Original Paper

The Clinical Significance of Physical Activity in Maintenance Dialysis Patients

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Key Words

Physical activity • Quality of life • Peritoneal dialysis • Hemodialysis • Frailty • Disability • Exhaustion

Abstract

Background: The aim of the present study was to evaluate the effects of physical activity on various aspects in Asian dialysis patients. **Methods:** This was a retrospective cohort study. Study participants were recruited from 27 hospitals or dialysis centers in Korea (n = 1611). The participants were divided into 3 groups according to the degree of regular exercise: Inactive group, Intermediate group, and Active group. **Results:** The proportions of patients with frailty and the presence of each component decreased as physical activity increased. The presence and numbers of disabilities decreased as physical activity increased. The number of participants with a history of fall during the last 12 months was 149 (20.5%) in the Inactive group, 88 (16.9%) in the Intermediate group, and 48 (13.2%) in the Active group. Physical component scale and mental component scale scores increased as physical activity increased. The survival rate for all-cause death at 500 days was 95.5% in the Active group, 95.2% in the Intermediate group, and 93.5% in the Inactive group. **Conclusion:** High physical activity was associated with favorable results for most health-related quality of life scale scores, including frailty, disability, and exhaustion, in Korean dialysis patients.

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Published by S. Karger AG, Basel

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Introduction

Dialysis patients are particularly susceptible to decreased health-related quality of life (HRQoL) or physical performance compared with patients who undergo kidney transplantation [1-4]. Therefore, many studies have focused on these issues in dialysis patients. Previous studies showed that various factors including anemia, malnutrition, and metabolic disturbances are associated with HRQoL or physical performance; however, there has not been much improvement in these problems [6-8]. Further investigations of new risk factors or proper interventions are needed to improve HRQoL or physical performance in dialysis patients.

Physical activity is a well-known factor that improves HRQoL, physical performance, and other clinical outcomes in the general population [9]. Physical inactivity is associated with an imbalance of energy expenditure that can increase comorbidities, such as hypertension, diabetes mellitus (DM), coronary artery disease (CAD), and depressive mood, which can aggravate such issues [9]. Considering these associations in the general population, physical activity in patients with chronic kidney disease (CKD) can also be associated with improvements in these issues. In addition, Kielstein et al. investigated the association between physical activity and endogenous nitric oxide inhibitor asymmetric dimethylarginine (ADMA) as a uremic toxin even without comorbidities [10]. They showed that ADMA infusion alone without CKD significantly decreased brain-derived neutrophic factors and physical activity. These reveal that patients with CKD are inherently at risk of decreased physical activity regardless of various comorbidities.

Barcellos et al. reviewed the effects of exercise in patients in various CKD stages [11]. For dialysis patients, exercise significantly improved oxygen peak consumption and strength. The association between exercise and C-reactive protein (CRP) level or HRQoL was not consistent. For non-dialysis patients, exercise significantly improved oxygen peak consumption and HRQoL. However, the association between exercise and CRP level or progression of CKD was also not consistent. Most included studies enrolled only dialysis patients. The effect of exercise in dialysis patients had relatively strong evidences, but not in pre-dialysis patients.

Previous studies showed favorable effects of physical activity in dialysis patients; however, these have mainly focused on Western populations or mortality only [12-23]. Few studies have comprehensively assessed the effects of physical activity on various factors, including HRQoL, frailty, disability, exhaustion, and mortality, in Asian populations. The aim of the present study was to evaluate the effects of physical activity on these various aspects in Asian dialysis patients.

Patients and Methods

Study population

The study participants were initially enrolled in a previous study [24]. Briefly, study participants were recruited from 27 hospitals or dialysis centers in Daegu/Kyungsangpook-do between July and December 2012. A total of 2737 participants who underwent dialysis were included. Participants were excluded from the present study if they met the following criteria: age < 20 years (n = 12), hospitalization during the previous 3 months except for vascular access problems (n = 351), dialysis duration < 6 months (n = 164), inability to walk with or without an assistive device (n = 79), lack of laboratory findings (n = 117), refusal to participate (n = 254), or inability to communicate with interviewers (n = 149). As a result, 1611 participants were ultimately included in this study. There were no dialysis units to encourage exercise during the dialysis session. The hospital's ethics committee approved the study protocol, and the study was conducted in accordance with the principles originating from the Declaration of Helsinki.

Study variables

Demographic and laboratory data collected at enrollment included the following: age, sex, body mass index (BMI; kg/m²), DM, CAD, cerebrovascular disease (CVD), dialysis vintage (years), education level, and levels of hemoglobin (mg/dL), blood urea nitrogen (BUN; mg/dL), creatinine (mg/dL), calcium (mg/dL), phosphorus (mg/dL), total cholesterol (mg/dL), intact-parathyroid hormone (i-PTH; pg/mL), and high-sensitivity CRP (hs-CRP; mg/dL). DM was defined as a self-reported history and medical record of DM diagnosis or a fasting glucose level ≥ 126 mg/dL. CAD was defined as a self-reported history and medical record of angina, myocardial infarction, or congestive heart failure. CVD was defined as a self-reported history and medical record of stroke. All-cause and cardiovascular mortalities up to December 2014 were retrieved from the patients' medical records.

Assessment of HRQoL scale scores

HRQoL was assessed by the Kidney Disease Quality of Life (KDQOL)-SF™ 1.3 Korean version [25]. KDQOL-SF™ 1.3 includes the SF-36 scale (36 items) and kidney disease-specific scale (11 items). The SF-36 includes the following 8 domains: physical functioning (PF), role limitations due to physical health problems (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), mental health (MH), and overall health rating (OHR). A total score of 0–100 is calculated for each domain. A low score indicates a low quality of life. These scales have been used to calculate the physical component scale (PCS) and mental component scale (MCS) [26, 27]. The 11 kidney disease-specific items consist of symptom/problem, kidney disease effects, kidney disease burden, work status, cognitive function, quality of social interaction (QSI), sexual function, sleep, social support, patient satisfaction, and dialysis staff encouragement. Questionnaires were completed during the dialysis session.

Definitions

We evaluated disability using 4 questions regarding activities of daily living (ADLs) to assess whether the participants currently needed help from another person to have a meal, dress/undress, get in or out of bed, or take a bath or shower. For each question, they answered one of 3 responses: no help needed, some help needed, or complete help needed. Disability was defined as the inability to perform at least one of the 4-ADL domains without help [28].

Exhaustion was measured using 2 questions from the Center for Epidemiological Studies Depression Scale [29]: (1) I felt that everything I did was an effort; and (2) I could not get going. The question asked was: "How often did you feel this way?" The answer was rarely or none of the time, some or a little of the time, a moderate amount of the time, or most of the time. The participants answering moderate or most of the time to either or both of the 2 questions were identified as having exhaustion. A fall was defined as an event that resulted in a participant coming to rest unintentionally on the ground or a lower level with or without losing consciousness during the last 12 months. Serious falls were defined as head injury requiring hospitalization, joint dislocations, severe sprains, or a laceration requiring sutures [30].

Physical activity was defined as the presence of regular exercise during leisure time for the past 3 months. The participants were divided into 3 groups according to exercise amount. The Active group was defined as engaging in moderate activity for > 30 min/day for 5 days a week or at a high intensity for > 20 min/day for 3 days a week [9]. The Inactive group was defined as engaging in physical activity < 1 time per week during their leisure time for the previous 3 months. The Intermediate group was defined as participants whose activity levels were between those of the Inactive and Active groups. Most of the participants in the Inactive group provided the following causes of their low physical activity: pain, fatigue, lack of will to exercise, depressive mood, lack of time to exercise, unsure how to exercise, unsure about the importance of exercise, lack of equipment or place to exercise, and fear of injury. Participants answered non-open questions and chose from multiple choices.

Frailty was defined using modified criteria previously described elsewhere [31]. Components included slowness, poor endurance, physical inactivity, and unintentional weight loss. Slowness and poor endurance were determined by the PF scale of the SF-36 (2 points for PF scale < 75) and the VT scale of the SF-36 (1 point for VT scale < 55), respectively. Participants who were physically inactive were classified into the Inactive group (1 point for physical inactivity). Unintentional weight loss was defined as unintentional body weight loss > 4.5 kg or 5% of the baseline value over the past year (1 point for weight loss). All points of

Table 1. Participants' clinical characteristics

	Inactive (n = 728)	Intermediate (n = 520)	Active (n = 363)	P-value
Age (years)	55.0 ± 14.0	56.1 ± 12.2	57.3 ± 11.6*	0.021
Sex (male, %)	378 (51.9%)	282 (54.2%)	240 (66.1%)	0.000
Body mass index (kg/m ²)	22.5 ± 3.5	22.2 ± 3.0	22.2 ± 2.9	0.155
Diabetes mellitus (%)	274 (37.6%)	209 (40.2%)	154 (42.4%)	0.293
Coronary artery disease (%)	120 (16.5%)	75 (14.4%)	59 (16.3%)	0.591
Cerebrovascular disease (%)	58 (8.0%)	49 (9.4%)	37 (10.2%)	0.428
Dialysis vintage (years)	5.4 ± 4.8	5.1 ± 4.3	4.8 ± 4.1	0.118
Education level				0.050
≤ 6 th grade	180 (24.7%)	97 (18.7%)	76 (20.6%)	
7 th – 12 th grade	142 (19.5%)	96 (18.5%)	80 (22.0%)	
> 12 th grade	406 (55.8%)	327 (62.9%)	207 (57.0%)	
Hemoglobin (mg/dL)	10.4 ± 1.0	10.5 ± 0.9	10.5 ± 0.8	0.665
Serum albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.4	3.8 ± 0.4	0.073
Blood urea nitrogen (mg/dL)	56.6 ± 15.3	60.0 ± 14.6	61.0 ± 15.1	0.329
Creatinine (mg/dL)	10.4 ± 2.9	10.5 ± 3.1	10.6 ± 3.0	0.515
Calcium (mg/dL)	8.7 ± 0.8	8.7 ± 0.8	8.7 ± 0.8	0.512
Phosphorus (mg/dL)	5.4 ± 1.4	5.3 ± 1.3	5.2 ± 1.3	0.181
Total cholesterol (mg/dL)	154.5 ± 36.5	153.6 ± 36.9	153.6 ± 39.3	0.886
Intact parathyroid hormone (pg/mL)	314.5 ± 424.7	255.7 ± 271.2*	234.0 ± 220.9*	0.000
Dialysis modality (hemodialysis, %)	567 (77.9%)	414 (79.6%)	266 (73.3%)	0.079
High sensitivity C-reactive protein (mg/dL)	0.73 ± 1.39	0.72 ± 2.08	0.54 ± 1.36	0.397

Data are expressed as numbers (percentages) for categorical variables and mean ± standard deviations for continuous variables. P values were tested by one-way analysis of variance, followed by a post-hoc Tukey comparison for continuous variables and Pearson's χ^2 or Fisher's exact tests for categorical variables. *P < 0.05 versus the Inactive group.

scoring of each frailty component were summed. Those participants with ≥ 3 points, 1 or 2 points, and 0 points were defined as having frailty, pre-frailty, and non-frailty, respectively.

Statistical analyses

The data were analyzed using the statistical software SPSS version 21 (Chicago, IL, USA). Categorical variables were expressed as both counts and percentages. Continuous variables were expressed as mean ± standard deviation (SD) or mean ± standard error (SE). The Pearson's χ^2 or Fisher's exact test was used to analyze categorical variables. For continuous variables, means were compared using the *t*-test or analysis of variance, followed by a post-hoc Tukey comparison. The survival estimates were calculated using Kaplan-Meier curves. Multivariate analysis was performed using analysis of covariance. For analysis of covariance, the covariates were age, sex, BMI, education level, dialysis vintage, DM, CVD, CAD, serum albumin level, i-PTH level, and dialysis modality. The level of statistical significance was set at *P* < 0.05.

Results

Participants' clinical characteristics

The number of participants in the Inactive, Intermediate, and Active groups was 728, 520, and 363, respectively (Table 1). The numbers of participants with hemodialysis (HD) and peritoneal dialysis (PD) were 364 (22.6%) and 1247 (77.4%), respectively. Among the HD patients, the numbers of participants who underwent 2 and 3 HD sessions/week were 77 (6.2%) and 1170 (93.8%), respectively. The numbers of participants who underwent 2 HD sessions/week were 29 (5.1%) in the Inactive group, 29 (7.0%) in the Intermediate group, and 19 (7.1%) in the Active group (*P* = 0.464). The most common dialysis modality in our study was HD and most of these participants underwent 3 HD sessions/week. There were no significant differences in dialysis modality or frequency of HD session among the 3 groups.

In the patients in the Inactive group, the most common cause of physical inactivity was unwillingness to exercise (302 participants, 41.5%). The numbers of participants who cited fatigue, lack of time to exercise, pain, unsure how to exercise, depressive mood, fear of injury, lack of equipment or place to exercise, and unsure about the importance of exercise were 287 (39.4%), 186 (25.6%), 185 (25.4%), 72 (9.9%), 62 (8.5%), 49 (6.7%), 41 (5.6%), and 24

(3.3%), respectively. We have divided the participants in the Inactive group into those with unwillingness only (n = 130) and others (n = 598). Comparison of clinical characteristics is shown in Table 2. Participants with unwillingness only had a younger age and higher education levels than those in others.

Table 2. Clinical characteristics according to the cause of physical inactivity

	Unwillingness only (n = 130)	Others (n = 598)	P-value
Age (years)	50.4 ± 12.4	56.0 ± 14.1	0.000
Sex (male, %)	66 (50.8%)	312 (52.2%)	0.423
Body mass index (kg/m ²)	22.3 ± 3.1	22.6 ± 3.6	0.260
Diabetes mellitus (%)	48 (36.9%)	226 (37.8%)	0.468
Coronary artery disease (%)	16 (12.3%)	104 (17.4%)	0.097
Cerebrovascular disease (%)	7 (5.4%)	51 (8.5%)	0.153
Dialysis vintage (years)	5.4 ± 5.5	5.4 ± 4.6	0.972
Education level			0.001
≤ 6 th grade	18 (13.8%)	162 (27.1%)	
7 th – 12 th grade	22 (16.9%)	120 (20.1%)	
> 12 th grade	90 (69.2%)	316 (52.8%)	
Hemoglobin (mg/dL)	10.4 ± 0.9	10.5 ± 1.0	0.533
Serum albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.4	0.894
Blood urea nitrogen (mg/dL)	58.2 ± 13.8	59.9 ± 15.6	0.235
Creatinine (mg/dL)	10.5 ± 3.0	10.3 ± 2.9	0.524
Calcium (mg/dL)	8.8 ± 0.8	8.7 ± 0.9	0.607
Phosphorus (mg/dL)	5.3 ± 1.1	5.4 ± 1.4	0.658
Total cholesterol (mg/dL)	153.7 ± 35.2	154.7 ± 36.8	0.762
Intact parathyroid hormone (pg/mL)	322.0 ± 533.3	312.9 ± 397.7	0.854
Dialysis modality (hemodialysis, %)	96 (73.8%)	471 (78.8%)	0.135
High sensitivity C-reactive protein (mg/dL)	0.82 ± 1.53	0.70 ± 1.35	0.561

Data are expressed as numbers (percentages) for categorical variables and mean ± standard deviations for continuous variables. P-values were tested by the *t*-test for continuous variables and Pearson's χ^2 or Fisher's exact tests for categorical variables.

Comparison of frailty and disability by physical activity level

The numbers of participants with pre-frailty and frailty were 343 (47.1%) and 384 (52.7%) in the Inactive group; 246 (47.3%) and 119 (22.9%) in the Intermediate group; and 152 (41.9%) and 54 (14.9%) in the Active group, respectively ($P < 0.001$). For each frailty component, the numbers of participants with slowness, poor endurance, and unintentional weight loss were 348 (47.8%), 560 (76.9%), and 91 (12.5%) in the Inactive group; 147 (28.3%), 325 (62.5%), and 42 (8.1%) in the Intermediate group; and 65 (17.9%), 182 (50.1%), and 32 (8.8%) in the Active group, respectively ($P < 0.001$ for slowness, $P < 0.001$ for poor endurance, and $P = 0.024$ for unintentional weight loss). The proportions of patients with frailty and the presence of each component decreased as physical activity increased.

The proportions of participants with disability in the Inactive, Intermediate, and Active groups were 171 (23.5%), 93 (17.9%), and 40 (11.0%), respectively (Fig. 1A; $P < 0.001$). The mean numbers of disabilities (means ± SE) were 0.46 ± 0.04 in the Inactive group, 0.33 ± 0.04 in the Intermediate group, and 0.18 ± 0.03 in the Active group ($P < 0.001$). The multivariate analysis showed similar results (0.48 ± 0.03 in the Inactive group, 0.32 ± 0.04 in the Intermediate group, and 0.15 ± 0.04 in the Active group; $P < 0.001$). The presence and numbers of disabilities decreased as physical activity increased.

Comparison of exhaustion and falls by physical activity level

The proportions of participants with exhaustion in the Inactive, Intermediate, and Active groups were 262 (36.0%), 132 (25.4%), and 77 (21.2%), respectively ($P < 0.001$). The numbers of exhaustion (means ± SE) were 0.55 ± 0.03 in the Inactive group, 0.37 ± 0.03 in the Intermediate group, and 0.31 ± 0.03 in the Active group (Fig. 1B, $P < 0.001$). The multivariate analysis showed similar results (0.56 ± 0.03 in the Inactive group, 0.38 ± 0.03 in the Intermediate group, and 0.30 ± 0.04 in the Active group; $P < 0.001$). The presence of exhaustion decreased as physical activity increased. The number of patients with exhaustion was higher in the Inactive group than in the other groups. The numbers of participants with a history of fall during the last 12 months were 149 (20.5%) in the Inactive group, 88 (16.9%)

Fig. 1 Comparison of the numbers of disabilities (A) or exhaustion (B) among the groups by physical activity (data are expressed as mean and standard errors). (A) The number of disabilities (Univariate: 0.46 ± 0.04 in the Inactive group, 0.33 ± 0.04 in the Intermediate group, and 0.18 ± 0.03 in the Active group; Multivariate: 0.48 ± 0.03 in the Inactive group, 0.32 ± 0.04 in the Intermediate group, and 0.15 ± 0.04 in the Active group; $P < 0.001$ for both analyses). (B) The number of exhaustion (Univariate: 0.55 ± 0.03 in the Inactive group, 0.37 ± 0.03 in the Intermediate group, and 0.31 ± 0.03 in the Active group; Multivariate: 0.56 ± 0.03 in the Inactive group, 0.38 ± 0.03 in the Intermediate group, and 0.30 ± 0.04 in the Active group; $P < 0.001$ for both analyses). * $P < 0.05$ versus the Inactive group. # $P < 0.05$ versus the Intermediate group

in the Intermediate group, and 48 (13.2%) in the Active group ($P = 0.011$). The numbers of participants with history of serious falls included 27 (3.7%) in the Inactive group, 11 (2.1%) in the Intermediate group, and 9 (2.5%) in the Active group ($P = 0.219$).

Comparison of HRQoL scale scores according to physical activity level

Table 3 shows the differences in HRQoL scale scores according to physical activity. On univariate analysis, PF, GH, VT, PCS, MCS, and QSI scores increased as physical activity increased. RP, BP, SF, MH, OHR, symptom/problems, kidney disease effects, kidney disease burden, cognitive function, sleep, social support, and dialysis staff encouragement scores were lower in the Inactive group than in the other groups. The mean RE score was higher in the Active group than in the Inactive group.

The SF-6 scale scores showed the same trends on multivariate analysis. The mean symptom/problems score was highest in the Active group. Scores for kidney disease burden, QSI, and dialysis staff encouragement were higher in the Active group than in the Inactive group. The social support score was higher in the Intermediate group than in the Inactive group.

Survival analysis by physical activity level

The survival rate for all-cause death was 99.7% at 100 days and 95.5% at 500 days in the Active group, 99.4% at 100 days and 95.2% at 500 days in the Intermediate group, and 99.9% at 100 days and 93.5% at 500 days in the Inactive group (Fig. 2A; $P = 0.232$). The survival rate for cardiovascular death was 99.7% at 100 days and 98.8% at 500 days in the Active group, 99.8% at 100 days and 98.3% at 500 days in the Intermediate group, and 100% at 100 days and 96.7% at 500 days in the Inactive group (Fig. 2B; $P = 0.064$).

Discussion

The present study was a multicenter cohort study and enrolled only relatively stable dialysis patients. The dialysis patients were divided into 3 groups by physical activity level. The most common cause of physical inactivity was unwillingness to exercise. The

Table 3. Comparison of quality of life scale scores between hemodialysis and peritoneal dialysis patients

SF-6 scale	Univariate (mean ± SD)				Multivariate (mean ± SE)			
	Inactive	Intermediate	Active	P-value	Inactive	Intermediate	Active	P-value
PF	67.3 ± 27.2	77.4 ± 20.4*	83.5 ± 15.5*#	<0.001	67.0 ± 0.7	77.3 ± 0.9*	84.4 ± 1.0*#	<0.001
RP	57.0 ± 43.2	68.7 ± 39.9*	74.3 ± 37.0*	<0.001	57.1 ± 1.5	68.2 ± 1.8*	74.8 ± 2.1*	<0.001
BP	72.5 ± 27.4	80.3 ± 22.3*	83.5 ± 24.0*	<0.001	72.9 ± 0.9	79.8 ± 1.1*	83.3 ± 1.3*	<0.001
GH	39.5 ± 21.2	46.5 ± 22.1*	50.9 ± 23.4*#	<0.001	39.5 ± 0.8	46.2 ± 1.0*	51.2 ± 1.2*#	<0.001
VT	38.7 ± 20.3	47.3 ± 19.9*	53.1 ± 21.4*#	<0.001	38.7 ± 0.7	47.0 ± 0.9*	53.5 ± 1.1*#	<0.001
SF	72.5 ± 28.9	76.5 ± 26.1*	80.0 ± 26.8*	<0.001	72.1 ± 1.0	76.5 ± 1.2*	80.8 ± 1.4*	<0.001
RE	67.1 ± 43.3	72.8 ± 40.2	75.4 ± 40.0*	0.003	67.2 ± 1.5	72.5 ± 1.8	75.7 ± 2.2*	0.004
MH	55.0 ± 20.8	61.0 ± 19.6*	63.6 ± 19.4*	<0.001	55.0 ± 0.7	60.7 ± 0.9*	63.9 ± 1.1*	<0.001
OHR	32.4 ± 26.2	40.3 ± 24.7*	43.5 ± 25.7*	<0.001	32.5 ± 0.9	40.0 ± 1.1*	43.6 ± 1.3*	<0.001
PCS	55.0 ± 21.6	64.0 ± 18.3*	69.1 ± 17.9*#	<0.001	55.0 ± 0.7	63.7 ± 0.8*	69.4 ± 1.0*#	<0.001
MCS	54.5 ± 20.6	60.8 ± 19.3*	64.6 ± 20.2*#	<0.001	54.5 ± 0.7	60.6 ± 0.9*	65.0 ± 1.0*#	<0.001
KD-specific scale								
Sx	77.2 ± 16.3	81.7 ± 13.7*	83.9 ± 12.7*	<0.001	80.6 ± 1.0	82.3 ± 1.1	88.1 ± 1.4*#	<0.001
KD effects	70.1 ± 20.2	74.5 ± 17.7*	76.8 ± 18.3*	<0.001	73.9 ± 1.3	73.9 ± 1.5	78.4 ± 1.8	0.099
KD burden	32.5 ± 25.7	36.5 ± 26.7*	38.0 ± 27.0*	<0.001	36.2 ± 2.0	37.6 ± 2.2	45.3 ± 2.7*	0.023
Work status	29.0 ± 36.0	27.7 ± 36.6	25.8 ± 36.1	0.381	42.3 ± 3.0	40.2 ± 3.3	37.8 ± 4.2	0.673
Cognitive function	83.6 ± 19.3	87.8 ± 15.3*	88.3 ± 15.6*	<0.001	88.3 ± 1.1	89.6 ± 1.2	91.8 ± 1.5	0.175
QSI	72.3 ± 22.7	76.3 ± 21.1*	80.1 ± 20.0*#	<0.001	76.5 ± 1.5	78.0 ± 1.7	83.7 ± 2.2*	0.024
Sexual function	76.3 ± 28.0	76.8 ± 25.6	80.6 ± 23.1	0.427	75.3 ± 2.0	76.7 ± 2.2	82.7 ± 2.8	0.094
Sleep	61.8 ± 21.4	65.0 ± 20.7*	66.7 ± 21.8*	<0.001	65.5 ± 1.5	66.7 ± 1.7	71.5 ± 2.2	0.072
Social support	64.3 ± 27.4	70.3 ± 26.2*	71.0 ± 26.6*	<0.001	64.3 ± 2.0	73.4 ± 2.2*	72.0 ± 2.8	0.006
Patient satisfaction	64.5 ± 23.1	66.3 ± 22.4	67.7 ± 22.7	0.077	65.4 ± 1.8	67.5 ± 2.0	69.6 ± 2.5	0.392
DSE	84.0 ± 19.8	87.4 ± 17.7*	89.1 ± 16.0*	<0.001	84.8 ± 1.4	88.3 ± 1.5	90.5 ± 1.9*	0.039

Univariate analyses were tested by one way analysis of variance, followed by a post hoc Tukey comparison. Multivariable analyses were adjusted for age, sex, body mass index, education level, dialysis vintage, diabetes mellitus, cerebrovascular disease, coronary artery disease, serum albumin level, intact-parathyroid hormone level, and dialysis modality. * $P < 0.05$ versus the Inactive group. # $P < 0.05$ versus the Intermediate group. Abbreviations: SD, standard deviation; SE, standard error; SF, short form; PF, physical functioning; RP, role limitations due to physical health problems; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role limitations due to emotional problems; MH, mental health; OHR, overall health rating; PCS, physical component scale; MCS, mental component scale; KD, kidney disease; Sx, symptom/problems; QSI, quality of social interaction; DSE, dialysis staff encouragement

Fig. 2 Kaplan-Meier curves (A, all-cause mortality; B, cardiovascular mortality).

proportions of frailty, disability, and exhaustion decreased as physical activity increased. More participants in the Inactive group had a history of falls during the last 12 months. Most of the HRQoL scale scores were highest in the Active group. No statistical significance was observed; however, the trend showed highest survival rates in the Active group.

Previous studies showed positive associations between physical activity and PCS, MCS, or survival in dialysis patients [12, 14, 15, 18]. However, those studies mainly enrolled

Western populations. Many factors, such as differences in disease burden, socioeconomic status, social support, or insurance, can influence HRQoL scale scores. Ethnicity per se is associated with differences in HRQoL results in dialysis patients [32, 33]. Therefore, further investigations are needed to identify the similarity or difference in the association between 2 variables in Korean dialysis patients compared with the results from Western dialysis patients. The present study enrolled only Korean dialysis patients. To the best of our knowledge, few studies have examined the association between physical activity and HRQoL in Korean dialysis patients. In addition, the present study enrolled only relatively stable dialysis patients and may have excluded the potential effects, such as acute medical or psychological problems, that can develop in incident dialysis patients. Our results revealed that physical activity was associated with most SF-36 components, including kidney disease burden, QSI, and dialysis staff encouragement. Our results were similar to those of previous studies. However, the survival analyses did not show statistical significance. The non-significance of the findings of the survival analyses would be associated with the relatively short follow-up period and low mortality rate owing to its enrollment of relatively stable dialysis patients. In addition, our study was a retrospective study. However, considering the intergroup differences in survival rate and Kaplan-Meier curve shapes, further studies with longer follow-up periods may reveal statistical significance in both all-cause and cardiovascular mortality rates.

There are no guidelines regarding the optimal time to evaluate HRQoL in dialysis patients, and only few studies are conducted. We believe that the optimal time to evaluate HRQoL in dialysis patients or the significant differences in HRQoL before, during, or after dialysis are very interesting issues. Most participants in our study were evaluated during dialysis sessions.

Our study investigated the cause of physical inactivity and found that the most common cause was unwillingness to exercise. Unwillingness to exercise, fatigue, lack of time to exercise, pain, unsure how to exercise, depressive mood, lack of equipment or place to exercise, and unsure about the importance of exercise may be reversible or resolvable. Of the total dialysis patients, 45.2% were included in the Inactive group; however, proper psychological or medical supports can be used to move participants from the Inactive group to the Active or Intermediate group. For example, lack of time, equipment, or place would be main a challenge of physical inactivity or exercise in dialysis patients; however, these may be overcome by exercise during dialysis sessions. Saitoh et al. have recently investigated the effects of intradialytic exercise in dialysis [34]. Their preliminary results showed that intradialytic exercise was safe and improved physical activity and malnutrition. Although further investigations are needed to identify the effects and safety of intradialytic exercise and establish protocols for exercise, intradialytic exercise may be an option to overcome physical inactivity or increase exercise in dialysis patients. In our study, the specific causes of unwillingness to exercise were not included. The purpose of our study was to evaluate the association between physical activity and various clinical outcomes in dialysis patients. Further analyses regarding specific causes of unwillingness, which were beyond the scope of our study, may be useful in future investigations.

Frailty is defined as a state of high vulnerability to adverse outcomes including disability and dependency combined with decreased body energy, protein reserve, and strength [35]. The association between physical activity and frailty is well-known. One review showed that the prevalence of frailty is approximately 24–78% in prevalent dialysis patients [36]. In our study of relatively stable dialysis patients, the prevalence of frailty was 34.6%, and those in the Inactive and Active groups were 52.7% and 14.9%, respectively. The prevalence of frailty in the total participants was similar to those of a previous report; however, there was a significant difference in this prevalence between the Inactive and Active groups.

Our study showed an association between physical activity and frailty or exhaustion. Frailty includes physical inactivity as a diagnostic criterion for frailty; thus, the comparison of physical activity and frailty may be duplicated. Endurance is a diagnostic criterion for

frailty and interchangeable with exhaustion. Therefore, we compared each component for frailty, including slowness, poor endurance, and unintentional weight loss. The proportion of participants with each component decreased as physical activity increased. In addition, considering the accuracy of the exhaustion definition, we defined exhaustion using another 2 questions drawn from the Center for Epidemiological Studies Depression Scale [29]. The Classical Center for Epidemiologic Studies Depression Scale (CESD) was created for evaluation of depressive symptoms and included a 20-item self-report measure [27]. Two items among the 20 items are associated with exhaustion [37]. Data on all items would be useful. However, we want to evaluate exhaustion rather than depression, and considering the limitations of time or effort, we have evaluated only the 2 items associated with exhaustion.

Disability is defined as difficulty or dependency in performing activities essential to independent living [38, 39]. Classical disability measurements published by Katz et al. include 6 items [40]. However, the incontinence item was highly associated with urinary incontinence and age [41]. Many authors have used modified ADL scales, including meal, dress/undress, get in or out of bed, toileting, and bathing. However, not all 5 items were sometimes asked because of limitation of time or effort [42]. Some surveys have also combined 2 similar activities, such as toileting and bathing into 1 item [26]. Our study had evaluated disability using 4 items (meal, dress/undress, get in or out of bed, and take a bath or shower) among the 6 classical items. Although the reliability or validity for the 4 items was not investigated, we think that only 4 items would be sufficient to identify the disability considering limitations of time or effort. Disability is a status that includes both social and medical entities [38]. Disability can be a cause of frailty; however, frailty can also be a risk factor for the development of disability. Disability and frailty can overlap; however, these 2 clinical entities are distinct and can exist independently [43]. Disability per se can be associated with poor clinical outcomes. Therefore, we evaluated both disability and frailty. In addition, frailty, disability, or exhaustion can be conclusively associated with development of falls in dialysis patients [44]. In our study, the proportion of participants with a history of falls during the last 12 months increased as physical activity decreased. The highest proportion of participants with a history of serious falls was found in the Inactive group; however, no statistical significance was observed.

In our study, there were older participants and higher comorbidities in the Active group than the other groups. These would misinterpret older participants and those with high comorbidities to be more physically active. However, there were no significant differences in the proportions with CAD or CVA among the 3 groups. Although statistical significance in age was obtained, we think that the mean differences in age may be not enough to induce clinical effects. In addition, the Active group had higher proportions of men than the other groups. Sex differences among the 3 groups would influence physical activity and compensate for age effects.

The present study has a few limitations. First, it was retrospective study and used participants enrolled in a previous study [24]. Second, physical activity was assessed by using only a self-reported questionnaire. This subjective method may be associated with overestimation or underestimation of physical activity. Objective methods, such as accelerometer or physical activity monitor have more clinical importance or accuracy than our method. Unfortunately, our study did not include other methods and used only a self-reported questionnaire. This is an inherent limitation of our study. However, many previous studies have also assessed physical activity using this questionnaire; WHO also defined physical activity level using this questionnaire. This may be associated with frailty, disability, or exhaustion inaccuracies. Third, data on dialysis adequacy, use of opioid, antihistamine, or antidepressant, and residual renal function were not included. We did not compare physical activity with changes in dialysis dose nor evaluate the difference in dialysis dose among the 3 groups by physical activity. Whether the dialysis of the participants was adequate or not can be associated with physical activity. KDOQI recommend $\text{spKt/V} \geq 1.2$ as a minimally adequate dialysis for HD [45]. In our study, most common dialysis modality was HD. From the 2015

Korean Registry data, spKt/V in men and women who underwent HD was 1.43 ± 0.25 and 1.71 ± 0.29 , respectively [46]. Therefore, most Korean dialysis patients, including the patients in our study, may undergo adequate dialysis. In addition, use of opioid, antihistamine, or antidepressant can be associated with decreased physical activity and cognitive function. Although our study did not evaluate these medications, all participants in our study were relatively stable dialysis patients and able to walk and communicate with the interviewer. We think that the number of participants significantly affected by these medications would be small. Fourth, the associations between physical activity and variables, including HRQoL, frailty, exhaustion, and disability were evaluated using data collected at enrollment. Analysis of the changes between data at enrollment and those at follow-up may accurately identify the associations better. A prospective study including additional parameters such as other physical performance-based measurements and follow-up data is warranted to overcome these limitations.

Conclusion

In conclusion, high physical activity was associated with favorable results for most HRQoL scale scores, including frailty, disability, and exhaustion, in Korean dialysis patients. Patients on dialysis should be encouraged to increase their physical activity, which may improve their prognosis.

Disclosure Statement

The authors declare that they have no conflict of interest.

Acknowledgements

This work was supported by the Medical Research Center Program (2015R1A5A2009124) through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning.

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