



Physical Activity Dose for Hemodialysis Patients: Where to Begin? Results from a Prospective Cohort Study

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Objective: Greater physical activity is associated with lower risk of mortality in persons with kidney disease; however, little is known about the appropriate dose of physical activity among hemodialysis patients. Here detected the minimum level of habitual physical activity to help inform interventions aimed at improving outcomes in the dialysis population.

Design: The design was prospective cohort study.

Subjects: Clinically stable outpatients in a hemodialysis unit from October 2002 to March 2014 were assessed for their eligibility to be included in this 7-year prospective cohort study. We used the Youden index to determine the optimal cutoff points for physical activity. The prognostic effect of physical activity on survival was estimated by Cox proportional hazards regression analysis. The number of steps per nondialysis day was recorded by accelerometer at study entry.

Main Outcome Measure: The main outcome measure was all-cause mortality.

Results: There were 282 participants who had a mean age of 65 ± 11 years and 45% were female. A total of 56 deaths occurred during the follow-up period (56 months [interquartile range: 29-84 months]). The cutoff value for the physical activity discriminating those at high risk of mortality was 3,752 steps. After adjustment for the effect of confounders, the hazard ratio in the group of <4,000 steps was 2.37 (95% confidence interval: 1.22-4.60, $P = .01$) compared with the others.

Conclusions: Engaging in physical activity is associated with decreased mortality risk among hemodialysis patients. Our findings of a substantial mortality benefit among those who engage in at least 4,000 steps provide a basis for as a minimum initial recommendation kidney health providers can provide for mobility disability-free hemodialysis patients.

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Introduction

THE END-STAGE RENAL disease population has a high prevalence of physical frailty characterized by physical inactivity.^{1,2} Low physical activity, assessed by

questionnaire¹⁻⁵ or accelerometer⁶-based methods, is strongly associated with poor prognosis in chronic kidney disease patients on hemodialysis. Despite evidence suggesting increased physical activity among dialysis patients improves performance-based outcomes, little is known about the appropriate dose of habitual physical activity from epidemiologic studies to help guide recommendations for minimum daily physical activity in this population.

Goal setting of physical activity is well known as 1 of the most popular techniques to promote it in elderly people or people with chronic illnesses.⁷⁻⁹ A meta-analysis, which investigated the effectiveness of pedometer used intervention on physical activity in community-dwelling people, concluded that setting a physical activity goal is a key motivational factor for increasing physical activity and is absolutely essential for successful intervention.¹⁰

Hemodialysis patients confront many challenges to improving their physical activity including time constraint caused by the 4-hour hemodialysis procedure, postdialysis fatigue, and poor physical function. These challenges make it difficult for these patients to meet the goal of at least 30 minutes of moderate-to-vigorous activity¹¹ or 7,000 to 10,000 steps per a day.¹² Therefore, more realistic and

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specific goal of physical activity for hemodialysis patients is needed. However, it is unclear whether how much physical activity hemodialysis patients need in their daily livings.

The purpose of this study was to detect the minimum level of habitual physical activity to help inform interventions aimed at improving outcomes in the dialysis population.

Methods

Study Population

Clinically stable outpatients in a hemodialysis unit from October 2002 to March 2014 were assessed for their eligibility to be included in this prospective cohort study. Patients were undergoing maintenance hemodialysis therapy at 3 times a week, which is most common in Japan according to the data of the Japanese Society for Dialysis Therapy. Patients were excluded from our study if they had been hospitalized within 3 months before the study, suffered from a recent myocardial infarction or angina pectoris, had uncontrolled cardiac arrhythmias, hemodynamic instabilities, uncontrolled hypertension, or renal osteodystrophy with severe arthralgia, or needed assistance in walking from another person. This study was approved by the Research Ethics Committee.

Patients Characteristics

Information on demographic factors (age, sex, and time on hemodialysis), physical constitution (body mass index [BMI]), primary kidney disease, and comorbid conditions were collected at the time of the patients' entry into the study. The following laboratory parameter was extracted from patient hospital charts: serum albumin level. A comorbidity index, which was developed for dialysis patients and composed of end-stage renal disease primary causes, atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, dysrhythmia, other cardiac diseases, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, cancer, and diabetes, was used to quantify comorbid illnesses in this study. This score was calculated using the method previously described and performed well in analysis for survival in hemodialysis patients.¹³ The geriatric nutritional risk index¹⁴ was also calculated based on serum albumin level and BMI as an index of nutritional condition.

Exposure Measurement

Habitual physical activity (Lifecorder; Suzuken Co., Ltd., Nagoya, Japan) was measured using an accelerometer. The device obtains objective information on physical activity patterns because it can continuously measure the intensity, duration, and frequency of activities. The accuracy and reliability of the instrument have been reported in previous studies.^{15,16} The vector magnitude in the vertical direction that was recorded for every 2-minute period reflects the intensity of the physical activity, as described elsewhere.¹⁷

The number of steps and energy expenditure of physical activity were recorded by the accelerometer.

The instrument was worn around the waist, and it measured motion as the acceleration of the body. Patients were instructed to wear the accelerometer continuously during their waking hours for 7 days and to avoid getting it wet, such as during bathing. Patients were asked to maintain their typical weekly schedules. To ensure that the measurement periods were typical of their weekly activity patterns, data were excluded when patients traveled or manifested as acute illness.

Before the analysis, the accelerometer data were inspected to ensure that there were no obvious errors, such as a failure to acquire data or if the patient forgot to wear the accelerometer. The measurements from 4 nondialysis days during the week were analyzed.

Outcome

All-cause mortality was assessed by death registry at the clinic. Recruitment started on October 2002, and date of death was determined on February 2016. We truncated the data for the follow-up to 7 years.

Statistical Methods

Data were presented as mean \pm standard deviation or number (percentage). Baseline patient characteristics and physical activity were compared by unpaired *t*-test, one-way analysis of variance, or chi-square test. The Pearson product moment correlation was used to explore the correlation between number of steps and energy expenditure of physical activity. To calculate the area under the curves (AUCs) in number of steps and energy expenditure of physical activity, receiver operating characteristic (ROC) curve analysis was performed. We compared AUCs between number of steps and energy expenditure of physical activity. We used the Youden index to determine the optimal cutoff points for physical activity.^{18,19} Youden index is used as a measure of the overall combined specificity and sensitivity of prognostic factor and is defined as the maximum vertical distance between the ROC curve and the diagonal of chance line and is calculated as maximum [sensitivity + specificity - 1]. The best Youden index is used to determine the best cutoff point of physical activity. To calculate the discrimination ability of combined use of physical activity, ROC analysis, net reclassification improvement (NRI), and integrated discrimination improvement (IDI) were also performed for the logistic regression models of patient characteristics only and patient characteristics plus physical activity index. NRI and IDI have been developed as more sensitive statistical methods to quantify model improvement with the addition of a new variable to an existing clinical model.²⁰

For the Kaplan-Meier estimate of the survival curves, we truncated the data for the follow-up period of 7 years to avoid the number at risk being too small. We adopted the

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