# 学位論文

Evaluation of physical activity and its relationship to health-related quality of life in patients on chronic hemodialysis

香川大学大学院医学系研究科 社会環境病態医学専攻

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# REGULAR ARTICLE

# Evaluation of physical activity and its relationship to health-related quality of life in patients on chronic hemodialysis

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#### Abstract

Objective The aim of this study was to investigate the relationship between physical activity and health-related quality of life (HRQOL) in patients on chronic hemodialysis.

Methods A total of 31 men (69.0  $\pm$  11.1 years) and 17 women (66.9  $\pm$  10.0 years) among 61 male and 30 female patients on chronic hemodialysis at Innoshima General Hospital, Onomichi, Japan, were enrolled in this cross-sectional study. Physical activity was evaluated using triaxial accelerometers. HRQOL and psychological distress were also evaluated using the EuroQol questionnaire (EQ-5D) and the K6 questionnaire, respectively.

Results Physical activity evaluated by  $\Sigma$ [metabolic equivalents  $\times$  h per week (METs·h/w)] was  $8.1 \pm 6.0$  METs·h/w, and EQ-5D score was  $0.754 \pm 0.177$ . Among all patients, EQ-5D scores were significantly correlated with physical activity over 4 METs on non-hemodialysis treatment days (r = 0.426, p = 0.003). In women, EQ-5D scores were also correlated with physical activity over 4 METs on hemodialysis treatment days and non-hemodialysis treatment days. By stepwise multiple regression analysis, physical activity over 4 METs on non-hemodialysis treatment days was a determinant factor of EQ-5D even after adjusting for age and K6 scores.

Conclusion Physical activity over 4 METs on non-hemodialysis treatment days might be associated with EQ-5D in patients on chronic hemodialysis, especially in women.

**Keywords** Hemodialysis · Health-related quality of life (HRQOL) · EuroQol (EQ-5D) · Psychological distress · Physical activity

### Introduction

Patients on hemodialysis are dramatically increasing and this has become a public health challenge in Japan. Over 300,000 patients are undergoing hemodialysis [1]. Therefore, adequate management of patients on chronic hemodialysis is urgently required.

Patients on chronic hemodialysis are thought to be much less active in their daily lives than healthy subjects, and lower physical activity may affect the various clinical parameters in patients on chronic hemodialysis. Recently, a very small tri-axial accelerometer called the Actimarker (Panasonic, Osaka, Japan) has been developed [2, 3]. This accelerometer can monitor physical activity continuously for over 1 month, and it can be easily used by simply attaching it to the waist.

In addition, in recent years, health-related quality of life (HRQOL) has become a prevalent concept worldwide. The EuroQol questionnaire (EQ-5D) [4-6], which is a widely used questionnaire evaluating HRQOL, has been translated into Japanese, and an official version was developed in May 1998 [7, 8]. However, the relationship between physical activity accurately evaluated by tri-accelerometer and HRQOL still remains to be investigated in patients on chronic hemodialysis in Japan. Therefore, in this study, we evaluated the effect of physical activity on HRQOL using

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EQ-5D in patients on chronic hemodialysis in a crosssectional study.

## Subjects and methods

### Subjects

We used data on 31 men ( $69.0 \pm 11.1$  years) and 17 women ( $66.9 \pm 10.0$  years) among 91 patients who met the following criteria: (1) wanted to be enrolled voluntarily in this cross-sectional study at Innoshima General Hospital, Onomichi, Japan, (2) received anthropometric parameter, physical activity, HRQOL, and psychological distress measurements, and (3) provided written informed consent (Table 1).

Ethical approval for the study was obtained from the Ethical Committee of Innoshima General Hospital, Onomichi, Japan (Innoshima General Hospital H24-3-28).

Anthropometric and body composition measurements

Anthropometric and body compositions were evaluated based on the following parameters: height, body weight, and body fat percentage. Body mass index (BMI) was calculated by weight/(height)<sup>2</sup> (kg/m<sup>2</sup>). The body fat percentage was measured by the impedance method (MLT-50, SEKISUI MEDICAL CO. LTD., Tokyo, Japan).

# Physical activity

In this study, we used the Actimarker, a small and lightweight (36.0 g) accelerometer which can continuously monitor physical activity for over one month. It can be easily used by simply attaching it to the waist. Actimarker collects tri-axial acceleration data at 20 Hz. Furthermore, the standard deviation of the data of 1 min is defined as a average value of acceleration. The METs value can be calculated using a linear regression formula of the relationship between the average value of acceleration and the METs value measured by the gas metabolic system [2, 3]. The subjects were taught how to use the instrument, and were told to wear it on their belt or waist band at the right midline of the thigh from the moment they awoke until they went to bed, except while bathing or swimming, for seven consecutive days. The activity monitor was firmly attached to their clothes at the waist by a clip as previously described [9].

# EO-5D score

EQ-5D is a brief, self-completed instrument for describing and valuing quality of health status defined by the EQ-5D scores. This descriptive system classifies respondents into one of 243 distinct health states. The descriptive system consists of five dimensions: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort, and (5) anxiety/depression. Each dimension has three levels, allowing for 3<sup>5</sup> (i.e., 243) possible health combinations. In addition, for completeness, the states "dead" and "unconscious" were also incorporated in the framework [4–8]. The unique EQ-5D health state is defined by combining one level from each of the five dimensions and producing a set of utility values for 245 health states. We used the Japanese EQ-5D instrument to assess the OOL of the subjects [8, 10].

#### The K6 score

As shown in previous reports [11], the K6 was used as an index of psychological distress [12, 13]. The questionnaire consisted of six questions. "Over the last month, how often did you feel: (1) nervous, (2) hopeless, (3) restless or fidgety, (4) so sad that nothing could cheer you up, (5) that everything was an effort, (6) worthless?" The subjects were requested to respond by choosing from the following: "all of the time" (4 points), "most of the time" (3 points), "some of the time" (2 points), "a little of the time" (1 point), and "none of the time" (0 points). The total point score range was 0-24. The K6 is based on modern psychometric measurement theory. In the field of psychometric current, the K6 is an excellent measurement method [14-16]. Using the standard back-translation method, the Japanese version of K6 has been developed, and it has been validated [12]. As suggested by Kessler et al. [16], we have classified subjects with scores of 13 points or more.

# Statistical analysis

Data are expressed as mean  $\pm$  standard deviation (SD) values. Simple correlation analysis was performed as well to test for the significance of the linear relationship among continuous variables, where p < 0.05 was considered to be statistically significant. In addition, stepwise multiple regression analysis was also performed on factors affecting HRQOL.

# Results

Written informed consent was obtained from 72 patients, and clinical profiles of enrolled patients on chronic hemodialysis for analysis (31 men and 17 women) are summarized in Table 1. Physical activity evaluated by  $\Sigma$ [metabolic equivalents  $\times$  h per week (METs-h/w)] was  $8.1 \pm 6.0$  METs-h/w (0.5–29.9). EQ-5D scores and K6 scores were 0.754  $\pm$  0.177 and 3.6  $\pm$  3.7, respectively, among all patients on chronic hemodialysis.

Table 1 Clinical characteristics of patients on hemodialysis

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	Total			Men			Women		
	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum
Patients enrolled as subjects	48			31			17		
Age (years)	$68.3 \pm 10.7$	45.0	88.0	$69.0 \pm 11.1$	45.0	88.0	$66.9 \pm 10.0$	50.0	83.0
Height (cm)	$156.4 \pm 8.3$	138.7	171.2	$160.6 \pm 5.7$	148.7	171.2	$148.7 \pm 6.7$	138.7	161.0
Body weight (dry weight) (kg)	$53.4 \pm 10.0$	32.7	89.4	$56.6 \pm 8.7$	40.1	89.4	$47.5 \pm 9.8$	32.7	71.7
Body mass index (kg/m²)	$21.7 \pm 3.0$	16.6	30.5	$21.9 \pm 2.7$	16.8	30.5	$21.4 \pm 3.6$	16.6	30.2
Body fat percentage (%)	$28.5 \pm 9.6$	10.2	50.1	$27.2 \pm 9.3$	10.2	50.1	$31.0 \pm 9.8$	14.7	49.2
EQ-5D scores	$0.754 \pm 0.177$	0.419	1.000	$0.757 \pm 0.170$	0.444	000.1	$0.746 \pm 0.194$	0.419	1.000
K6 score	$3.6 \pm 3.7$	0.0	16.0	$3.6 \pm 3.5$	0.0	11.0	3.5 ± 4.2	0.0	16.0
Daily step counts (steps per day)	$3770.3 \pm 2065.4$	422.4	9043.3	$3569.0 \pm 2093.7$	422.4	8523.9	$4137.3 \pm 2022.5$	1628.6	9043.3
Daily step counts on hemodialysis treatment days (steps per day)	3473.2 ± 1903.5	376.7	8944.3	$3294.4 \pm 2071.9$	376.7	8944.3	$3799.3 \pm 1555.3$	1426.3	7194.7
Daily step counts on non-hemodialysis treatment days (steps per day)	$3993.0 \pm 2407.5$	456.8	10429.8	$3774.9 \pm 2345.6$	456.8	9814.5	$4390.7 \pm 2539.7$	1295.3	10429.8
Physical activity (METs-h/w)	$8.1 \pm 6.0$	0.5	29.9	$7.2 \pm 6.4$	0.5	29.9	$9.7 \pm 5.2$	3.8	20.3
Physical activity on hemodialysis treatment days (METs·h/w)	$7.2 \pm 5.3$	9.0	21.3	<b>6.3</b> ± 5.4	9.0	21.3	8.9 ± 4.9	2.9	18.7
Physical activity on non-hemodialysis treatment days (METs-h/w)	8.8 ± 7.4	0.4	36.4	$7.9 \pm 8.1$	0.4	36.4	$10.4 \pm 5.9$	2.9	21.4
Physical activity over 4 METs·h/w (METs·h/w)	$1.2 \pm 1.4$	0.0	5.6	$1.1 \pm 1.3$	0.0	5.6	$1.4 \pm 1.5$	0.2	5.2
Physical activity over 4 METs-h/w on hemodialysis treatment days (METs-h/w)	1.0 ± 1.4	0.0	8.8	$0.9 \pm 1.7$	0.0	8.8	$1.0 \pm 0.9$	0.0	3.3
Physical activity over 4 METs·h/w on non-hemodialysis treatment days (METs·h/w)	1.4 ± 1.8	0.0	8.1	$1.2 \pm 1.5$	0.0	5.3	$1.7 \pm 2.1$	0.1	8.1



Table 2 Simple correlation analysis between EQ-5D scores and physical activity in patients on hemodialysis

	Total		Men		Women	
	r	p	$\overline{r}$	p	r	p
Daily step counts (steps per day)	0.204	0.164	0.317	0.830	0.032	0.904
Daily step counts on hemodialysis treatment days (steps per day)	0.146	0.321	0.182	0.328	0.095	0.718
Daily step counts on non-hemodialysis treatment days (steps per day)	0.220	0.133	0.374	0.038	0.001	0.998
Physical activity (METs h/w)	0.268	0.066	0.219	0.237	0.413	0.099
Physical activity on hemodialysis treatment days (METs·h/w)	0.159	0.164	0.740	0.693	0.350	0.169
Physical activity on non-hemodialysis treatment days (METs·h/w)	0.297	0.040	0.266	0.148	0.417	0.096
Physical activity over 4 METs h/w (METs h/w)	0.355	0.013	0.154	0.409	0.671	0.003
Physical activity over 4 METs·h/w on hemodialysis treatment days (METs·h/w)	0.109	0.462	-0.054	0.774	0.609	0.009
Physical activity over 4 METs·h/w on non-hemodialysis treatment days (METs·h/w)	0.426	0.003	0.281	0.126	0.624	0.007

Bold values are statistically significant (p < 0.05)

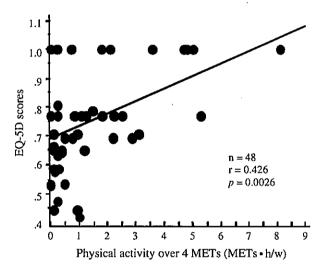


Fig. 1 Simple correlation analysis between EQ-5D scores and physical activity over 4 METs on non-hemodialysis treatment days (METs-h/w) in all patients

We evaluated the relationship between EQ-5D scores and physical activity measured by the Actimarker (Table 2). EQ-5D scores were positively and significantly correlated with physical activity over 4 METs on non-hemodialysis treatment days (r = 0.426, p = 0.003) among all patients (Fig. 1). In women, EQ-5D scores were positively and significantly correlated with physical activity over 4 METs on hemodialysis treatment days and non-hemodialysis treatment days (Table 2). However, in men, a clear relationship between EQ-5D and physical activity was not noted.

Psychological distress might affect HRQOL. Therefore, we also investigated the relationship between the K6 scores and physical activity (Table 3). The K6 scores were negatively and significantly correlated with physical activity on hemodialysis treatment days in women (r = -0.491, p = 0.045).

Finally, we performed stepwise regression analysis, and used EQ-5D scores as the dependent variable, and age, K6

scores, physical activity on hemodialysis treatment days and non-hemodialysis treatment days, and physical activity over 4 METs on hemodialysis treatment days and non-hemodialysis treatment days, as independent variables to adjust for confounding factors. Among all patients on chronic hemodialysis, only physical activity over 4 METs on non-hemodialysis treatment days was a determinant factor of EQ-5D [EQ-5D scores = 0.043 (physical activity over 4 METs on non-hemodialysis treatment days) + 0.695,  $r^2 = 0.181$ , p = 0.0026].

### Discussion

We first evaluated the relationship between HRQOL and physical activity using a tri-axial accelerometer in Japanese patients on chronic hemodialysis in a cross-sectional study. A level of 4 METs and over might be associated with EQ-5D scores, especially in women.

Wong et al. [17] reported that, using the global physical activity questionnaire (GPAQ), none of the hemodialysis patients had high physical activity levels. Johansen et al. [18] also reported that patients on hemodialysis were less active than healthy sedentary controls, and this difference was more pronounced among older subjects using a three-dimensional accelerometer and with an activity questionnaire. In addition, engaging in habitual physical activity among outpatients undergoing maintenance hemodialysis was associated with decreased mortality risk in Japanese patients on chronic hemodialysis for 7 years [19]. In this study, we evaluated the physical activity in patients on chronic hemodialysis using a newly developed tri-axial accelerometer. The average daily step count was 3770.3  $\pm$  2065.4 (422.4–9043.3) and that of physical activity was  $8.1 \pm 6.0$  METs·h/w (0.5-29.9). Therefore, the subjects in this study were less active than subjects in previous studies.

There have been some reports on HRQOL in patients on chronic dialysis. In peritoneal dialysis patients, the EQ-5D

Table 3 Simple correlation analysis between K6 scores and physical activity in patents on hemodialysis

	Total		Men		Women	
	$\overline{r}$	p	$\overline{r}$	p	r	p
Daily step counts (steps per day)	-0.260	0.075	-0.353	0.051	-0.111	0.670
Daily step counts on hemodialysis treatment days (steps per day)	-0.227	0.122	-0.323	0.076	-0.040	0.880
Daily step counts on non-hemodialysis treatment days (steps per day)	-0.255	0.080	-0.337	0.064	-0.137	0.600
Physical activity (METs·h/w)	-0.370	0.010	-0.332	0.068	-0.472	0.056
Physical activity on hemodialysis treatment days (METs·h/w)	-0.397	0.005	-0.359	0.048	-0.491	0.045
Physical activity on non-hemodialysis treatment days (METs·h/w)	-0.314	0.030	-0.279	0.129	-0.420	0.093
Physical activity over 4 METs·h/w (METs·h/w)	-0.232	0.112	-0.159	0.394	-0.337	0.186
Physical activity over 4 METs·h/w on hemodialysis treatment days (METs·h/w)	-0.136	0.356	-0.103	0.580	-0.257	0.319
Physical activity over 4 METs·h/w on non-hemodialysis treatment days (METs·h/w)	-0.238	0.103	-0.159	0.392	-0.330	0.196

Bold values are statistically significant (p < 0.05)

score was  $0.65 \pm 0.23$  in Thai patients [20]. Kusleikaite et al. [21] showed that both baseline HRQOL and decline of HROOL are independent predictors of mortality in hemodialysis patients using a short form 36 questionnaire (SF-36) in a longitudinal analysis. Less severe depression and fewer anxiety symptoms were also associated with higher HRQOL [22], and regular exercise was correlated with more positive patients and fewer depressive symptoms in the Dialysis Outcomes and Practice Patterns Study [23]. In healthy Japanese [24], HROOL (SF-36 scores) was higher in individuals spending >25 % of their total activity at an intensity >3 METs [24]. We evaluated HRQOL in patients on chronic hemodialysis using EQ-5D and the score was  $0.754 \pm 0.177$ . It is noteworthy that EQ-5D scores were associated with physical activity over 4 METs (METs·h/w), especially in women. By stepwise regression analysis, the relationship between EQ-5D scores and physical activity over 4 METs on non-hemodialysis treatment days (METs·h/ w) still remained even after adjusting confounding factors in all patients. Mustata et al. [25] showed that long-term exercise training improved physical impairment, arterial stiffness, and HRQOL in patients on predialysis. Ota et al. [26] reported that a gymnastics program including stretching and isotonic muscle conditioning using two tennis balls (2-3 METs using a sitting position) improved physical fitness and instrumental activity of daily living (IADL) in elderly hemodialysis patients.

We evaluated the relationship between physical activity and HRQOL in patients on chronic hemodialysis, and physical activity was evaluated on hemodialysis treatment days and non-hemodialysis treatment days. When promoting increased physical activity in patients on chronic hemodialysis, it is generally important to evaluate their situation and fitness level. In addition, physical activity on hemodialysis treatment days and non-hemodialysis treatment days might be meaningful for instructors. However, increasing physical activity may be difficult for patients on

chronic hemodialysis, especially on hemodialysis treatment days. In this study, physical activity over 4 METs on non-hemodialysis treatment days was associated with HRQOL in women and total subjects. However, this association was not observed in men. In fact, men were less active and parameters of physical activity in men [over 4 METs on non-hemodialysis treatment days:  $1.2 \pm 1.5$  METs·h/w (0-5.3)] were lower than those in women. Nevertheless, this reference value may be a useful milestone for some patients on chronic hemodialysis.

Potential limitations remain in this study. First, this study was a cross-sectional and not a longitudinal study. Second, 48 patients on chronic hemodialysis in this study voluntarily underwent measurements. Third, we could not identify the mechanism that links physical activity and HRQOL. Fourth, the small sample size, especially of women, makes it difficult to validate this study. We could not analyze the relationship between EQ-5D scores and physical activity by stepwise regression analysis in women. Bayoumi et al. [27] reported that gender differences may affect QOL scores in patients on chronic hemodialysis. In addition, other potential factors that may influence physical activity could not be evaluated accurately in this study.

Nonetheless, it seems reasonable to suggest that promoting physical activity might result in improved HRQOL in some patients on hemodialysis. To demonstrate this clearly, further prospective and detailed studies in patients on chronic hemodialysis are needed.

Conflict of interest There is no conflict of interest.

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