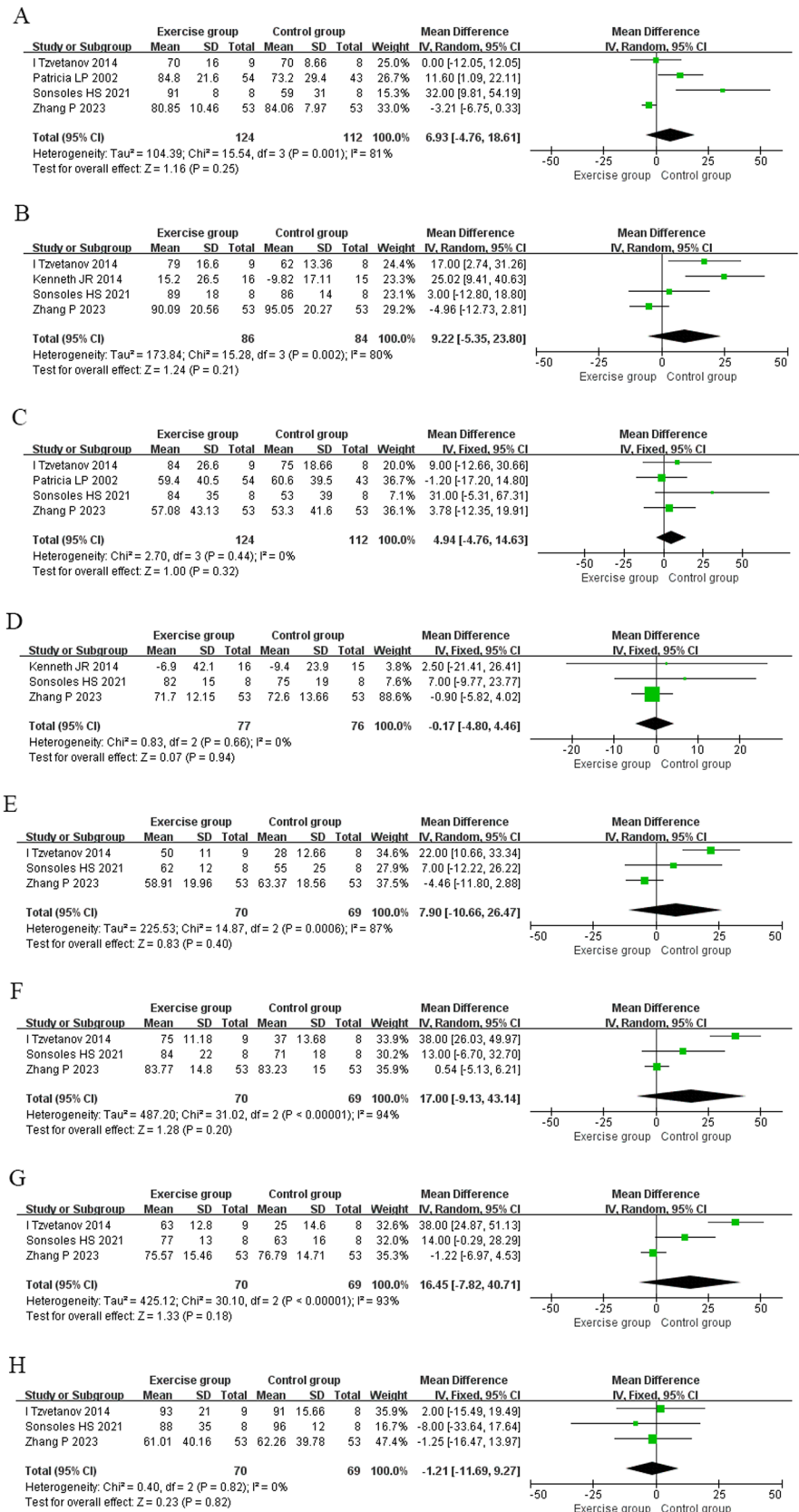
**Handgrip strength** Because of  $p < 0.05$ , we used a random-effects model to analyze the handgrip strength between the exercise intervention and control groups from two RCTs (Fig. 3D). The pooled estimate of MD was 3.66, 95% CI was –5.80 to 13.11,  $I^2$  was 75%, and  $\text{Chi}^2$  was 4.02 ( $p = 0.45$ ). These results reflect no statistical difference in handgrip strength between the two groups after the intervention treatment.

#### Quality of life short form-36 questionnaire (SF-36)

**Physical function score** Four RCTs reported the changes between the two patients after the intervention regarding physical function score (Fig. 4A). Since  $p < 0.05$ , a random-effects model was employed to analyze group differences. The model revealed that the MD was 6.93, the 95% CI was –4.76 to 18.61, the  $I^2$  was 81%, and the  $\text{Chi}^2$  value was 15.54 ( $p = 0.25$ ). The results suggested that the exercise intervention and control groups were similar in physical function scores.



**Fig. 4** Forest plots showing changes in **A** physical function score; **B** social function score; **C** role-physical score; **D** mental composite score; **E** general health score; **F** body pain score; **G** vitality score; **H** role-emotional score



**Social function score** Four RCTs analyzed the changes in social function scores of 170 patients after the intervention (Fig. 4B). We performed a random-effects model to analyze differences between groups. The model revealed that the MD was 9.22, the 95% CI was  $-5.35$  to  $23.80$ , the  $I^2$  was 80%, and the  $\text{Chi}^2$  value was 15.28 ( $p=0.21$ ). There was no significant difference between the two groups about the social function score.

**Role-physical score** Four RCTs analyzed differences in role-physical scores (Fig. 4C). Pooled results from a fixed-effects model suggested that the exercise intervention group had no significant effect on the role-physical score (MD = 4.94, 95% CI  $-4.76$  to  $14.63$ ,  $p=0.32$ ).

**Mental composite score** Our study included three RCTs (Fig. 4D). A fixed-effects model suggested that the MD was  $-0.17$ , the 95% CI was  $-4.80$  to  $4.46$ , the  $I^2$  was 0%, and the  $\text{Chi}^2$  value was 0.83 ( $p=0.94$ ), thus indicating that there was no significant difference between the two groups about the mental composite score.

**General health score** Three RCTs analyzed the changes in the general health score of 139 patients after the intervention (Fig. 4E). We performed a random-effects model to analyze differences between groups. The model revealed that the MD was 7.90, the 95% CI was  $-10.66$  to  $26.47$ , the  $I^2$  was 87%, and the  $\text{Chi}^2$  value was 14.87 ( $p=0.40$ ). There was no significant difference between the two groups about the general health score.

**Body pain score** Three RCTs analyzed differences in body pain scores (Fig. 4F). Pooled results from a random-effects model suggested that the exercise intervention group had no significant effect on the body pain score (MD = 17.00, 95% CI  $-9.13$  to  $43.14$ ,  $p=0.20$ ).

**Vitality score** Our study included three RCTs (Fig. 4G). A random-effects model suggested that the MD was 16.45, the 95% CI was  $-7.82$  to  $40.71$ , the  $I^2$  was 93%, and the  $\text{Chi}^2$  value was 30.10 ( $p=0.18$ ), thus indicating that there was no significant difference between the two groups about the vitality score.

**Role-emotional score** Because of  $p>0.05$ , we analyzed the role-emotional score between the exercise intervention and control groups from three RCTs using a fixed-effects model (Fig. 4H). The pooled estimate of MD was  $-1.21$ , 95% CI was  $-11.69$  to  $9.27$ ,  $I^2$  was 0%, and  $\text{Chi}^2$  was 0.40 ( $p=0.82$ ). The exercise intervention group had a similar role-emotional score compared to the control group.

## Discussion

Many patients with ESRD eventually ultimately require kidney transplantation to stay alive. Although advances have been made in surgical procedures, many difficult clinical issues remain in the management of patients during post-transplant. The incidence of postoperative cardiovascular disease (CVDS) is 4–6 times higher in kidney transplant recipients than in the general population [26, 27]. It is currently the leading cause of death in kidney transplant recipients [28]. Relevant studies have reported that kidney transplant recipients are also at increased risk of dyslipidemia, possibly related to using immunosuppressive drugs such as cyclosporine, glucocorticoids, and sirolimus [29]. In addition, patients after kidney transplantation often present with significant motor dysfunction [30]. Therefore, post-transplant management is important for patient recovery, and adjuvant treatment strategies may have important prognostic potential.

Exercise intervention therapy is a rehabilitation method that focuses on functional exercise. Over recent years, exercise training has generated interest as an adjunctive treatment strategy for surgical procedures. Many studies pointed out that perioperative exercise intervention in patients with gastrointestinal tumors can reduce the risk of complications [31] and shorten postoperative hospital stays [32]. Cavalheri et al. [33] suggested training can improve exercise capacity and quadriceps strength in patients after lung cancer surgery. Besides, many studies also analyzed the effects of exercise intervention programs on patients after solid organ transplantation. Raphael et al. [34] found that exercise intervention can significantly improve heart transplantation patients' peak heart rate and aerobic capacity. Langer et al. [35] concluded that exercise training improves functional recovery in postoperative uncomplicated lung transplant patients and that postoperative exercise intervention programs should be strongly encouraged in elderly lung transplant recipients. Stefan [36] demonstrated that exercise training is safe for liver transplant recipients, improves physical functional aspects, and may benefit cardiopulmonary and muscle health. Emily et al. [37] proved that an exercise training intervention can improve exercise capacity and quality of life in patients after lung transplantation.

$\text{VO}_{2\text{peak}}$  is an important measure to evaluate cardiorespiratory fitness [17]. It is commonly used to analyze various patients' aerobic work capacity [38, 39] and physical exercise effects [40]. In addition, some research confirmed excellent test–retest reliability for  $\text{VO}_{2\text{peak}}$  [41, 42]. Our study considered  $\text{VO}_{2\text{peak}}$  as an index to evaluate cardiopulmonary function in patients after kidney transplantation.

The SF-36 is a commonly used tool to evaluate subjective health-related quality of life [43]. It is now widely available for evaluating the quality of life in various diseases. The SF-36 comprises eight items, each reflecting different health aspects: physical function, role-physical, body pain, general health, vitality, social function, role-emotional, and mental health. In the present study, we used the SF-36 scores to analyze the patients' quality of life.

Our study included 16 RCTs containing 827 patients. We analyzed the effects of exercise intervention in kidney transplant recipients from eight dimensions, including anthropometric characteristics, body composition, renal function, cardiorespiratory function, blood parameters, serum cytokine levels, physical performance, and SF-36 scores. Analysis of the results revealed that exercise intervention had some positive effects on improving renal function. Specifically, patients in the exercise intervention group showed significantly improved creatinine and urea than the control group. In terms of cardiorespiratory function, patients following the exercise intervention program had significant superiority in improving  $VO_{2\text{ peak}}$ . Moreover, exercise intervention induced improvements in HDL-C, 60-STS, 6-MWD, and 6-MWT. And no difference was found between groups in terms of anthropometric characteristics, body composition, serum cytokine levels, and SF-36 scores. These findings laid a theoretical foundation for introducing exercise intervention in kidney transplant recipients.

In contrast to previously published studies [44, 45], we found that exercise intervention had shown advantages in improving renal function and dyslipidemia in kidney transplant recipients. These findings may be more clinically relevant. Additionally, this study analyzed the efficacy of exercise intervention in patients with kidney transplants from multiple dimensions and involved more evaluation indicators, offering more comprehensive results. Finally, our study, with more RCTs and a larger sample size, included, may provide more reliable results.

There are some shortcomings in the present study. First, the intervention duration and exercise programs of each RCT included were not unified, which may also result in bias of results. Second, given that many studies in recent years have reported on the effects of exercise intervention on renal transplant recipients, our study was limited by its lack of novelty. Therefore, we will continue the research topic and focus on the latest RCTs to address this.

## Conclusions

Our meta-analysis concluded that appropriate exercise intervention can improve renal function, cardiopulmonary function, dyslipidemia, physical performance, and quality of life in renal transplant recipients. The patients should be

encouraged to participate in an exercise training intervention after kidney transplantation. These findings will assist clinicians in developing and applying exercise rehabilitation programs specifically designed for kidney transplant recipients as part of standard medical care. In addition, our study will help bridge the gap in knowledge about the importance of exercise intervention programs in kidney transplant patients.

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**Author contributions** HXP and LP designed the research, interpreted the data and revised the paper. ZDX, YLQ, XBW and ZX performed the data extraction and carried out the meta-analysis. ZDX and YLQ drafted the paper. All of the authors approved the submitted and final versions.

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**Data availability** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Conflict of interest** The authors declare that they have no competing interests.

**Research involving human participants and/or animals** Not applicable.

**Informed consent** Not applicable.

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