

## ORIGINAL ARTICLE

# The effects of a physical exercise program in Chinese kidney transplant recipients: a prospective randomised controlled trial

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## ABSTRACT

**Background.** Kidney transplant has become the preferred therapy for end-stage renal disease. However, kidney transplant recipients (KTRs) still face several challenges, such as physical inactivity. The purpose of this study was to explore the effects of a nurse-led physical exercise program in Chinese KTRs.

**Methods.** A total of 106 participants were enrolled from the Third Xiangya Hospital of Central South University between July 2021 and June 2022 and randomly assigned to the control or intervention groups. Participants in the control group were provided with routine nursing care and participants in the intervention group received a nurse-led rigorous physical exercise program that was divided into two stages: the pre-discharge stage and the post-discharge stage. The pre-discharge stage included the non-ambulatory and ambulatory stages. The Chinese traditional exercise Baduanjin was incorporated into the physical exercise during the ambulatory stage. The post-discharge stage continued the same exercise as the ambulatory stage at home. After 3 months of intervention, both groups received the same follow-up for 3 months. The primary and secondary outcomes of all participants were collected. The data were analysed with repeated measures analysis of variance to examine the effectiveness of the intervention.

**Results.** Compared with the control group, the intervention group had less fatigue and more motivation to be active in primary outcomes. Moreover, patients in the intervention group had a higher phase angle, a longer 6-minute walk distance, more 30-second chair stand times and decreased anxiety and depression levels in secondary outcomes. No adverse events were observed during the intervention. There were no significant differences in all dimensions of the quality-of-life questionnaire between the intervention and the control group.

**Conclusion.** Chinese KTRs could benefit from the nurse-led physical exercise program post-operatively.

**Trial registration.** ChiCTR2100048755

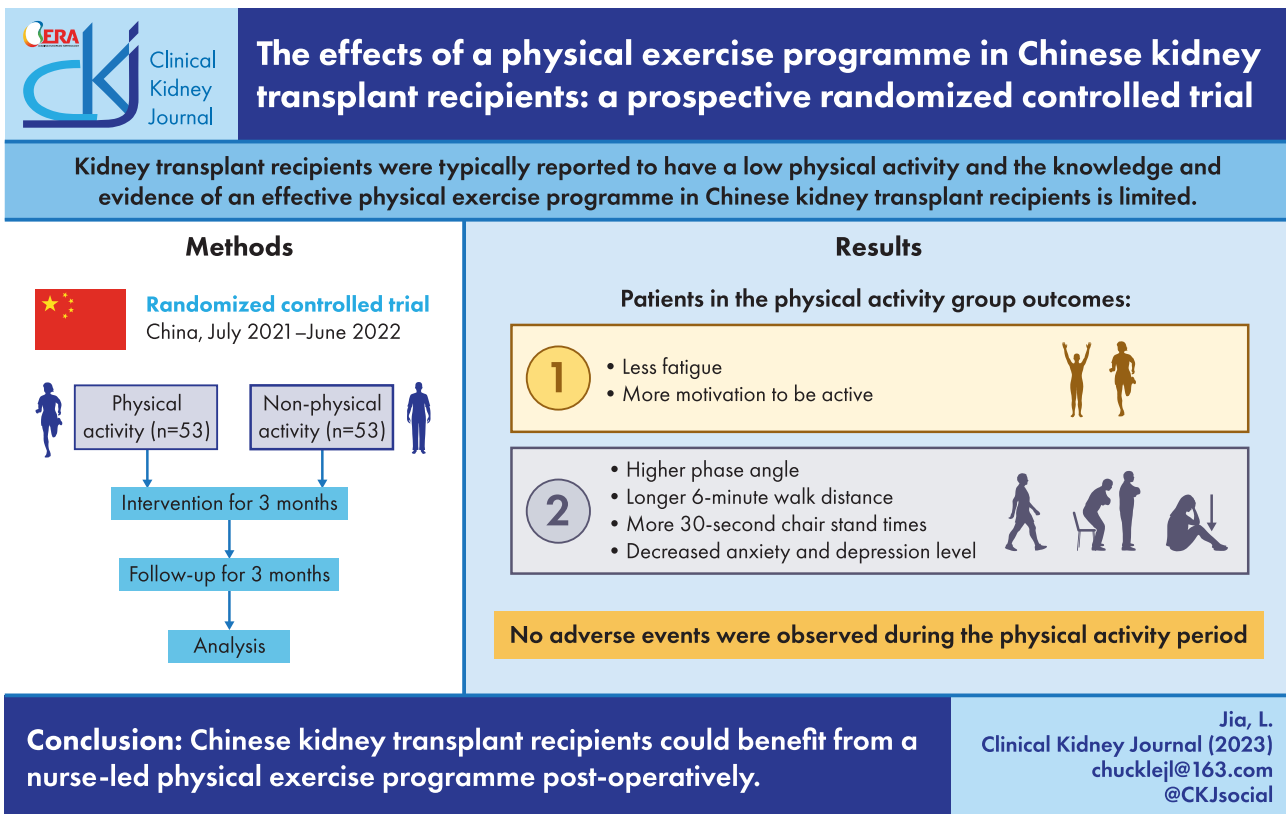
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## LAY SUMMARY

Kidney transplant has become the preferred therapy for end-stage renal disease. However, in real life, patients undergoing kidney transplantation were typically reported to have less physical activity and more barriers to exercise, including low energy and fatigue. The knowledge and evidence of effective physical exercise programs in Chinese kidney transplant recipients (KTRs) are limited. Our study initiated the first and largest sample study to explore the effect of a physical exercise program in Chinese KTRs. Our results indicated that Chinese KTRs could benefit from the physical exercise program, showing less fatigue, more motivation to be active, a higher phase angle, a longer 6-minute walk distance, more 30-second chair stand times and decreased anxiety and depression levels in the intervention group. More importantly, no adverse events were observed during the intervention period in KTRs.

## GRAPHICAL ABSTRACT



**Keywords:** fatigue, kidney transplant, physical exercise program, randomized controlled trial, sport motivation

## INTRODUCTION

Kidney transplant has become the preferred therapy for end-stage renal disease. A series of advancements, including refined surgical techniques, improved immunosuppressive protocols and optimised perioperative management of transplant patients, have been used to improve recipient and graft survival rates and quality of life [1–4]. The guideline for the care of kidney transplant recipients (KTRs) recommends adopting a healthy lifestyle with regular physical activity [5]. However, in reality, this is not the case for patients undergoing kidney transplant, who typically report having less physical activity [6] and more barriers to exercise, including low energy and fatigue [7].

Physical inactivity is strongly associated with an increased risk of cardiovascular and all-cause mortality in KTRs [8]. KTRs receive multiple immunosuppressive medications, including antimetabolite agents, which can cause the development of metabolic syndrome [9]. KTRs have a higher risk of muscle loss and osteoporosis because of corticosteroid use [10]. In addition, transplant recipients exhibit various psychological disorders, including depression and anxiety, because of long periods of physical and psychosocial stress from pre-transplant to post-transplant [11, 12]. Physical activity provides numerous physiological and psychosocial benefits [13–15]. Fatigue is a frequent and underestimated symptom of KTRs and leads to significant functional impairment, poor adherence to immunosuppressive therapy and a serious deterioration in quality of life [16, 17].

Physical inactivity is associated with fatigue in KTRs [18]. Therefore, physical exercise for KTRs may be particularly important.

Physical exercise helps with the rehabilitation of KTRs [6, 19]. Several studies have indicated that resistance training could increase exercise capacity, muscular strength, cardiorespiratory fitness and health-related quality of life [20–23]. A recent study indicated that moderate exercise, including aerobic and resistance training, could inhibit inflammatory cytokines and have beneficial effects on the immune system [24], which are closely associated with outcomes in kidney transplant [25, 26]. Barroso et al. [27] reported that KTRs with exercise training had better sleep quality and lower anxiety and depression levels than those without exercise training. Furthermore, a recent systematic review summarised that the adult KTRs benefited from a structured physical exercise program, showing improved aerobic capacity and better muscle performance [28]. No study has explored the impact of physical exercise in Chinese KTRs. In addition, in most studies the intervention primarily focussed on the post-discharge timeframe, so there is a scarcity of evidence regarding physical exercise in the pre-discharge stage after a kidney transplant.

In particular, the Chinese traditional exercise Baduanjin, which originated from the North Song dynasty and has a history of 800 years in China, was part of our exercise program. Baduanjin, which is similar to Tai Chi, has been documented to have positive effects on cognitive and physical functions in a wide range of populations [29]. In reviewing the literature, no study has explored the relationship between Baduanjin and physical performance in KTRs.

The present randomised controlled trial (RCT) attempted to investigate the feasibility and effectiveness of a nurse-led physical exercise program in Chinese KTRs in both the pre-discharge and post-discharge stage.

## MATERIALS AND METHODS

### Study design and ethics approval

This RCT was conducted between July 2021 and June 2022 and has been registered with the Chinese Clinical Trial Registry Centre (ChiCTR2100048755). This study was conducted in a single centre and approved by the Ethics Committee of the Third Xiangya Hospital Central South University (R21033). Written informed consent was obtained from all the study participants. This report follows the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomised studies [30].

### Participants

Participants were recruited from the Third Xiangya Hospital of Central South University and were eligible for inclusion in the study if they met the following criteria: 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. Participants were excluded if they presented one or more of the following conditions: cognitive or mental disabilities, immediately transferred to another medical facility after discharge, had skeletal muscle problems that hindered their performance of the tests and exercises, had severe rejection shown on biopsy and had haemodynamic instability after kidney transplant (defined as systolic blood pressure <90 mmHg or

>140 mmHg without using vasoactive drugs intravenously, such as dopamine, aramine or sodium nitroprusside).

### Randomisation

All participants were informed about the outline of the study and signed the informed consent. After completion of a baseline evaluation (before the kidney transplant surgery), we divided the participants into intervention and control groups using a computer-generated random number. Each randomised number was placed in a sealed opaque envelope that was given to the participants by an independent research assistant. After randomisation, participants were not blinded to the allocation owing to the pragmatic nature of the trial. Nevertheless, the research assistant was unaware of the specific grouping of the participants when collecting data after 3 months of intervention and 3 months of follow-up. During the study, the research assistant could stop the test immediately if adverse events were observed.

### Sample size

With consideration of the study intentions and the importance of fatigue outcomes, sample size was calculated from a similar study using exercise intervention in cancer patients, which indicated that exercise significantly reduced cancer-related fatigue by a mean effect size of 0.32 and 0.38 during and following cancer treatment, respectively [31]. Given  $\alpha = 0.05$ , power = 0.9 and effect size = 0.35, the required sample size was 43 in each group according to the calculation results of G\*Power statistical software (<https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower>) [32]. Allowing for a possible dropout rate of 20%, a total of 53 participants were recruited for each group.

### Intervention

Participants in the control group were provided with routine nursing care and management, including oral health education at the admission and hospitalisation phase, and a written discharge summary (including the diagnosis, treatment record, medications, diet and exercise suggestions etc). The exercise suggestions included routine daily activities after discharge, such as moderate walking and climbing, but did not refer to the items of the physical exercise program in our study.

Participants in the intervention group underwent a physical exercise program, except for routine nursing care and management. The physical exercise program was developed by the research team based on a literature review and related guidelines and revised by five experts (two kidney transplant specialists, two kidney transplant nursing specialists and one exercise rehabilitation specialist). The intervention group received a nurse-led standard physical exercise program for 3 months and then a follow-up for 3 months before data collection (a total of 6 months), which is shown in Table 1 and Fig. 1. The physical exercise training of the intervention group started on post-operative day 3 after a safety assessment by the two kidney transplant specialists and one rehabilitation specialist. The physical exercise program was divided into two stages: the pre-discharge stage and the post-discharge stage. The pre-discharge stage included the non-ambulatory stage [from day 3 to passing the Timed Up and Go (TUG) Test] and the ambulatory stage (from passing the TUG test to discharge). The exercise

Table 1: The non-ambulatory and ambulatory model of a standardised rehabilitation exercise program after kidney transplant (before passing the TUG test).

Time after kidney transplant	Exercise training				
	Exercise time	Items	Position	Times of repetition	Training time
The non-ambulatory model of a standardised rehabilitation exercise programme (before passing the TUG test)					
Day3	Twice a day (morning and afternoon)	Upper limb: dumbbell training Lower limb (non-operative side): straight leg raising training Lower limb (non-operative side): resistance hip flexion and knee extension training	Semi-reclining position Horizontal position Horizontal position	10 times x 2 6-8 times x 2 10 times x 2	2 min 3 min 5 min
Day4		Upper limb: dumbbell training Stand and move by the bed with help	Sitting position Standing position	10 times x 2 10 times x 2	2 min 15~20 min
Day5		Upper limb: dumbbell training	Sitting/Standing position	10 times x 2	2 min
Day6		Stand and move by the bed without help Upper limb: dumbbell training	Standing position Sitting/Standing position	10 times x 2 10 times x 2	15~20 min 2 min
Day7		Short walks with help Upper limb: dumbbell training	/ Sitting/Standing position	/ 10 times x 2	15~20 min 2 min
		Short walks without help The TUG test on Day 5: <10 seconds, starting with ambulatory model of a standardised rehabilitation exercise program; <20 seconds, try to transition to ambulatory model of a standardised rehabilitation exercise program; >20 seconds, repeating to non-ambulatory model of a standardised rehabilitation exercise program	/ /	/ /	15~20 min
Rehabilitation exercise					
Training steps					
Warm up		Exercise		Stretch	
Items	Motion	Time	Motion	Motion	Time
The ambulatory model of a standardised rehabilitation exercise programme (after passing the TUG test)					
Exercise training	Aerobic exercise	Warm up the upper and lower limbs	5 min	Baduanjin exercise (shown in video)	15 min
	Anti-resistance exercise	Rotating arms and shoulders	1 min	Lift the dumbbells up; stretch belt forward and side flat; leg resistance training	15 min
				Stretch the upper and lower limbs	5 min
				Biceps and triceps stretch	2 min
					Twice a day (morning and afternoon) Twice a day (morning and afternoon)
Resistance training should start with light weights, focus on good physical condition and complete each motion through a full range of movements. The exercise prescription progress should be first increase the number of repetitions, then increase the number of sets from 1 to 2 and finally increase the resistance levels of dumbbells or elastic bands. Meanwhile, we encourage patients to do 3-4 sets of 8-12 repetitions per motion.					

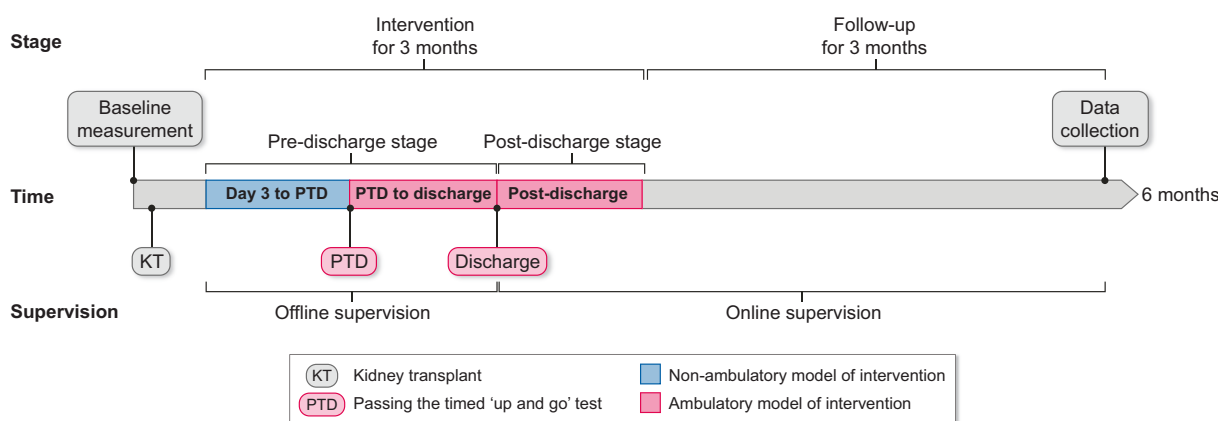


Figure 1: The schema of the physical exercise program.

training intervention changed from the non-ambulatory stage to the ambulatory stage if the participants passed the TUG test on postoperative day 7. If not, the participants continued the non-ambulatory exercise until they passed the TUG 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. The nurses would answer questions and provide recommendations to patients when needed. A participant was considered a dropout if he/she missed the physical exercise program three times in a row during the intervention. The period of intervention was 3 months. The video of the whole physical exercise program including Baduanjin was also uploaded to YouTube (<https://www.youtube.com/watch?v=ffVjhDLdD3o>).

During follow-up, all participants in the control and intervention groups received the same general health consultations and outpatient follow-up reminders by telephone. The period of follow-up in the two groups was 3 months.

### Feasibility assessment

The feasibility of the physical exercise program was assessed by the adherence of participants ( $\geq 90\%$ ) and no exercise-related adverse events, such as non-healing wounds ( $\geq 14$  days after surgery), wound dehiscence and bleeding, muscle strain and so on.

### Outcome variables and measures

After 3 months of intervention and 3 months of follow-up, the primary and secondary outcomes of all participants were recorded. Primary outcomes included fatigue and sport motivation. Secondary outcomes included heart rate, body mass index, blood glucose level, creatinine level, triglyceride level, body composition measurements (phase angle, body hydration status, fat free mass and body fat percentage), 6-minute walk test

(6-MWT), 30-second chair stand test (30s-CST), anxiety, depression and quality of life.

### Primary outcomes

#### Fatigue

Fatigue was assessed with the 20-item multidimensional fatigue inventory (MFI-20) scale, which was established by Smets *et al.* [33] and has been validated in Chinese research [34]. The MFI-20 consists of five dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. For each scale, two items were oriented in the direction of fatigue, while the other two items were oriented in the opposite direction. All items were scored on a 5-point Likert-type scale ranging from 1 to 5, with higher scores representing higher levels of fatigue. The MFI-20 questionnaire has well-established reliability and validity among Chinese patients; the Cronbach's  $\alpha$  coefficient was 0.8 [35].

#### Sport motivation

Sport motivation was assessed with the Sport Motivation Scale (SMS). The SMS contains 28 items that refer to seven dimensions of motivation according to the self-determination theory, including intrinsic motivation (motivation to know, motivation to accomplish, motivation to experience stimulation), extrinsic motivation (identification, introjection, external regulation) and amotivation. The task of the respondent was to determine to what extent a given statement referred to him/her on a 7-point scale [36]. Higher scores indicate more intrinsic motivation, extrinsic motivation or amotivation. The SMS questionnaire has well-established reliability and validity among Chinese patients; the Cronbach's  $\alpha$  coefficient was 0.78–0.85 [37].

### Secondary outcomes

#### Clinical characteristics

The clinical characteristics of these participants, including heart rate, body mass index, blood glucose level, creatinine level and triglyceride level, were collected from the medical data system of

the Third Xiangya Hospital, which recorded all patients' follow-up information.

### Body composition measurements

Body composition measurements were detected by InBody S10 (Seoul, Korea). At baseline and 3 months, participants were asked to stand on the device without shoes and hold the device handle with both hands for 1 minute. From the detection report, we obtained phase angle, body hydration status, fat free mass and body fat percentage. The phase angle, a bioimpedance analysis parameter that is calculated from the raw data of resistance and reactance at a frequency of 50 kHz [38] has been described as a global health indicator given its predictive capacity for health problems [39].

### 6-MWT

The 6-MWT was performed in a tiled 20-m hallway with two marked end lines. Participants were asked to walk as fast as possible for 6 minutes and cover the farthest possible distance between the two end lines [40]. Participants were not allowed to run, but were allowed to rest during the test. Distance was recorded in metres.

### 30s-CST

The 30s-CST was performed according to the protocol described in Goda *et al.* [41]. Participants sat in the middle of a chair with their back straightened (height: 42 cm, without leaning against the chair) and their hands crossed in front of their chests. At the researcher's request, the person stands and sits repeatedly for 30 seconds and the number of sit-stand-sit cycles completed within 30 seconds is recorded.

### Anxiety and depression scales

Anxiety and depression were assessed with the Self-Rating Anxiety Scale (SAS) [42] and Self-Rating Depression Scale (SDS) [43], respectively. The Chinese versions of the SAS and SDS were used to evaluate anxiety and depression [44]. Both the SAS and SDS scales are self-reported instruments composed of 20 items and all items were scored on a 4-point Likert-type scale that quantified the relevant levels of anxiety and depression. Higher scores indicated more severe anxiety or depression. The SAS and SDS are well-established with reliability and validity among Chinese patients; the Cronbach's  $\alpha$  coefficients were 0.882 and 0.896, respectively [45].

### Quality of life

The quality of life was assessed with the 36-item Short Form Health Survey (SF-36), which has been validated in the Chinese population [46]. The SF-36 questionnaire included eight domains: general health (5 items), social functioning (2 items), role-emotional (3 items), role-physical (4 items), bodily pain (2 items), physical functioning (10 items), vitality (4 items) and mental health (5 items). Each question was scored on a scale of 0–100. Higher scores indicate a better quality of life. The SF-36 questionnaire has well-established reliability and validity among Chinese patients; the Cronbach's  $\alpha$  coefficient was 0.821 [47].

### Statistical analysis

SPSS Statistics for Windows version 22.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Mean and standard deviation (SD) were used to describe continuous variables, and number and constituent ratios were used to describe categorical variables. The Kolmogorov–Smirnov test was used to check the normal distribution of the continuous variables. Unpaired Student's *t*-tests (for continuous variables) and chi-squared tests (for categorical variables) were used to assess differences between groups in demographic and clinical characteristics at baseline. Two-way repeated measure analysis of variance (ANOVA) was used to explore how primary and secondary outcomes changed over time and between groups, as well as the interaction of times and groups. *P*-values < .05 were considered statistically significant.

## RESULTS

### Patient characteristics at baseline

The flowchart of the study is shown in Fig. 2. In total, 124 participants were enrolled in the study; 16 patients were excluded before allocation because they did not meet the criteria for inclusion and 2 patients dropped out because they were too busy or were lost to follow-up during the post-discharge stage (1 in the intervention group and 1 in the control group). Finally, 53 patients in the intervention group and 53 patients in the control group (a total of 106) were enrolled in the study. The adherence rate in the intervention group was 98.11%. As shown in Table 2, no significant differences were observed in any of the sociodemographic variables or medical characteristics upon entry into the study. The baseline of all primary and secondary outcome measurements did not significantly differ between the intervention and control groups (Table 3). There were no adverse events reported among the participants in the intervention group during the study.

### Primary outcomes

The effects of the physical exercise intervention on primary outcomes are shown in Table 4. There was a significant group effect and group  $\times$  time interaction effect for fatigue scores. The fatigue scores in all five dimensions (general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue) among patients in the intervention group were significantly lower than those in the control group. The sport motivation scores in five dimensions in the intervention group (motivation to know, motivation to accomplish, identification, external regulation and amotivation) were significantly higher than those in the control group, except for the dimension of motivation to experience stimulation and introjection.

### Secondary outcomes

The effects of the physical exercise intervention on secondary outcomes are shown in Table 5. Although only phase angle and 30s-CST were observed to be significant in the group effect, a group  $\times$  time interaction effect was observed for phase angle, 6-MWT and 30s-CST. In detail, the intervention group had a higher phase angle than the control group by body composition measurements. Regarding the 6-MWT, patients in the intervention group had longer walking distances than patients in the control group. The 30s-CST showed that the number of sit-stand-sit cycles in the intervention group was greater than in the control

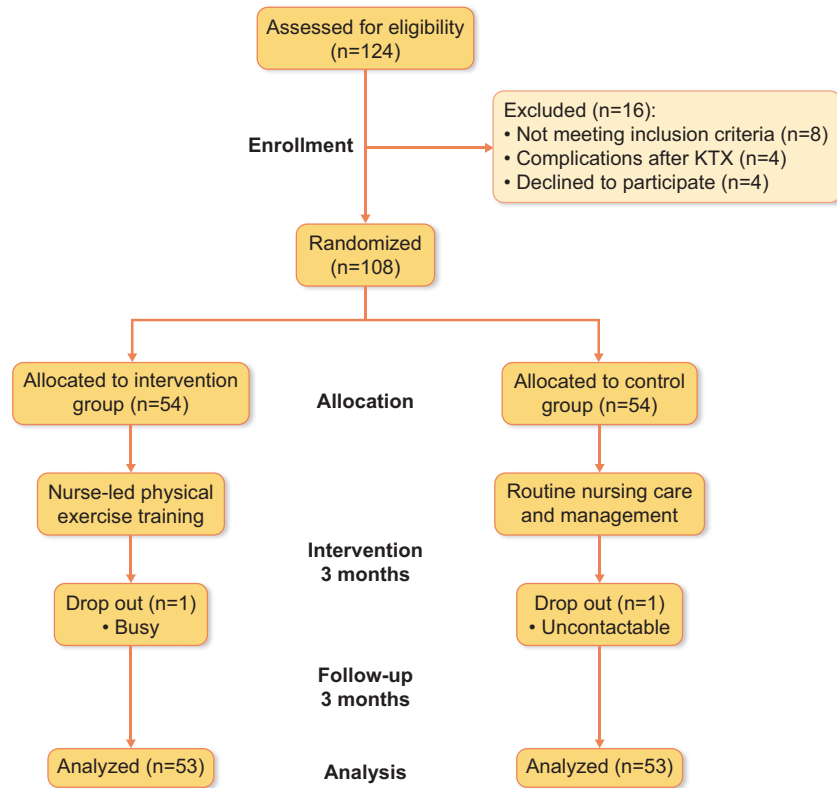


Figure 2: Flow diagram depicting participant recruitment and retention.

Table 2: Main demographic and clinical characteristics at baseline by groups.

Variables		Intervention group (n = 54)	Control group (n = 54)	t/ $\chi^2$	P-value
Age (years), mean $\pm$ SD		43.16 $\pm$ 10.76	42.06 $\pm$ 9.51	0.536	.593
Gender, n	Male	41	40	0.052	.819
	Female	12	13		
Marital status, n	Unmarried/divorced	9	8	0.070	.791
	Married	44	45		
Education, n	$\geq$ Doctor	1	4	3.852	.418
	Master	7	7		
	Undergraduate	17	10		
	High school	25	29		
	$\leq$ Secondary school	3	3		
Occupation, n	Farmer	30	25	3.856	.288
	Worker	16	13		
	Freelance work	5	12		
	Unemployed	2	3		
Family income (CNY), n	1500–2000	4	10	3.141	.370
	2600–3600	17	15		
	3700–4700	20	16		
	4800–5800	12	12		
Organ source, n	Relative donor	4	3	/	1.000
	Deceased donor	49	50		
Hospital readmission, n	None	45	44	2.401	.575
	1	7	5		
	2	1	2		
	$\geq$ 3	0	2		
Hospitalization time of transplant (days), mean $\pm$ SD		24.77 $\pm$ 6.25	24.62 $\pm$ 6.28	0.124	.902

CNY: Chinese yuan.

Table 3: The baseline of all objective and subjective measurements.

Variables	Intervention group (n = 54)	Control group (n = 54)	t/ $\chi^2$	P-value
<b>Clinical characteristics</b>				
Heart rate (beats/min)	88.77 ± 13.75	89.15 ± 14.68	-0.137	.892
Body mass index	22.76 ± 2.93	23.33 ± 2.85	-1.027	.307
Blood glucose (mmol/L)	4.85 ± 0.85	4.76 ± 0.72	0.615	.540
Creatinine ( $\mu$ mol/L)	917.23 ± 261.53	878.75 ± 239.67	0.786	.434
Triglyceride (mmol/L)	1.27 ± 0.62	1.16 ± 0.56	0.987	.345
<b>Body composition measurements</b>				
Phase angle (rad)	4.99 ± 0.70	4.85 ± 0.71	1.037	.302
Body hydration status(kg)	35.54 ± 5.72	35.07 ± 6.24	0.407	.685
Fat free mass (kg)	47.47 ± 7.52	47.05 ± 8.42	0.276	.783
Body fat (%)	23.95 ± 7.70	23.34 ± 7.60	0.413	.681
<b>Exercise capacity</b>				
6-MWT (m)	520.17 ± 74.61	508.02 ± 74.21	0.841	.403
30s-CST (times)	17.81 ± 2.47	17.62 ± 2.40	0.398	.691
<b>Fatigue scores</b>				
General fatigue scores	8.77 ± 2.41	9.19 ± 2.31	-0.909	.365
Physical fatigue scores	9.85 ± 2.28	9.94 ± 2.39	-0.208	.836
Reduced activity scores	11.06 ± 3.34	10.77 ± 3.37	0.434	.665
Reduced motivation scores	8.02 ± 3.09	8.09 ± 2.74	-0.133	.894
Mental fatigue scores	9.49 ± 1.58	9.58 ± 1.93	-0.276	.783
SAS scores	44.46 ± 6.08	46.46 ± 5.35	-1.802	.074
SDS scores	58.23 ± 9.13	59.46 ± 7.18	-0.769	.444
<b>Sport motivation</b>				
Intrinsic motivation to know	18.02 ± 4.60	18.19 ± 4.60	-0.190	.850
Intrinsic motivation to accomplish	19.91 ± 5.52	19.19 ± .90	0.646	.520
Intrinsic motivation to experience stimulation	18.83 ± 4.57	19.19 ± 5.25	-0.375	.708
Extrinsic motivation introjected	19.04 ± 4.89	18.92 ± 5.10	0.117	.907
Extrinsic motivation identified	20.34 ± 4.94	20.08 ± 5.72	0.254	.800
Extrinsic motivation external regulation	15.94 ± 3.72	15.89 ± 4.05	0.075	.940
Amotivation	12.77 ± 4.59	13.13 ± 4.80	-0.393	.695
<b>Quality of life</b>				
Physical functioning score	83.49 ± 9.18	83.40 ± 8.37	0.055	.956
Role-physical score	55.66 ± 41.50	52.83 ± 39.73	0.359	.721
General health score	64.06 ± 17.84	65.57 ± 17.32	-0.442	.660
Bodily pain score	84.15 ± 14.11	85.13 ± 14.99	-0.347	.729
Vitality score	74.34 ± 15.60	78.11 ± 14.52	-1.289	.200
Social functioning score	94.58 ± 22.93	96.93 ± 20.64	-0.556	.579
Role-emotional score	59.75 ± 39.96	61.64 ± 37.78	-0.250	.803
Mental health score	71.40 ± 14.43	73.06 ± 12.16	-0.641	.523
Reported health transition score	83.49 ± 23.48	86.32 ± 24.30	-0.610	.543

Data are presented as mean ± SD.

group. Patients in the intervention group had lower SAS and SDS scores for depression and anxiety. However, there was no significant difference in any dimension of the quality-of-life questionnaire between the two groups.

## DISCUSSION

Multiple studies have shown that kidney transplant recipients could benefit from exercise [28, 48]. However, there were no available studies on physical exercise training in Chinese KTRs. Our study is the first study to explore the effect of a physical exercise program in Chinese KTRs and indicated that they could benefit from the physical exercise program, with less fatigue and more motivation to be active in the intervention group. Importantly, no adverse events were observed during the intervention period in KTRs.

Regarding the primary outcomes, we found that patients in the intervention group had lower fatigue scores in the five dimensions of the fatigue questionnaire than those in the control

group. Fatigue is present in  $\approx$ 40–50% of KTRs, with rates comparable to those of the haemodialysis population, leading to significant functional impairment [17, 18]. Several studies have reported that physical exercise significantly reduces fatigue in patients with chronic disease, such as breast cancer patients [49], type 2 diabetes [50] and multiple sclerosis patients [51]. In addition, physical inactivity was associated with fatigue in KTRs [18]. We should encourage KTRs to practise the rehabilitation exercise program early to decrease fatigue. SMS results showed that KTRs in the intervention group had stronger sports motivation than those in the control group. One noteworthy reason could be the rehabilitation specialist's supervision and the nurse's recommendations or guidance during the follow-up.

For the secondary outcomes, we found that no difference was observed between the intervention and control groups in the indicators of body composition measurements except the phase angle. The intervention group had a higher phase angle than the control group. The phase angle is directly associated with muscle strength in individuals with different health



Table 4: Primary outcomes in intervention and control groups.

Variables	Control group			Intervention group			Group effect		Time effect		Interaction effect	
	Baseline (n = 54)	Post-follow-up (n = 53)	Change post – baseline within groups (95% CI)	Baseline (n = 54)	Post-follow-up (n = 53)	Change post – baseline within groups (95% CI)	F-value	P-value	F-value	P-value	F-value	P-value
Fatigue scores												
General fatigue	9.19 ± 2.31	9.47 ± 2.25	0.28 (-0.65–1.05)	8.77 ± 2.41	6.08 ± 1.44	-2.69 (-3.4 to -2.02)	37.795	.000	18.423	.000	28.096	.000
Physical fatigue	9.94 ± 2.39	10.34 ± 2.20	0.40 (-0.56–1.28)	9.85 ± 2.28	6.23 ± 1.34	-3.62 (-4.33 to -2.92)	55.290	.000	30.419	.000	47.197	.000
Reduced activity	10.77 ± 3.37	11.30 ± 3.12	0.53 (-0.85–1.76)	11.06 ± 3.34	7.58 ± 1.78	-3.47 (-4.41 to -2.63)	16.381	.000	14.0402	.000	25.932	.000
Reduced motivation	8.09 ± 2.74	9.04 ± 3.09	0.94 (0.02–1.91)	8.02 ± 3.09	5.81 ± 1.49	-2.21 (-2.95 to -1.43)	15.952	.000	3.948	.050	24.529	.000
Mental fatigue	9.58 ± 1.93	9.98 ± 1.67	0.40 (-0.27–1.05)	9.49 ± 1.58	7.91 ± 1.50	-1.58 (-2.21 to -1.05)	20.095	.000	7.466	.007	20.740	.000
Sport motivation	18.189 ± 4.60	17.96 ± 5.53	-0.23 (-2.00–1.58)	18.02 ± 4.60	21.85 ± 3.30	3.83 (2.17–5.33)	8.169	.005	8.854	.004	11.218	.001
Intrinsic motivation to know	19.19 ± 5.90	14.30 ± 4.16	-4.89 (-6.70 to -3.17)	19.91 ± 5.52	23.49 ± 2.77	3.58 (1.89–5.37)	57.077	.000	1.003	.319	42.480	.000
Intrinsic motivation to accomplish	19.19 ± 5.25	19.04 ± 5.53	-0.15 (-2.15–1.79)	18.83 ± 4.57	20.70 ± 3.84	1.87 (0.26–3.42)	0.878	.351	1.834	.179	2.535	.114
Intrinsic motivation to experience stimulation	18.92 ± 5.10	17.38 ± 5.04	-1.55 (-3.42–0.35)	19.04 ± 4.89	19.87 ± 2.91	0.83 (-0.68–2.46)	4.313	.040	0.323	.571	3.553	.062
Extrinsic motivation	20.08 ± 5.72	16.58 ± 4.88	-3.49 (-5.58 to -1.41)	20.34 ± 4.94	25.40 ± 2.39	5.06 (3.56–6.65)	50.712	.000	1.489	.225	44.366	.000
Extrinsic motivation identified	15.89 ± 4.05	15.89 ± 4.04	0.00 (-1.42–1.60)	15.94 ± 3.72	18.32 ± 2.97	2.38 (1.16–3.54)	5.442	.022	5.935	.017	5.935	.017
Extrinsic motivation external regulation	13.13 ± 4.80	13.25 ± 4.98	0.11 (-1.86–2.12)	12.77 ± 4.59	7.92 ± 1.94	-4.85 (-6.08 to -3.54)	24.145	.000	15.947	.000	17.508	.000
Amotivation												

Data are presented as mean ± SD. CI: confidence interval.

Table 5: Secondary outcomes in intervention and control groups.

Variables	Control group		Intervention group		Group effect		Time effect		Interaction effect			
	Baseline (n = 54)	Post-follow-up (n = 53)	Change post – baseline within groups (95% CI)	Baseline (n = 54)	Post-follow-up (n = 53)	Change post – baseline within groups (95% CI)	F-value	P-value	F-value	P-value	F-value	P-value
<b>Clinical characteristics</b>												
Heart rate (times/min)	89.15 ± 14.68	85.21 ± 12.35	-3.94 (-5.85 to -2.08)	88.77 ± 13.75	86.11 ± 12.98	-2.66 (-4.64 to -1.04)	0.011	.917	23.939	.000	0.904	.344
Body mass index	23.33 ± 2.85	22.63 ± 3.02	-0.70 (-1.59-0.17)	22.76 ± 2.93	22.85 ± 2.50	0.10 (-0.47-0.66)	0.136	.713	1.262	.264	2.181	.143
Blood glucose (mmol/L)	4.76 ± 0.72	5.45 ± 1.20	0.69 (0.37-1.06)	4.85 ± 0.85	5.23 ± 0.86	0.38 (0.16-0.62)	0.169	.682	25.816	.000	2.129	.148
Creatinine (µmol/L)	878.75 ± 239.67	107.66 ± 34.97	-771.54 (-844.69 to -711.36)	917.23 ± 261.53	117.08 ± 38.73	-800.15 (-876.67 to -731.29)	0.982	.324	979.256	.000	0.325	.570
Triglyceride (mmol/L)	1.16 ± 0.56	1.52 ± 0.93	0.36 (0.10-0.67)	1.27 ± 0.62	1.37 ± 0.69	0.66 (0.54-0.78)	0.034	.855	7.508	.007	2.627	.108
<b>Body composition measurements</b>												
Phase angle (rad)	4.85 ± 0.71	4.77 ± 0.81	-0.07 (-0.27-0.13)	4.99 ± 0.70	5.53 ± 0.52	0.55 (0.37-0.72)	14.870	.000	12.836	.001	22.094	.000
Body hydration status(kg)	35.07 ± 6.24	34.75 ± 5.97	-0.31 (-0.800.22)	35.54 ± 5.72	35.10 ± 5.27	-0.44 (-0.98-0.08)	0.135	.714	4.193	.043	0.124	.725
Fat free mass (kg)	48.89 ± 7.10	47.05 ± 8.42	-1.85 (-3.96-0.31)	48.61 ± 7.28	47.47 ± 7.52	-1.14 (-2.50-0.30)	0.003	.957	4.896	.029	0.280	.598
Body fat (%)	22.84 ± 8.47	23.34 ± 7.60	0.20 (-2.20-2.40)	23.4 ± 8.49	23.95 ± 7.70	0.55 (-0.10-1.17)	0.258	.613	0.365	.547	0.078	.781
<b>Exercise capacity</b>												
6-MWT (meter)	508.02 ± 74.21	493.45 ± 83.06	-14.57 (-31.59-3.76)	520.17 ± 74.61	530.56 ± 72.52	10.39 (4.68-16.53)	3.066	.083	0.204	.652	7.279	.008
30s-CST (times)	17.62 ± 2.40	17.66 ± 2.97	0.04 (-0.51-0.59)	17.81 ± 2.47	20.17 ± 2.43	2.36 (1.85-2.95)	8.671	.004	34.847	.000	32.687	.000
AS scores	46.46 ± 5.35	46.91 ± 5.66	0.45 (-1.30-2.22)	44.46 ± 6.08	37.69 ± 4.54	-6.77 (-8.73 to -4.73)	47.623	.000	22.042	.000	28.736	.000
SDS scores	59.46 ± 7.18	61.11 ± 6.18	1.65 (-0.59-4.10)	58.23 ± 9.13	41.53 ± 6.60	-16.70 (-19.96 to -13.22)	106.968	.000	54.814	.000	81.510	.000
<b>Quality of life</b>												
General health	65.57 ± 17.33	63.37 ± 18.56	-2.19 (-9.16-5.31)	64.06 ± 17.84	58.91 ± 19.96	-5.15 (-11.47-1.62)	1.391	.241	2.100	.150	0.342	.560
Bodily pain	85.13 ± 14.99	83.23 ± 15.00	-1.91 (-7.61-3.59)	84.15 ± 14.11	83.77 ± 14.80	-0.38 (-5.14-4.38)	0.010	.920	0.362	.549	0.162	.688
Vitality	78.11 ± 14.52	76.79 ± 14.71	-1.32 (-6.86-4.08)	74.34 ± 15.60	75.57 ± 15.46	1.23 (-5.00-7.41)	1.498	.224	0.001	.982	0.368	.545
Social functioning	96.93 ± 20.64	95.05 ± 20.27	-1.89 (-10.26-6.60)	94.58 ± 22.93	90.09 ± 20.56	-4.48 (-12.75-3.38)	1.578	.212	1.210	.274	0.201	.655
Role-emotional Mental health	61.64 ± 37.78	62.26 ± 39.78	0.63 (-12.66-12.96)	59.75 ± 39.96	61.01 ± 40.16	1.26 (-12.66-16.05)	0.075	.784	0.034	.853	0.004	.951
Reported health	73.06 ± 12.16	72.60 ± 13.66	-0.45 (-4.87-4.18)	71.4 ± 14.43	71.70 ± 12.15	0.30 (-4.656-5.31)	0.473	.493	0.002	.966	0.047	.829
Role-physical Physical functioning	86.32 ± 24.30	87.26 ± 22.80	0.94 (-8.33-10.27)	83.49 ± 23.48	84.43 ± 25.58	0.945 (-7.94-10.71)	0.722	.397	0.083	.774	0.000	1.000
Role-physical Physical functioning	52.83 ± 39.73	53.30 ± 41.61	0.47 (-13.21-15.86)	55.66 ± 41.50	57.08 ± 43.13	1.42 (-14.15-17.93)	0.319	.573	0.029	.865	0.007	.932
Physical functioning	83.40 ± 8.37	84.06 ± 7.97	0.66 (-2.30-3.84)	83.49 ± 9.18	80.85 ± 10.46	-2.64 (-6.18-1.19)	1.477	.227	0.679	.412	1.886	.173

Data are presented as mean ± SD.  
CI: confidence interval.

conditions, such as chronic obstructive pulmonary disease (COPD) and kidney transplantation. De Blasio et al. [52] reported that the phase angle could provide useful information for evaluating body composition and better assess muscle strength and physical fitness in COPD. Several studies have already explored the effect and function of phase angle in KTRs and indicated that the phase angle could be used as a predictor and was inversely associated with the mortality of KTRs by nutritional assessment [53–55]. Our results showed that physical exercise could increase the phase angle, which was consistent with a recent systematic review showing that exercise programs were associated with a positive effect on the phase angle [56]. Therefore, our study provides evidence that the phase angle might be an inexpensive, easy-to-perform and non-invasive health indicator in Chinese KTRs. Further studies on the relationship of physical exercise, phase angle and mortality in Chinese KTRs are needed in the future.

The 6-MWT and 30s-CST are commonly used to estimate cardiopulmonary fitness and exercise capacity in clinical and research settings [57–59]. A prior study indicated a significant correlation between walking distance and oxygen consumption [60]. Many patients were found to have an important deficit in the walking distance after kidney transplantation [61, 62]. A previous study reported that a change of 14.0–30.5 m for the 6-MWT may be a minimal clinically important difference (MCID) across multiple patient groups [63]. In our study, the change in 6-MWT was 37.11 m, which was more than the previous reported MCID values. Our results showed that KTRs in the intervention group had longer walking distances than patients in the control group, suggesting that physical exercise may improve peak pulmonary oxygen uptake and cardiopulmonary function. Similarly, the 30s-CST is a simple test of lower limb function. The 30s-CST has been shown to correlate with the 6-MWT, and these two tests are usually conducted simultaneously [64, 65]. Several studies have verified that the 30s-CST provides a meaningful metric of functional performance in patients with COPD [66, 67]. Some recent studies have also used it to assess physical performance in KTRs and patients with end-stage renal disease [57, 68]. Also, a change of at least 2 repetitions in the 30s-CST may be clinically important [69, 70] and the change in the 30s-CST in our study was 2.51 repetitions, which was in agreement with previously reported MCID values. Our results showed that the number for the 30s-CST in the intervention group increased compared with the control group, which indicated that the exercise program could increase physical performance in Chinese KTRs. For the traditional Chinese exercise Baduanjin, Wu et al. [71] reported that Tai Chi interventions could improve older adults' 30s-CST, which was consistent with our results. Our study was the first to look at the relationship between Baduanjin and physical performance in KTRs using the 30s-CST.

Physical exercise also significantly improved the incidence of anxiety and depression in Chinese kidney transplant recipients. Anxiety, depression or psychosocial pain is experienced by 20–60% of KTRs [72]. Depression and anxiety are also highly prevalent psychological disorders in patients with end-stage renal disease, which may have a negative clinical impact on the endogenous creatinine clearance rate after kidney transplantation [73, 74]. Furthermore, anxiety and depression have an inverse correlation with the ability to self-manage [74]. In our physical exercise program, KTRs in the intervention group after discharge created a daily exercise rehabilitation video and sent the video by smartphone. These activities might have improved their self-management ability and decreased anxiety and depression.

In our study, the comparison group showed no significant differences in any dimension of the quality-of-life questionnaire over time, which was not consistent with a previous report [75]. Short intervention and follow-up time may be responsible for the results of the study. Further studies are needed to examine the effect of physical training on the quality of life in the future. Finally, the participants did not experience adverse events in our study. However, the physical exercise program included extensive stretching motions, which had the potential for adverse events, such as wound dehiscence and bleeding and muscle strain. We suggest that the participants should be educated about the clinical manifestations of potential adverse events prior to starting an exercise program and were guided and accompanied by the nurses and exercise rehabilitation specialist when they did the exercise program during the pre-discharge stage.

### Limitations

Our study had several limitations. All participants enrolled in this study came from the Third Xiangya Hospital. Multicentre trials in different regions and different levels of hospitals are warranted. Additionally, the period of our RCT was only 6 months, including intervention for 3 months and follow-up for 3 months. Only outcomes at one time point after the intervention were collected. Sustained effectiveness remains to be confirmed. The repeated measure ANOVA analyses indicated that the time effect was also included in some variables, such as the 6-MWT. Therefore, measurements need to be taken at more time points to capture the effects of intervention in the future.

### CONCLUSION

The present study verified that Chinese KTRs could benefit from a rigorous and standardised physical exercise program. This study can be used as a reference for subsequent evidence-based, nurse-led physical exercise interventions in Chinese KTRs.

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### AUTHORS' CONTRIBUTIONS

P.Z. and J.L. were responsible for conceiving and designing the experiments. X.Z., L.D., H.L. and L.Z. collected and analysed the data. P.Z. was responsible for writing and revising the manuscript. S.L. made important intellectual contributions to the research design, provided technical guidance and revised the manuscript. All the authors read and approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

The datasets analysed during the current study are available from the corresponding author upon reasonable request.

## CONFLICT OF INTEREST STATEMENT

None declared.

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