

CLINICAL TRIAL REPORT

# Does Intradialytic Group Exercise Programme Influence Patient-Reported Outcomes, Laboratory Parameters, and Anthropometric Parameters in Maintenance Hemodialysis Patients? A Single-Group Repeated-Measures Trial

Lijuan Zhou 1,2,\*, Dan Shi 2, Liyuan Zhang2,\*, Qian Wang2, Li Chen2, Honglin Chen3

Correspondence: Honglin Chen, Email honglinyjs@126.com

**Background:** Maintenance hemodialysis(MHD) patients often suffer from fatigue and are recommended to undertake physical activities. The optimal format of exercise rehabilitation for MHD patients remains uncertain despite demonstrated health benefits. This study aimed to evaluate the effectiveness of an intradialytic group exercise programme for MHD patients.

**Methods:** This was a single-centre, single-group repeated-measures design study. The 12-week, three times per-week intradialytic group exercise programme was conducted for around 30 min during the first 2 hours of each dialysis session. Patient-reported outcomes including fatigue, anxiety, depression and health-related quality of life, laboratory parameters including haemoglobin, albumin, pre-albumin and hypersensitive C-reactive protein, and anthropometric parameters including triceps skinfold thickness, mid-upper arm circumference, mid-arm muscle circumference and handgrip strength, were measured at baseline, immediately post-intervention and 12-weeks post-intervention. The repeated-measures analysis of variance and Friedman test were used to compare the parametric and non-parametric data across time points, respectively.

**Results:** Ninety patients were enrolled and 75 completed. Participants reported significant improvements across time points in fatigue (F = 10.19, p < 0.01), depression (F = 19.20, p < 0.001), health-related quality of life (F = 5.36, p = 0.006), haemoglobin (F = 3.43, p = 0.047), albumin (F = 4.42, p = 0.032), hypersensitive C-reactive protein  $(\chi^2 = 50.39, p < 0.001)$ , pre-albumin  $(\chi^2 = 11.85, p = 0.003)$ , triceps skinfold thickness (F = 25.03, p < 0.001), mid-upper arm circumference (F = 6.32, p = 0.005), mid-arm muscle circumference (F = 4.89, p = 0.02), and handgrip strength (F = 13.59, p < 0.001). Although the mean anxiety score tended to reduce, the difference across time points was nonsignificant (F = 1.33, p = 0.27).

**Conclusion:** The findings suggested that the intradialytic group exercise programme could improve MHD patients' fatigue, depression, health-related quality of life, nutritional status, and inflammation.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2000034394 (04/07/2020).

**Keywords:** maintenance hemodialysis, group exercise, aerobic exercise, resistance exercise nutrition, quality of life

#### Introduction

Chronic kidney disease (CKD) has become a leading public health problem in the past decade, especially in developing countries. End-stage renal disease (ESRD), a major lethal factor for CKD patients, is incurable unless renal transplantation is available. Given the limited access to renal grafts, lifelong dialysis has been the sub-optimal treatment for ESRD patients. In China, maintenance hemodialysis (MHD) is the most widely used therapeutic approach for ESRD treatment, with the number

<sup>&</sup>lt;sup>1</sup>Medical School, Nantong University, Nantong, People's Republic of China; <sup>2</sup>Nursing Department, Taizhou People's Hospital, Taizhou, People's Republic of China; <sup>3</sup>School of Public Health, Nantong University, Nantong, People's Republic of China

<sup>\*</sup>These authors contributed equally to this work

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of MHD patients reaching 632 thousand in 2020.<sup>3</sup> Significant progress has been made in hemodialysis technology and patient care; however, MHD patients still face various problems impairing their health-related quality of life (HRQOL).<sup>2,4</sup>

Physical inactivity is common among MHD patients<sup>5</sup> and acts as one major modifiable risk factor for their poor HRQOL.<sup>6</sup> The level of physical activity in MHD patients is strikingly reduced due to consequences of renal failure per se (eg, abnormal skeletal muscle metabolism and structure, mitochondrial dysfunction and electrolyte disturbance), anaemia and malnutrition;<sup>7,8</sup> subsequently results in impaired exercise capacity, ultimately muscle wasting, poor HRQOL, and increased risks of hospitalization and mortality.<sup>8–11</sup> Given the negative impacts caused by physical inactivity, MHD patients are recommended to undertake physical activities,<sup>6,12</sup> and nephrology staff are encouraged to help patients engage in these activities.<sup>13</sup>

Exercise training is commonly used to improve MHD patients' physical activity. Exercise training for MHD patients can be categorized as intradialytic and extradialytic exercise according to exercise time. Intradialytic exercise is preferred considering the lower physical activity level on dialysis days compared to nondialysis days;<sup>5,14</sup> moreover, owing to the supervision of medical staff, intradialytic exercise is superior to interdialytic exercise in terms of patient adherence and safety.<sup>15,16</sup> Being different from the exercise time, the optimal type of exercise training remains uncertain. Aerobic exercise increases endurance and resistance exercise increases muscle strength. A combination of these are commonly prescribed in exercise training and have shown benefits for MHD patients.<sup>17,18</sup>

Despite the beneficial effects of exercise training on MHD patients, it remains neglected in dialysis care because of various barriers, <sup>19</sup> including the lack of motivation and resource restrictions. <sup>20,21</sup> Further studies should tackle these barriers to promote physical exercise for MHD patients.

Group exercise, involving social interactions and providing a sense of belonging, positively affects participants' motivation and keeps their adherence to the intervention. <sup>22,23</sup> Besides, group exercise can provide a resource-saved way of exercise training because several patients can get together and exercise under the supervision of the same health professionals. Furthermore, maintenance hemodialysis is a regular and long-term treatment allowing MHD patients to get familiar with each other in the dialysis units, making it suitable for conducting group exercises. Thus, group exercise has potential promising results for MHD patients, considering the two-way benefits for patients and health professionals; however, the effects of intradialytic group exercise on MHD patients remain unclear.

In terms of the effects of exercise on MHD patients, current studies mainly focused on biochemical and physiological parameters, 1,18,24,25 with limited attention on patient-reported outcomes, such as depression, anxiety, and fatigue. Considering the high prevalence and negative impacts of these patient-reported outcomes, 26,27 it is necessary to comprehensively assess the effects of exercise training on patient-reported outcomes in addition to objective parameters.

Therefore, this study aimed to examine the effects of a 12-week intradialytic group exercise programme for MHD patients on patient-reported outcomes, laboratory parameters and anthropometric parameters.

#### **Methods**

The 12-week study applied a repeated measure research design (the Chinese Clinical Trial Registry: ChiCTR2000034394). The study was conducted according to the Declaration of Helsinki and approved by the Ethics Committee of Taizhou People's Hospital, China (KY 202004001). All participants gave informed consent before participation.

## **Participants**

Patients who took regular maintenance hemodialysis in the Hemopurification Center at the Taizhou People's Hospital from September 2020 to April 2021 were available for enrollment. The study included participants who (1) aged  $\geq 18$  years, (2) took hemodialysis treatment for more than three months, (3) took hemodialysis four hours per time and three times per week (Monday-Wednesday-Friday or Tuesday-Thursday-Saturday), (4) had no physical disability and both upper and lower muscle strength were not less than grade III, and (5) gave informed consent. The exclusion criteria were as follows: (1) had serious complications such as uncontrolled cardiovascular disease, malignant tumours, severe infection, and active bleeding, (2) had aphasia or were deaf, and (3) had a doctor-diagnosed psychiatric illness.

## Study Intervention

The Hemopurification Center has 10 wards, with 4 to 10 beds each. The research staff grouped participants with good relationships under the same purification time into the same ward. After then, the purification bed was fixed unless the patients wanted a change. The intradialytic group exercise programme was conducted during the first two hours of each hemodialysis session<sup>8,28,29</sup> with a dose of 30 min per session, three sessions per week for 12 weeks. The exercise programme consisted of four parts: warm-up, aerobic, resistance, and cool-down (Table 1).

Resistance loop bands (PROIRON®, SHANXI REGENT, China) were applied in the resistance exercise. These bands had five tension levels, including X-Light (5–10lbs), Light (15–20lbs), Medium (25–30lbs), Heavy (35–40lbs), and X-Heavy (45–50lbs). The tension levels were set according to the MHD patients' tolerance every time before the session. During the resistance exercise, the patient could reduce the tension level by changing the resistance band or taking a rest if s/he reported the Rating of Perceived Exertion (RPE) was over 15 points. 18,30

Actions were taken to guarantee the safety of MHD patients. Vital signs and weight would be measured when patients came to the centre; those with abnormal vital signs (blood pressure > 200/100 mmHg or < 110/50 mmHg, heart rate per minute< 60, or oxygen saturation < 80%) or having interdialytic weight gain (IDWG) > 5% would not take the current exercise session. Besides, during the exercise session, nurses in the centre performed continuous supervision, and patients should stop their exercise immediately when (1) their blood pressure was >200/100 mmHg or < 110/50 mmHg; (2) their heart rate were over 80% of the maximum heart rate (maximum heart rate = 220-age); or (3) they had hypoglycemia, dizziness, headache, pale complexion, chest pain, dyspnea, etc.

#### Data Collection and Outcomes

Data were collected by a research assistant (LC) at baseline (T0), immediately post-intervention (T1), and three months post-intervention (T2).

Table I Components of the Intradialytic Group Exercise Programme

Exercise	Time	ne Contents			
Warm-up exercise	5min	Standing position			
		Circumduction of Wrists, Arms, Ankles and Legs – two sets of eight repetitions for each			
		Shoulder flexion, elevation and extension – two sets of eight repetitions			
		Marching in place – two sets of eight repetitions			
Aerobic exercise	8-10min	Lying position			
		• Upper limb without arteriovenous fistula: fist clenching-relaxing movements, wrist forward-reverse rotation			
		movements, and elbow extension-flexion movements - four sets of eight repetitions for each			
		• Lower limbs: ankle forward-reverse rotation movements, keen extension-flexion movements and leg raising			
		movements - four sets of eight repetitions for each			
Resistance exercise	10–15min	Lying position			
		• Upper limb training: stepping on a cushioned handle with the foot arch of the nondialysis side and holding the			
		other cushioned handle firmly by the nondialysis upper limb, with the palm side up and upper arm fixed; ding			
		elbow extension-flexion movements and trying to bring the fist close to the chest - 10 sets of eight			
		repetitions and taking a 10-second-rest between every two sets			
		• Lower limb training - straight-leg-raising movements: circling the loop band around the ankles of feet; taking			
		turns to raise feet as high as the patient can; holding for I second before slowly putting down the foot - five sets of IO repetitions and taking a IO-second-rest between every two sets			
		• Lower limb training - clamshell exercise: looping a band around both thighs, just above the knees; lying on the			
		side without arteriovenous fistula, with the head resting on the nondialysis arm, the hand with the			
		arteriovenous fistula placed on the hip, knees bending 90 degrees, and the feet in line with the butt; Keeping			
		feet together, raising the above knee as far as the patient can without rotating the hip or lifting the knee			
		below off the bed; hold for one second before slowly putting the knee down - five sets of eight repetitions			
		and taking a 10-second-rest between every two sets			
Cool-down	5min	Lying position			
		Deep breath			
		Peer communications			

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#### Patient-Reported Outcomes

Multidimensional fatigue inventory (MFI): Fatigue was measured by the MFI, which included five subscales of fatigue, namely general fatigue (4 items), physical fatigue (4 items), reduced activity (4 items), reduced motivation (4 items), and mental fatigue (4 items). Each item was scored using a Likert 5-point scale, with a total score ranging from 20 to 100.31 The higher the score, the patient had higher level of fatigue. The Chinese version of MFI had robust psychometric properties, with Cronbach's alpha coefficient ranging from 0.83 to 0.92 and a contracts validity index of 0.93.<sup>32</sup>

Hospital anxiety and depression scale (HADS): Depression and anxiety were measured by the HADS, which consisted of 14 items and seven items for assessing anxiety (HADS-A) and depression (HADS-D), respectively.<sup>33</sup> Each item was assessed as 0 to 3 points, with a total score of 21 for anxiety and depression, with higher scores indicating more severe psychological distress. The Cronbach's alpha coefficient for the Chinese version of HADS-A was 0.78 and for the HADS-D was 0.76.34

Kidney disease quality of life-short form (KDQL-SF<sup>TM</sup>, Version 1.3): The KDQL-SF consisted of a 36-item shortform health survey (SF-36) and a 12-filed survey in kidney disease-targeted areas (KDTA). The Chinese version of KDQL-SF<sup>TM</sup> demonstrated good reliability, with good internal consistency (Cronbach's alpha ranging from 0.69–0.78) and test-retest reliability (ranging from 0.70 to 0.86).<sup>35</sup> The scores ranged from 0 to 100, and the higher the KDOOL-36<sup>TM</sup> score, the better QOL the patients had.<sup>35</sup>

#### Laboratory Parameters

Blood sampling was analyzed after an overnight fast on dialysis-free days in the hospital's laboratory. Haemoglobin (Hb) was analyzed on a haematology analyzer (XN-20, Sysmex<sup>®</sup>, Kobe-shi, Japan). Albumin (Alb), pre-albumin (pre-Alb) and hypersensitive C-reactive protein (hs-CRP) were analyzed on a bio-analysis machine (AU5800, Beckman Coulter, Shanghai, China).

#### Anthropometric Parameters

The following five anthropometric parameters were measured. (1) Triceps Skinfold Thickness (TSF): TSF was measured using skinfold callipers, and the needle was read to the nearest 0.5mm. The measurement point was at the midpoint between the olecranon and the acromion tip of the nondialysis arm.<sup>36</sup> The averages of two consecutive measurements were recorded; (2) Mid-Upper Arm Circumference (MUAC): MUAC was measured in the nondialvsis side by a tape ruler at the midpoint of the upper arm, with the arm dropping naturally. Results were recorded to the nearest 0.1cm, and the averages of two consecutive measurements were recorded; (3) Mid-Arm Muscle Circumference (MAMC): the MAMC was calculated according to the formula MAMC(cm) =  $MUAC(cm) - 3.14*TSF(cm);^{37}$  (4) Handgrip Strength (HGS); The HGS of the nondialysis hand was measured by an electronic hand dynamometer (KYTO<sup>®</sup>, Dongguan, Guangdong, China) before the start of dialysis treatment. Results were recorded to the nearest 0.1kg, and the larger of two consecutive measurements were recorded.

## Statistical Analysis

Data analysis was conducted using SPSS 22.0 (IBM, Armonk, NY, USA). The analysis was carried out on a per-protocol approach. The kurtosis and skewness tests were used to test the normal distribution of the data; data with normal distribution were described using means and standard deviation (SD); those without normal distribution were described using medians and quartiles [q25, q75]. The repeated-measures analysis of variance (rANOVA) and Friedman test were used to compare the parametric and non-parametric data at three time points, respectively. All statistical tests were twotailed, and p < 0.05 was considered statistically significant.

#### Results

## Demographic and Clinical Characteristics

A total of 178 MHD patients were screened, among which 90 were recruited. Among the 90 recruited MHD patients, 75 (35 males) completed the 12-week intradialytic group exercise. The flow chart of patients during the study is shown in Figure 1. The mean age of the participants was 55.03 (10.69) years, ranging from 25 to 77 years. Most participants were married (92.0%) and had no religious beliefs (84.0%). More than half of people (68%) had a duration of dialysis longer than 36 months. The details of demographic and clinical characteristics are reported in Table 2.

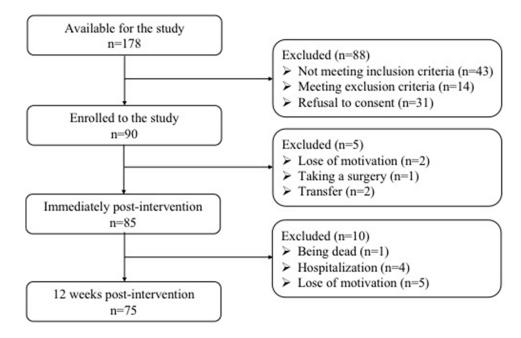


Figure I Flow chart of participants.

## Effects of the Intradialytic Group Exercise

#### Effects on Patient-Reported Outcomes

The results of rANOVA indicated significant improvements in fatigue (F = 10.19, p < 0.01), depression (F = 19.20, p < 0.001), and HRQOL (F = 5.36, p = 0.006) across time points. Although the mean anxiety score tended to reduce, the difference across time points was not significant (F = 1.33, p = 0.27).

Table 2 Demographic and Clinical Characteristics

Characteristics	N=75	
Age (years)		
Mean ± SD	55.03 ± 10.69	
Gender, n (%)		
Man	35 (46.7)	
Women	40 (53.3)	
Education level, n (%)		
Primary school education or illiteracy	16 (21.3)	
Secondary school or high school education	50 (66.7)	
College or higher education	9 (12.0)	
Marital status, n (%)		
Married	69 (92.0)	
Divorced, Single or Widowed	6 (8.0)	
Work status, n (%)		
Employment	14 (18.7)	
Resignment	24 (32.0)	
Retirement	37 (49.3)	
Religious belief, n (%)		
Buddhism	10 (13.3)	
Christianity	2 (2.7)	
None	63 (84.0)	

(Continued)

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Table 2 (Continued).

Characteristics	N=75	
Payment way, n (%)		
Private expenses	2 (2.6)	
Medical insurance	73 (97.3)	
Average income monthly, n (%)		
≤ 1000 yuan	35 (46.7)	
1001~3000 yuan	26 (34.7)	
3001~5000 yuan	10 (13.3)	
> 5000 yuan	4 (5.3)	
Primary disease, n (%)		
Glomerulonephritis nephropathy	21 (28.0)	
Hypertensive renal disease	37 (49.3)	
Diabetic nephropathy	9 (12.0)	
Systemic lupus erythematosus	2 (2.7)	
Others	6 (8.0)	
Duration on dialysis (month)		
Median, Q25 - Q75	55, 32–91	

The results of rANOVA showed significant improvements in laboratory parameters, including Hb (F = 3.43, p =0.047) and Alb (F = 4.42, p = 0.032) across time points. The results of the Friedman test showed that MHD patients attain significant improvements in hs-CRP ( $\chi^2 = 50.39$ , p < 0.001) and pre-Alb ( $\chi^2 = 11.85$ , p = 0.003).

In terms of anthropometric parameters, significant improvements were obtained in TSF (F = 25.03, p < 0.001), MUAC (F = 6.32, p = 0.005), MAMC (F = 4.89, p = 0.02), and HGS (F = 13.59, p < 0.001). Comparisons of outcomes at different time points are reported in Table 3.

Table 3 Comparisons of Patient-Reported Outcomes at Different Time Points

Outcomes	Pre-Intervention Mean ± SD/Medium (q25, q75)	Post-Intervention Mean ± SD/Medium (q25, q75)	3m Follow-Up Mean ± SD/Medium (q25, q75)	Flχ <sup>2</sup>	Þ
Patient-reported outcomes					
MFI	57.36 ± 14.24	54.87 ± 12.64	53.07 ± 12.68	10.19	< 0.001
HADS-A	8.36 ± 2.96	8.05 ± 2.75	8.03 ± 2.84	1.33	0.27
HADS-D	9.09 ± 4.08	7.44 ± 2.59	7.28 ± 2.69	19.20	< 0.001
KDQL-SF	65.24 ± 12.62	69.23 ± 10.15	67.99 ± 9.09	5.36	0.006
Laboratory parameters					
Hb, g/L	108.15 ± 14.22	109.40 ± 15.75	110.21 ± 13.21	3.43	0.047
hs-CRP, mg/L <sup>a</sup>	5.4 (4.2, 6.7)	4.2 (3.6, 5.6)	4.3 (3.7, 5.2)	50.39	< 0.001
Alb, g/L	39.23 ± 3.40	39.98 ± 3.41	40.09 ± 3.13	4.42	0.032
Pre-Alb, mg/L <sup>a</sup>	331 (283, 380)	331 (284, 381)	332 (290, 376)	11.85	0.003
Anthropometric parameters					
TSF, mm	12.03 ± 1.46	12.73 ± 1.41	12.84 ± 1.45	25.03	< 0.001
MUAC, cm	25.41 ± 3.05	26.00 ± 3.04	26.13 ± 2.92	6.32	0.005
MAMC, cm	20.63 ± 2.49	21.22 ± 2.62	21.31 ± 2.41	4.89	0.02
HGS, kg	22.41 ± 5.78	24.20 ± 6.78	23.01 ± 6.58	13.59	< 0.001

Note: <sup>a</sup>Friedman test.

Abbreviations: MFI, multidimensional fatigue inventory; HADS-A, hospital anxiety and depression scale-anxiety; HADS-D, hospital anxiety and depression; KDQL-SF, kidney disease quality of life-short form; Hb, haemoglobin; hs-CRP, hypersensitive C-reactive protein; Alb, Albumin; pre-Alb, pre-albumin; TSF, Triceps Skinfold Thickness; MUAC, Mid-Upper Arm Circumference; MAMC, Mid-Arm Muscle Circumference; HGS, Handgrip Strength.

#### **Discussion**

Of the 90 MHD patients enrolled, 15 dropped out of the study. In addition to death, hospital transfer, hospitalization, surgery and other irresistible factors, 7 patients (7.7%) dropped out of the study due to loss of motivation, the proportion is lower than in previous studies. Buring the first data collection, 2 patients were unwilling to continue the study because data collection occupied too much of their time. During the intervention, 5 patients lost motivation and dropped out of the study. Among them, 3 patients thought the exercise was too much for their body to withstand, and 2 patients because they did not get along with other patients in the same group. In future studies, some time can be reserved for each group of patients before intervention to help a group of patients communicate effectively and adapt to the amount of exercise. In future studies, some time can be reserved for each group of patients before intervention, so as to help patients in a group to have effective communication and adapt to the amount of exercise. Make detailed explanations with the patient before intervention, including the amount of data to be collected. Ultimately, these controllable factors can avoid the loss of participants.

MHD patients tend to be sedentary,<sup>40</sup> which can induce a catabolic state including reduced neuromuscular functioning, reduced exercise tolerance and reduced cardiorespiratory fitness.<sup>6,41</sup> Over time, these catabolic adaptations may lead to functional limitations that interfere with activities of daily living and affect quality of life. Some studies<sup>29,39</sup> suggest that exercise can change these conditions. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend that patients be physically active.<sup>42</sup> Recent systematic reviews have shown that intradialytic exercise could improve the removal of solutes, systemic inflammation, exercise tolerance, walking ability, muscle strength, and QOL;<sup>43–47</sup> however, limited attention has been put on patient-reported outcomes, and the optimal exercise type and format for MHD patients remains uncertain. This study applied the intradialytic group exercise programme for MHD patients; moreover, the study comprehensively examined the intervention effects on patient-reported outcomes, laboratory parameters and anthropometric parameters.

Aerobic exercise, using large muscle groups, primarily improves oxidative capacity and cardiovascular function, so as to improve endurance. Individual aerobic exercise in MHD patients is safe and has a significant effect on the control of hypertension, physical capacity, sleep quality and QOL. A3,48 Resistance exercise can increase muscle size and strength, and it may help in reducing microinflammatory reactions and protein-energy wasting. As a recent systematic review showed, differences between combined exercise and aerobic or resistance exercise alone did not reach statistical significance, however the combined one resulted in the largest effect sizes. Furthermore, given the social atmosphere in dialysis units and the benefits of group exercise concluded in available systematic reviews, around exercise programme consisted of both aerobic exercise and resistance exercise may be suitable and beneficial for MHD patients. Therefore, this study applied an intradialytic group exercise programme consisted of both aerobic exercise and resistance exercise.

Results of the study showed that the intradialytic group exercise could improve patients' fatigue, depression and HRQOL. The results were consistent with former studies. 17,57,58 Although the anxiety score reduced over time, we found a nonsignificant improvement in patients' anxiety. The finding was in line with the systematic review of Hargrove, El Tobgy, Zhou, Pinder, Plant, Askin, Bieber, Collister, Whitlock, Tangri, Bohm, 59 which looked at the effectiveness of aerobic exercise on patients' anxiety and demonstrated inconclusive results. Techniques such as deep breathing, 60 guided imagery, 61 and cognitive-behavioural interventions 2 may be needed to reduce the level of anxiety. In addition to patient-reported outcomes, this study also used anthropometric and laboratory indicators to reflect MHD patients' nutritional state and systemic inflammation. The findings suggested that the intradialytic group exercise positively affected malnutrition and systemic inflammation in MHD patients, which were consistent with previous studies. Furthermore, seven out of 90 patients dropped out for losing motivation, which was lower compared to former studies related to intradialytic exercise in MHD patients. 8,18,29,63

Exercise training has been proven to be important to MHD patients, yet, it has received limited attention from both MHD patients and health providers for diverse reasons, among which the fear of injuries, the lack of motivation and resources restrictions are the common barriers.<sup>64</sup> This study found that the intradialytic group exercise could benefit

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MHD patients with a low attrition rate. With the supervision of medical staff and peer support from other patients, intradialytic group exercise seems to provide a way for MHD patients to overcome the fear of injuries and sustain motivation. Healthcare providers and patients may treat exercise as the new "normal" in a physical and social environment, thus limiting opportunities for sedentary behaviours.<sup>21</sup> Moreover, group exercise provides resource-saved exercise training because several patients can exercise under a health provider's supervision. The exercise culture cultivated by fostering a common identity among participants and increasing social interaction during the group exercise may be the main reason for the low dropout rate.

Although the study generates some new knowledge in exercise rehabilitation in MHD patients, there are still some limitations. Firstly, this is a single-centre study, while results from a multicenter study enrolling more participants may be more reliable. Secondly, this is a single-group repeated-measures design study. Studies with a control group (such as randomized controlled trials) are needed to assess the effectiveness of the intradialytic group exercise. Thirdly, due to the sudden outbreak of COVID-19 in the city after the 3-month follow-up, thus, outcomes were not measured as scheduled at 6-month follow-up. A study with a more extended period is required to evaluate longer-term health impacts.

#### **Conclusions**

The findings of this study provided preliminary evidence that aerobic exercise combined with resistance exercise program could improve fatigue, depression, health-related quality of life, nutrition state and inflammation in patients undergoing maintenance hemodialysis. Further study using randomized controlled trials is needed to examine the effectiveness of the aerobic exercise combined with resistance exercise program for maintenance hemodialysis patients.

#### **Abbreviations**

CKD, Chronic kidney disease; ESRD, End-stage renal disease; MHD, maintenance hemodialysis; HRQOL, healthrelated quality of life; RPE, Rating of Perceived Exertion; IDEG, interdialytic weight gain; KDTA, kidney diseasetargeted areas; MFI, Multidimensional fatigue inventory; HADS-A, Hospital anxiety and depression scale-anxiety; HADS-D, Hospital anxiety and depression scale-depression; KDQL-SF, Kidney disease quality of life-short form; Hb, Haemoglobin; hs-CRP, hypersensitive C-reactive protein; Alb, Albumin; pre-Alb, pre-albumin; TSF, Triceps Skinfold Thickness; MUAC, Mid-Upper Arm Circumference; MAMC, Mid-Arm Muscle Circumference; HGS, Handgrip Strength; SD, standard deviation; rANOVA, The repeated-measures analysis of variance.

# **Data Sharing Statement**

The authors are willing to permanently share data supporting the results and analysis presented in the paper after publication. The data can be used for scientific research beneficial to human health. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### **Ethical Statement**

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted following the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Taizhou People's Hospital, China (NO. KY 202004001) and informed consent was taken from all individual participants.

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#### **Disclosure**

The authors report no conflicts of interest for this work.

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