Renal Replacement Therapy

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Effect of intradialytic exercise on fall occurrences in older patients undergoing hemodialysis: a single-center non-randomized study

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Abstract

Background Given rapid aging of the global population, preventing adverse events such as falls is essential for preserving functional capacity and quality of life among older adults, especially those at high risk due to hemodialysis (HD) treatment. We aimed to investigate the effects of a 3-year intradialytic exercise intervention on fall occurrence and physical performance in older patients undergoing HD.

Methods Sixty-one patients were non-randomly assigned to the exercise ($n = 31$) and control groups ($n = 30$). The exercise group performed aerobic and resistance training during HD three times per week for 3 years. Handgrip strength, lower extremity muscle strength, 10-m walking speed, and Short Physical Performance Battery (SPPB) scores were assessed at baseline. Physical function was reassessed every year in the exercise group. All participants were followed up until the first fall or the end of the study period.

Results There were no significant between-group differences in baseline data. Over a median follow-up of 35 months, 10 (16.3%) falls occurred, including 1 (3.2%) in the exercise group and 9 (30%) in the control group. Kaplan–Meier analysis revealed that the exercise intervention significantly reduced the occurrence of falls. No significant differences in physical function were observed among four time points in patients who completed the 3-year program.

Conclusion Intradialytic exercise may represent an essential intervention for preventing falls in older patients undergoing HD.

Trial registration: This study was retrospectively registered with the University Hospital Medical Information Network (UMIN 00044821, February 4, 2021).

Keywords Hemodialysis, Falls, Older adults, Intradialytic exercise

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Introduction

Falls represent the primary cause of chronic disability in older patients undergoing hemodialysis (HD). Fall risk is higher among patients undergoing HD than among the general population, and HD has been associated with high fall-related morbidity [1]. In older patients, HD contributes to poor physical function, frailty, and sarcopenia, all of which are associated with falls and fall-related fractures. In addition, the pathological characteristics of chronic kidney disease with mineral and bone disease (CKD-MBD) may increase the incidence of fall-related fractures among those with HD, and a previous study reported that the risk of hip fractures is 4.4 times higher in patients undergoing HD than in age-matched healthy controls [2]. As such, developing effective strategies for fall prevention is essential for improving quality of life and daily functioning among the HD population.

Exercise therapy may effectively mitigate fall risk in older adults, as demonstrated in a recent meta-analysis [3]. However, a 2018 report by the US Preventive Services Task Force indicated that exercise was associated with a "non-significant reduction in falls" [4], while other studies have shown no effect of exercise interventions on fall risk among older participants with a history of falls [5, 6]. Thus, whether such interventions are effective in older adults with a high risk of falls, such as those undergoing HD, remains controversial given the dearth of available evidence.

Evidence from some meta-analytic studies indicates that intradialytic exercise can improve physical function [7] and reduce the incidence of adverse events requiring hospitalization among patients undergoing HD when compared with controls [8]. Another study reported better prognosis among those who had completed the exercise program than among those who had not in a cohort of patients with CKD, non-dialysis CKD, HD, peritoneal dialysis, and kidney transplant [9]. However, there is no evidence regarding the effectiveness of intradialytic exercise for fall prevention in older patients undergoing HD. In the present study, we aimed to evaluate the hypothesis that intradialytic exercise can reduce the occurrence of falls and improve physical function in these patients.

Patients and methods

Study participants

We evaluated the eligibility of all patients who regularly attended the outpatient HD unit of Sanaru Sun Clinic, Japan, in July 2018. The inclusion criteria were as follows: (a) age $\geq$ 70 years; (b) undergoing maintenance HD therapy for 4 h, three times per week; (c) on HD for > 6 months; and (d) independently ambulatory without assistive equipment. The exclusion criteria were as follows: (a) lower-limb amputation, (b) motor paralysis due to central nervous system disease, (c) cognitive dysfunction, and (d) refusal to provide consent to participate. All patients were invited to participate in the intradialytic exercise program; however, only patients who agreed to perform exercise were assigned to the exercise group, while those who did not were assigned to the control group. Additionally, patients who were initially assigned to the control group and voluntarily began exercising during the study period were excluded from the analysis.

All procedures were approved by the Human Research Ethics Committee of Seirei Christopher University, and written informed consent was obtained from all participants (approval number: 20066). This study was retrospectively registered with the University Hospital Medical Information Network (UMIN 00044821, February 4, 2021).

Intervention

During the 3-year study period, intradialytic exercise sessions were conducted three times per week during the first half of the HD session and included three sets of warm-up exercises, as well as aerobic and resistance exercises. Exercise was performed with the participant in the supine position. Aerobic exercise was performed for 30 min using a cycle ergometer (Terasu ergo, Showa Denki Co. Ltd., Osaka, Japan) at an intensity of 11–13 (somewhat hard) on the Borg rating of perceived exertion scale. Resistance exercise consisted of four exercises performed using an elastic tube (TheraBand Resistance Band Loops, THERABAND, Akron, OH, USA): leg extension, straight leg raises, hip abduction, and hip flexion. The stiffness of the tube was adjusted to achieve a target intensity of 13 on the Borg scale. Participants completed two to three sets of each resistance exercise, with each set consisting of 10 repetitions. The exercise protocols were based on those adopted in previous studies [10] and were designed by a physical therapist, and all sessions were supervised by a nurse. The control group received standard HD care.

Data collection

Patient characteristics and physical function were assessed at baseline, and physical function was reevaluated each year in the exercise group. All patients underwent follow-up until the first fall or the end of the study period (December 31, 2021). Fall occurrences were investigated via interviews during each dialysis session.

The clinical data collected before HD included age, sex, height, dry weight, body mass index (BMI), HD vintage, comorbidities, medication use, and levels of the following laboratory values: serum phosphorus, calcium, potassium, hemoglobin, and C-reactive protein. Kt/V was used as an index of dialysis adequacy. Nutritional status was assessed using the Geriatric Nutritional Risk Index (GNRI). GNRI was calculated by incorporating serum albumin levels, body weight, and height by modifying the nutritional risk index for older patients. The GNRI equation is as follows:

$$\mathrm{GNRI} = [14.89 \times \mathrm{albumin}(\mathrm{g/dL})] + [41.7 \times (\mathrm{body\ weight/ideal\ body\ weight})]$$

Bodyweight/ideal body weight was set to 1 when the patient's body weight exceeded the ideal body weight [11].

Physical function was assessed based on handgrip strength, lower extremity muscle strength (LES), 10-m walk speed, and Short Physical Performance Battery (SPPB) results. Handgrip strength was measured using a handgrip dynamometer (Grip-D T.K.K.5401; Takei Scientific Instruments, Nigata, Japan) with participants in the standing position and with arms at their sides. Grip strength was measured twice on each side at maximum effort. The results were recorded in kilograms to the nearest 0.1 kg as read from the digital display of the dynamometer, and the maximum value was used for analysis. LES was assessed using a handheld dynamometer (Mobie, Sakai Medical Corp., Tokyo, Japan) with the patient seated in a chair with the knees flexed at 90°, and the dynamometer pad was attached perpendicular to the leg immediately above the ankle. Patients were instructed to push against the dynamometer pad by attempting to straighten their knees for 5 s. Isokinetic knee extensor strength was measured twice on each side, and the highest values for the right and left legs were averaged. The values were standardized by dividing them by the dry weight. In addition, 10-m walking speed was measured with the patients walking at a comfortable pace on a 14-m walking course (2 m added before and after to account for acceleration/deceleration). The SPPB score includes the following three components: balance, gait speed, and lower-limb force, with scores for each component ranging from 0 to 4 points. In this study, the final score was calculated as the sum of the three test scores, ranging from 0 to 12 points.

Statistical analysis

Missing data related to baseline characteristics were complemented using a multiple assignment method based on the missing-at-random assumption to minimize bias [12]. Multiple assignment was performed using the missing value option in IBM SPSS. All data were tested for normality using the Shapiro–Wilk test. Normally distributed data are presented as the mean ± standard deviation, while non-normally distributed data are presented as medians and ranges. Between-group differences at baseline were compared using unpaired t tests, Mann–Whitney U tests, Chi-square tests, or Fisher's exact tests. The relationship between fall occurrences, fracture, or death and the intradialytic exercise intervention was investigated via Kaplan–Meier analysis with the log-rank test. All patients who continued the exercise program for at least six months were included in the survival analysis (exercise group). Additionally, between-group differences at each time point were evaluated using multiple comparison tests only for patients who completed the 3-year exercise program. All analyses were performed using IBM SPSS for Windows ver. 21 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

Results

Among 86 patients assessed for eligibility, 14 were excluded due to the need for assistance with walking, while 3 were excluded for medical reasons, resulting in 31 and 38 patients in the exercise and control groups, respectively. Eight patients of the control group were excluded from the analysis because they started the exercise program after allocation at their request. Therefore, 61 patients (31 in the exercise group and 30 in the control group) were included in the final analysis (Fig. 1). There were no significant differences in age, handgrip strength, LES, 10-min walking speed, SPPB score, or other laboratory values between the exercise and control groups at baseline (Table 1).

In the exercise group, all patients continued the program for at least 6 months. The number of patients who continued to exercise was 25 (80.6%) at 1 year, 21 (67.7%) at 2 years, and 18 (58.1%) at 3 years, and the median duration of exercise was 3 years (interquartile range [IQR]: 1.25–3 years). There were no adverse events associated with intradialytic exercise. Over a median follow-up of 35 months (IQR: 22–35 months), 10 (16.3%) falls occurred, including 1 (3.2%) in the exercise group and 9 (30%) in the control group. Follow-up was terminated for reasons other than falls in 11 cases of deaths (5 in the exercise and 6 in the control group) and 4 cases of transfers (all in the control group). In the control group, the causes of death were 1 case of heart failure, 1 case of bloody bowel discharge, 1 case of mesenteric artery occlusion, and 2 cases of unknown causes. In the exercise group, the causes of death were 2 cases of heart failure, 1 case of gastrointestinal bleeding, 1 case of gallstone, 1 case of suicide, and 1 case of unknown cause.

Three patients (10%) in the control group had femoral neck, lumbar compression, and rib fractures, respectively. No fractures were observed in the exercise group. Kaplan–Meier analysis revealed that the exercise intervention significantly reduced the incidence of falls

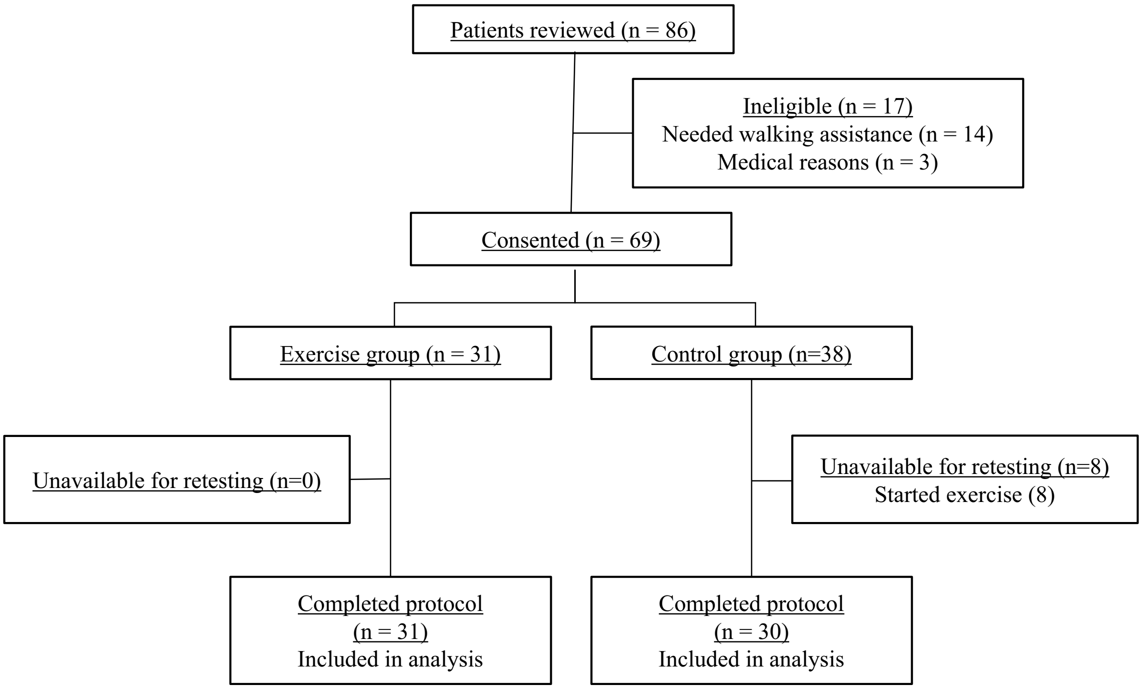

Fig. 1 Flowchart of patient selection

($p < 0.05$) but not that of fractures ($p = 0.08$) and death ($p = 0.63$) (Fig. 2).

Among the 18 patients who completed 3 years of exercise, handgrip strength values were 24.6 ± 6.6, 23.8 ± 8.3, 22.5 ± 7.7, and 22.3 ± 7.1 kg at baseline, 1 year, 2 years, and 3 years, respectively. The respective values for LES were 40 ± 9.7, 37 ± 14, 42.5 ± 10.9, and 36.6 ± 14.3%; those for 10-m walking speed were 1.5 ± 0.5, 1.3 ± 0.3, 1.3 ± 0.3, and 1.3 ± 0.3 m/s; and those for the SPPB were 12 (10.25–12), 12 (12–12), 12 (11–12), and 11 (9–12) points. The exercise group exhibited no significant differences in physical function among the measurement time points in the multiple comparison analyses (Fig. 3).

Discussion

Given rapid aging of the global population, preventing adverse events such as falls is essential for preserving functional capacity and quality of life among older patients, especially those at high risk due to HD treatment. Some prospective randomized controlled trials have examined the effect of exercise therapy on the incidence of adverse events in patients receiving HD, reporting reduced rates of hospitalization [8] and improved survival in the exercise only group [9]. However, these studies did not mention the effect of older age on adverse events and falls associated with intradialytic exercise. To our knowledge, this is the first prospective interventional study of a long follow-up period to demonstrate the effect of intradialytic exercise on fall occurrence in older patients undergoing HD. As this intervention is highly accessible and easily maintained, the current findings demonstrate the potential clinical value of intradialytic exercise programs in this population.

Patients undergoing HD experience a high incidence of falls, reaching rates of up to 24.4% [13], 25% [14], and 37.4% [15] over 1 year in previous studies. Notably, fall rates were relatively lower in our study (9.4% overall and 20.6% of controls at 3 years), which may be due to differences in the methods used to record fall occurrences. In many prospective observational studies, falls are reported daily using a fillable calendar. As we recorded the number of falls based on interviews conducted during dialysis sessions, some events may have gone unrecorded. However, a previous study reported that falls resulting in fractures were observed in 15% of patients at 1 year [16]. In other studies, serious fall-related injuries were observed in 7.6% [17] and 19% of patients [1] at 1 year, 7.6% of patients at 2 years [18], and 12.6% of patients at 9.9 years [19]. Thus, the fracture rate in this study (10% at 3 years) did not seem to be lower than that reported in previous studies.

According to a previous study, rates of fall-related injuries may be higher among younger patients who do not require assistance with activities of daily living during dialysis initiation periods [20]. Another study reported that the number of falls increased with medium- to

Table 1 Patient characteristics

	All ($n=61$)	Control ($n=30$)	Exercise ($n=31$)	p
Age (years)	76.2 ± 5.8	75.5 ± 5.4	76.9 ± 6.1	0.36
Sex (male/female (*n*))	39/22	22/8	17/14	0.13
Height (cm)	156.3 ± 10	154.3 ± 10.3	158.5 ± 9.4	0.1
Dry weight (kg)	53.5 ± 11.9	51.5 ± 11.2	55.6 ± 12.4	0.17
BMI (kg/m^2)	21.5 ± 3.4	21.4 ± 2.9	21.7 ± 3.9	0.74
HD vintage (months)	52.6 (22.2–110.3)	53.5 (32.7–96.8)	48.1 (9.3–118.9)	0.41
Disease (*n*(%))				
Chronic glomerulonephritis	22 (36.1)	11 (36.7)	11 (35.5)	0.92
Diabetes	17 (27.9)	9 (30)	8 (25.8)	0.71
Nephrosclerosis	16 (26.2)	8 (26.7)	8 (25.8)	0.94
Others	6 (9.8)	2 (6.7)	4 (12.9)	
Laboratory data				
Alb (g/dL)	3.8 ± 0.3	3.8 ± 0.3	3.8 ± 0.3	0.38
GNRI	95.6 ± 5.6	95.5 ± 5.8	95.8 ± 5.4	0.86
P (mg/dL)	5.5 ± 1.6	5.4 ± 1.6	5.6 ± 1.7	0.67
Ca (mg/dL)	8.6 ± 0.8	8.5 ± 0.8	8.8 ± 0.8	0.18
K (mEq/L)	4.6 ± 0.8	4.5 ± 0.9	4.8 ± 0.7	0.09
PTH-intact (pg/mL)	183.3 ± 119.2	178.5 ± 102.6	188.2 ± 135.9	0.75
Hb (g/dL)	10.9 ± 0.9	10.8 ± 1	11 ± 0.7	0.37
CRP (mg/dL)	0.4 ± 0.6	0.4 ± 0.6	0.4 ± 0.7	0.97
Kt/V	1.6 ± 0.3	1.6 ± 0.3	1.5 ± 0.3	0.62
Physical function				
Handgrip strength (kg)	23.5 ± 7.5	22.9 ± 6.9	24.1 ± 8.2	0.52
LES (%)	35.9 ± 12.4	34.5 ± 11.7	37.3 ± 13.2	0.39
10-m walking speed (m/s)	1.3 ± 0.4	1.3 ± 0.5	1.3 ± 0.4	0.88
SPPB (points)	11 (9–12)	11 (9–12)	11 (9–12)	0.78

Results are reported as means ± standard deviations or medians (interquartile range)

BMI body mass index, *HD* hemodialysis, *Alb* serum albumin, *GNRI* geriatric nutritional risk index, *P* serum phosphorus, *Ca* serum calcium, *K* serum potassium, *Hb* hemoglobin, *CRP* C-reactive protein, *LES* lower extremity muscle strength, *SPPB* Short Physical Performance Battery

high-intensity physical activity among patients with no limitations in daily mobility [21]. These studies suggest that older patients undergoing HD may be less likely to fall because of low physical activity levels. Nonetheless, the above data indicate that fracture risk may be higher in older patients, highlighting the need to adopt strategies for fall prevention.

Falls exhibit a complex pathological relationship with several indicators of physical health, such as muscle strength and exercise capacity [2], gait speed [22], and frailty [15]. In addition to physical function, previous studies have shown that falls among patients undergoing HD are associated with age [1, 23], sex [15], comorbidity [1], diabetes [15, 23], and psychosocial domains such as depressive symptoms and social participation [2]. Currently, the most common interventions known to effectively reduce fall risk in community-dwelling people involve modifications of the home environment to reduce the probability of falls, discontinuing use of psychotropic medications, increasing exercise frequency, and providing supplementation for older adults with vitamin D deficiency [24]. Critically, some systematic reviews have reported that exercise can reduce the fall rate by 23% [25], although other studies have shown no effect of such interventions in older adults with a history of falls [5, 6], highlighting the need for further research focused on fall prevention in the HD population.

Our pilot study results may accumulate small evidence that intradialytic exercise may reduce falls, apart from long-term improvements in physical function. Although intradialytic exercise is thought to improve physical function, its effects in older patients remain unknown. One meta-analysis demonstrated an effect of intradialytic exercise mainly in middle-aged patients but no effect in older patients undergoing HD [26]. Another study reported no improvements in physical function after 1 year of intradialytic exercise among older patients with HD, although decreases in physical function were observed in the control group [27]. In a similar study, the authors reported no significant

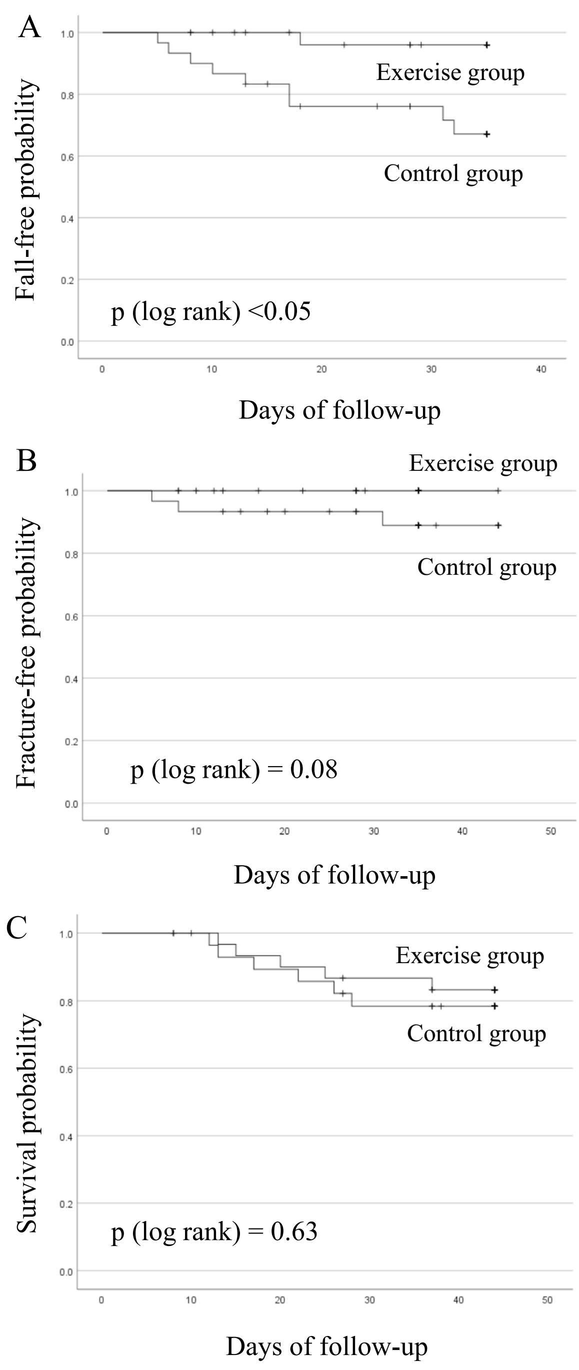

Fig. 2 Kaplan–Meier analysis of falls-fee provability (**A**), fractures-free provability (**B**), or survival provability (**C**) in the exercise and control groups

differences between the intradialytic exercise and control groups in terms of physical function or physical activity at either 12 or 24 months [28]. Our results are in accordance with these previous studies, suggesting that long-term exercise therapy exerts a limited effect on physical function in older adults undergoing HD. However, the results of this study on physical function are limited due to the absence of comparison with a non-exercise group. Therefore, further verification of the effectiveness of intradialytic exercise on physical function for older patients should include a comparison with non-exercise groups, and the assessment of effectiveness should consider indicators other than physical function.

Although the reasons underlying this decrease in fall incidence without an improvement in physical function remain unknown, a previous meta-analysis also reported a reduction in falls despite no significant group differences in balance or LES [29]. Similarly, a randomized clinical trial investigating the effects of a tai chi intervention reported reduced falls among older adults without group differences in balance or gait speed [30]. Together, these findings suggest that significant reductions in the fall rate can be observed without significant improvements in physical performance. As fall prevention represents an important treatment target in older patients undergoing HD, intradialytic exercise interventions that are effective in reducing fall risk may have great clinical value in this population.

This study had some limitations. First, as mentioned above, this study had a low fall rate. Although our analysis indicated that exercise significantly reduced the occurrence of falls, the true incidence of falls in the population and the rate of reduction due to exercise could not be calculated, necessitating further research. Second, selection bias was inherent because patients were assigned to groups in a non-randomized fashion, as patients were placed in the exercise group if they voluntarily requested inclusion. Positive feelings toward exercise in this group likely exerted a non-negligible impact on outcomes. Third, assessments of physical function in the control group and quality of life were not performed, and further research is required to analyze the long-term effects of intradialytic therapy relative to standard HD treatment. Fourth, this study did not consider the effects of bone density, history of osteoporosis, sleeping pills, or other medications that affect falls and fractures. These are important confounding factors that may affect the results. Finally, the results of this study have limited generalizability because of its single-center design and small sample size.

In conclusion, the current study may accumulate small evidence that intradialytic exercise might reduce fall occurrences in older patients undergoing HD, apart from long-term improvements in physical function. Intradialytic exercise may represent an essential intervention for preventing falls in this population.

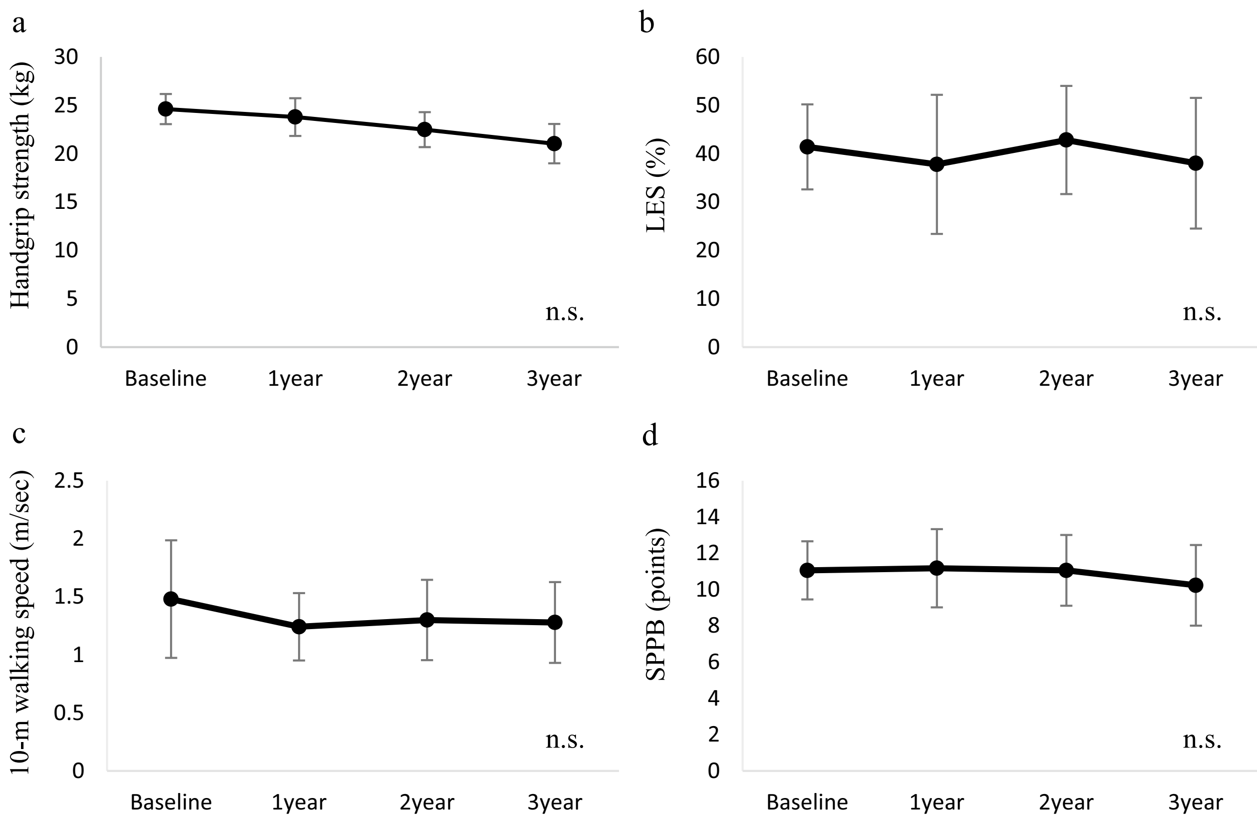

Fig. 3 Changes in physical function in patients who completed 3 years of intradialytic exercise ($n = 18$). **a** Handgrip strength; **b** LES; **c** 10-m walking speed; **d** SPPB. *LES* lower extremity muscle strength, *SPPB* Short Physical Performance Battery; *n.s.* not significant. There were no significant differences in any variables among the measurement points

Conclusion

The current study demonstrated that intradialytic exercise reduces fall occurrences in older patients undergoing HD without improving physical function. Intradialytic exercise may represent an essential intervention for preventing falls in this population.

Abbreviations

HD	Hemodialysis
CKD-MBD	Chronic kidney disease with mineral and bone disease
CKD	Chronic kidney disease
BMI	Body mass index
GNRI	Geriatric Nutritional Risk Index
LES	Lower extremity muscle strength
SPPB	Short Physical Performance Battery
IQR	Interquartile range

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Author contributions

H.Y and K.K were involved in research idea and study design; H.Y, A.S, H.S, and Y.I helped in data acquisition; H.Y and T.Y contributed to data analysis/interpretation; H.Y and T.Y were involved in statistical analysis; Y.Y and H.A helped in supervision or mentorship. Each author contributed important intellectual content during manuscript drafting and revision, agreed to be personally accountable for the individual's contributions, and to ensure questions about the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

All procedures were approved by the Human Research Ethics Committee of Seirei Christopher University, and written informed consent was obtained from all participants (Approval No. 20066). This study was retrospectively registered with the University Hospital Medical Information Network (UMIN 00044821, February 4, 2021).

Consent for publication

Not applicable.

Competing of interests

All the authors have declared that no conflict of interest exists.

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