Renal Replacement Therapy

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Interactional effects of depressive symptoms and physical function on daily physical activity in ambulatory patients receiving hemodialysis

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Abstract

Background Clarification of the factors associated with decreased physical activity is crucial for effective disease management in patients undergoing hemodialysis. Although evidence suggests that physical activity may be associated with physical function or depressive symptoms, limited studies have demonstrated these factors to be independently associated with the former in patients undergoing hemodialysis. This study aimed to examine whether physical function and depressive symptoms were independently or interactively associated with daily physical activity in patients undergoing hemodialysis.

Methods This cross-sectional study analyzed 157 clinically stable outpatients (median age: 68 years) receiving hemodialysis. Physical activity (steps/day) was measured using an accelerometer for four consecutive non-dialysis days. Physical function was evaluated by calculating usual walking speed along a 10-m walkway. The 10-item version of the Center for Epidemiologic Studies for Depression Scale was used to assess depressive symptoms.

Results The hierarchical multiple regression model (Model 2), constructed by adding physical function to Model 1 (clinical characteristics), showed a significant increase in coefficient of determination (R^2), compared to Model 1 ($\Delta R^2 = 0.15$, $P < 0.01$). There was no significant increase in R^2 between Models 2 and 3, where depressive symptoms were added to Model 2. The interaction term of physical function with depressive symptoms in Model 4 indicated an increase in R^2 ($\Delta R^2 = 0.01$, $P = 0.03$), compared with Model 3. The simple slope analysis demonstrated that the difference in physical activity between patients with or without depressive symptoms at higher levels of physical function was greater than that at its lower levels.

Conclusions Physical function was a strong and independent factor associated with physical activity, but no independent relationship between depressive symptoms and the physical activity was observed in patients undergoing hemodialysis. In contrast, physical function and depressive symptoms were interactively associated with daily physical activity in patients undergoing hemodialysis who were capable of walking independently. Our findings suggested that a two-step screening, primarily based on physical function and then depressive symptoms, can be useful to identify factors associated with physical inactivity in hemodialysis patients.

Keywords Chronic renal failure, Depressive symptoms, Physical activity, Physical function, Walking speed

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Background

Patients undergoing hemodialysis (HD) are significantly less active than those with normal kidney function [1–3]. Low physical activity (PA) leads to a decrease in activities of daily living (ADL), activity space, and quality of life as well as an increased risk of mortality in patients on HD [4–7]. Therefore, identifying factors associated with reduced PA is crucial for the development of useful disease management strategies for these patients.

PA is measured by energy expenditure, duration of activity, and number of steps taken. It is known to be closely associated with physical functions such as aerobic capacity, skeletal muscle strength, balance, and walking speed in healthy individuals and those with disease [8–10]. However, PA has been suggested to be associated not only with physical function, but also with psychological factors, such as depressive symptoms. [11–13]. The Dialysis Outcomes and Practice Patterns Study showed that 40% of patients on HD experienced depressive symptoms. Depression and depressive symptoms are the most frequent psychological problems among these patients and are associated with a high mortality risk and low quality of life [15, 16]. However, the relationships among physical activity, physical function, and psychological components are bidirectional [17]. Also, no consistent relationship has been found between physical activity and depressive symptoms [18]. In particular, few studies have examined whether depressive symptoms are independently associated with physical activity in patients undergoing HD.

Moreover, a previous report examining factors associated with mobility-based ADL revealed that depressive symptoms were associated with ADL in patients on HD [19]. However, this previous study, which examined lower- (e.g., sitting, standing, walking 100 m) and higher-difficulty (e.g., walking 600 m, walking 1000 m) ADL items separately for their association with PA, showed no association between ADL scores and depressive symptoms for lower-difficulty ADL items, whereas such an association was found for higher-difficulty ADL items. Acquisition of ADLs requires physical function commensurate with their level of difficulty, and ADL levels define daily PA.

In other words, to clarify the relationship between depressive symptoms and daily PA in patients on HD, it is necessary to examine not only whether depressive symptoms are associated with PA independent of physical function, but also whether the association between depressive symptoms and PA differs according to different levels of physical function. Although several reports have examined the relationship between depressive symptoms and PA [20, 21], no study has examined whether depressive symptoms are dependently associated with PA in patients on HD after adjusting for physical function of the lower limbs, such as walking speed.

We investigated whether physical function and depressive symptoms were independently associated with PA and examined their interactive effects on PA in patients on HD.

Methods

Population and study design

This cross-sectional study included clinically stable outpatients with end-stage kidney disease from a Japanese dialysis center between April 2018 and March 2019. In accordance with the Japanese Society for Dialysis Therapy guidelines, the center provided maintenance HD thrice per week. We excluded patients who had been hospitalized within three months before the study; required assistance for walking (from another person, cane, or walker); had recent myocardial infarction or angina pectoris, chronic heart failure (New York Heart Association classes III–IV), severe peripheral artery disease with intermittent claudication or critical limb ischemia, or uncontrolled hypertension (resting systolic and diastolic blood pressure > 180/110 mmHg); or disdialysis syndrome, such as hypotension, nausea, or muscle spasm while receiving HD. We performed the study in accordance with the 2013 revision of the 1975 Declaration of Helsinki. The study protocol was approved by the Research Ethics Committee of Kitasato University (2015-033). The study participants provided written informed consent before participation.

Clinical characteristics

We recorded the demographic factors (age, sex, and time on HD), body composition (body mass index), primary causes of end-stage kidney disease, laboratory findings, and comorbidities at the time of participant enrollment. Serum albumin and hemoglobin levels were obtained from hospital charts. We also recorded the presence of congestive heart failure because it may also affect PA, in addition to the factors listed in the exclusion criteria.

Physical activity (PA)

An accelerometer (Lifecorder; Suzuken Co. Ltd., Nagoya, Japan) was used to determine the PA, including continuous measurements of the intensity, duration, and frequency of activity. The accuracy, reliability, and validity of the accelerometer have been reported [6, 22, 23]. The accelerometer was worn around the waist to monitor the body acceleration and record the number of steps taken. The device was worn continuously during the waking hours of participants for seven days and to prevent contact with water. Additionally, they were requested to maintain typical weekly schedules. To ensure that the data collected indicated the weekly PA patterns, we excluded data obtained from patients when they were traveling or acutely ill. Before the accelerometer data were analyzed, they were evaluated to confirm the absence of obvious errors, such as failure to acquire data or wear the device. Data recorded from four consecutive non-dialysis days were analyzed.

Physical function

To measure the physical function, data related to the usual walking speed along a 10-m walkway before HD on a dialysis day were recorded. Walking speed is most frequently used to evaluate the walking ability and is strongly associated with the onset of disability, severe mobility limitation, and mortality in several populations, including healthy older adults and individuals with neurological disorders, orthopedic dysfunction, cardiovascular disease, and kidney disease. The reliability and validity of this method has been reported previously [10, 24–26]. The usual walking speed has recently been used to identify sarcopenia and frailty [27, 28]. Walking speed is calculated as distance (m) divided by time (s) during self-selected walking speed. It was calculated once and expressed in m/s.

Depressive symptoms

Depressive symptoms are commonly evaluated using the Center for Epidemiologic Studies for Depression (CES-D) scale in the general population and individuals with chronic diseases, including patients on HD [15, 16, 29–31]. We administered the short, 10-item Japanese version of CES-D to evaluate the depressive symptoms in the past week. The accuracy and validity of this scale have been reported in patients on HD [14, 32, 33]. The items are rated on a scale (range: 0–3); the total CES-D10 score was a sum of the item scores (range: 0–30). Higher scores indicated greater depressive symptoms; the presence of depressive symptoms was defined as score ≥ 10.

Statistical analysis

Dara are presented as medians (25–75 percentile) or numbers (percentage). Data were analyzed using hierarchical multiple regression and simple slope analyses to identify factors associated with PA.

PA was considered the dependent variable. Four models were created as independent in the hierarchical multiple regression analyses. First, age, sex (0 = female; 1 = male), time on HD, body mass index, hemoglobin level, serum albumin level, and congestive heart failure (0 = absence; 1 = presence) were entered (Model 1). Second, physical function was included in Model 1 to account for its effect (Model 2). Third, depressive symptoms (0 = absence; 1 = presence) were included in Model 2 (Model 3). Finally, the interaction term (physical function × depressive symptoms) was added to Model 3 (Model 4); if found to be significant, a simple slope analysis was performed. A two-tailed $P < 0.05$ indicated statistical significance. Data were analyzed using Stata (version 16) and JMP Pro 15 software (SAS Institute Inc.).

Results

Patient characteristics and PA

In total, 339 outpatients were evaluated for inclusion. Among them, 134 patients did not fulfill the inclusion criteria and were excluded, whereas 48 patients declined to participate. Consequently, 157 HD outpatients were included. Table 1 summarizes the characteristics of study participants. The median age of study participants was 68 years, 42% were males, and the median body mass index was 21.0 kg/m^2. The median time on HD was 8.0 years. The most frequent primary cause of end-stage kidney disease was glomerulonephritis/cystic kidney disease (33.8%), followed by diabetes (31.2%). The median serum albumin and hemoglobin levels were 3.9 g/dL and 10.8 g/dL, respectively. Overall, 12.7% of the participants

Table 1 Participant characteristics

Characteristics	*N* = 157
Demographic factors	
Age (years)	68.0 [60.0, 76.0]
Male (*n*, %)	91 (58.0)
Time on hemodialysis (years)	8.0 [3.0, 15.0]
Body composition	
Body mass index (kg/m^2)	21.0 [18.2, 24.3]
Primary kidney disease (*n*, %)	
Diabetes	49 (31.2)
GN/cystic kidney disease	53 (33.8)
Hypertension	11 (7.0)
Unknown	21 (13.3)
Other	23 (14.6)
Comorbidity	
Congestive heart failure (*n*, %)	20 (12.7)
Laboratory data	
Serum albumin (g/dl)	3.9 [3.6, 4.0]
Hemoglobin (g/dL)	10.8 [10.4, 11.4]
Physical function	
Walking speed (m/s)	1.2 [1.0, 1.4]
Depressive symptoms	
CES-D10 score ≥ 10 (*n*, %)	44 (28.0)
Physical activity	
Number of steps (steps/day)	3263.8 [1221.8, 5612.6]

GN, glomerulonephritis; CES-D10, 10-item version of the Center for Epidemiologic Studies for Depression scale. Data are presented as median [interquartile range] or number (%)

had congestive heart failure. The median number of steps on non-dialysis (i.e., PA) was 3263.8.

Physical function and depressive symptoms

The median, 25th, and 75th percentiles of usual walking speed as physical function were 1.2 m/s, 1.0 m/s, and 1.4 m/s, respectively. Overall, 28% of participants had depressive symptoms (Table 1).

Association of physical function and depressive symptoms with PA

Table 2 presents the hierarchical multiple regression analysis results for PA (steps). Model 2 demonstrated a significantly higher coefficient of determination (R^2) than Model 1 ($\Delta R^2 = 0.15$, $P < 0.01$). However, there was no significant increase in R^2 when comparing Model 2 to Model 3, indicating no independent relationship between depressive symptoms and PA. When the interaction term between physical function and depressive symptoms was included in Model 4, the two factors had a significant interaction effect on PA ($\beta = -0.13$, $P = 0.03$), with a significant increase in R^2 ($\Delta R^2 = 0.01$, $P = 0.03$). Therefore, a simple slope analysis was conducted to visualize the effects of the interaction term between physical function (walking speed) and depressive symptoms on PA (Fig. 1). Our results showed that the difference in PA (steps) between patients with and without depressive symptoms was greater in those with higher physical function (1 SD above the mean) than in those with lower physical function (1 SD below the mean).

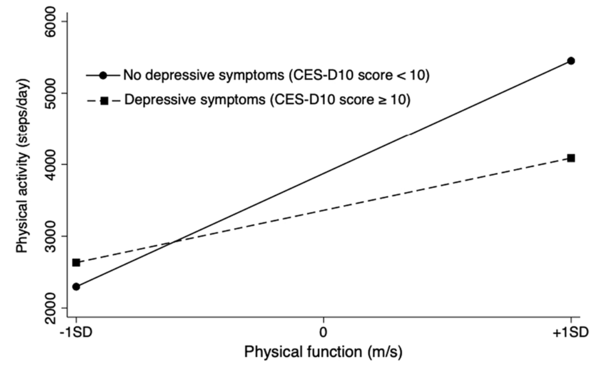

Fig. 1 Interactive effect of physical function (m/s) and depressive symptoms on physical activity (steps/day). Physical function was evaluated at the usual walking speed (m/s)

Discussion

We investigated the associations of physical function and depressive symptoms with daily PA in patients undergoing regular HD at the outpatient dialysis center. Our cross-sectional study showed that the interactive effects of physical function and depressive symptoms were associated with PA in clinically stable patients undergoing HD. Furthermore, the magnitude of the association between depressive symptoms and PA differed between patients with slow and fast walking speeds as physical function, with the latter being greater. These results may provide useful information for disease management (diagnosis and treatment procedures) of patients on HD, as a decrease in PA not only leads to a reduction in activities of daily living and quality of life, but also causes

Table 2 Hierarchical multiple regression analyses of the association of physical function and depressive symptoms with PA

	Model 1		Model 2		Model 3		Model 4	
	β	P_1	β	P_1	β	P_1	β	P_1
Age (years)	−0.47	<0.01	−0.23	0.01	−0.22	0.01	−0.23	0.01
Sex	0.02	0.79	0.07	0.31	0.07	0.30	0.06	0.39
Body mass index (kg/m^2)	−0.04	0.68	0.02	0.86	0.02	0.80	0.04	0.62
Hemodialysis vintage (year)	−0.06	0.43	−0.07	0.30	−0.07	0.28	−0.06	0.37
Congestive heart failure (%)	−0.15	0.02	−0.10	0.06	−0.10	0.05	−0.10	0.05
Serum albumin (g/dl)	0.02	0.75	−0.01	0.90	−0.01	0.88	−0.01	0.90
Hemoglobin (g/dL)	−0.06	0.46	−0.07	0.34	−0.07	0.35	−0.07	0.33
Physical function (m/s)			0.47	<0.01	0.47	<0.01	0.52	<0.01
Depressive symptoms					−0.04	0.52	−0.08	0.23
Physical function*depressive symptom							−0.13	0.03
R^2		0.24		0.40		0.40		0.41
ΔR^2				0.15		<0.01		0.01
P_2				<0.01		0.52		0.03

PA, physical activity; P1, P value for β; P2, P value for change in R^2; R, the coefficient of determination. Physical function was evaluated at the usual walking speed (m/s) adverse outcomes, such as high risk of hospitalization and mortality rate.

Our results are consistent with those of previous studies that have found that physical function is associated with PA. These findings indicate that physical function is a predominant factor in PA. [6, 34]. Walking speed is closely related to lower limb muscle strength, standing balance, and aerobic capacity, such as the 6-min walking distance. It is therefore a representative index reflecting lower limb function [10]. In 2019, the Asian Working Group for Sarcopenia proposed that walking speed is a useful indicator for diagnosing sarcopenia [28]. Recent studies have suggested that it is essential to detect physical frailty for effective treatment of elderly patients since it results in elevated rates of mortality and morbidity, greater dependence, difficulty in ADL, and major adverse clinical events. Walking speed is a representative index to determine physical frailty [6, 23]. Notably, most previous studies have shown that walking speed is independently associated with limited ADL and poor outcomes, even after adjusting for the effects of age and disease. These findings strongly support ours that state that walking speed is independently associated with PA in patients on HD. In addition, previous studies have reported that depressive symptoms are associated with PA [13, 35]. Although there are several potential mechanisms underlying the relationship between the two, the detailed mechanisms are unclear, and this relationship may be bidirectional [17]. Depression leads to reduced motivation and energy as well as increased fatigue. These symptoms may be linked to a sedentary lifestyle and inactivity [36, 37]. Additionally, there may also be direct physiological relationships between depression and lack of exercise, such as hyperactivity of the hypothalamic–pituitary–adrenal axis [38] and sympathetic nervous system [39, 40].

However, only a few have examined whether depressive symptoms are independently associated with PA [20, 21, 41]. Furthermore, even though some studies have assessed their relationship after adjusting for the effects of age, sex, and comorbidity [20, 21], none have applied physical function strongly reflecting lower limb function, such as walking speed, as adjustment factors.

The hierarchical multiple regression analysis showed a significant change in the coefficient of determination in Model 2, in which physical function (walking speed) was added to the patient characteristics (age, sex, dialysis duration, and comorbidities) as an adjustment factor; however, no significant change in the coefficient of determination was observed in Model 3, in which depressive symptoms were entered after physical function. Therefore, to the best of our knowledge, this is the first report showing that depressive symptoms are not independently associated with PA after adjustment for physical function in patients undergoing hemodialysis, whereas in the present analysis, we examined the interactive effect between physical function and depressive symptoms (Model 4), and the coefficient of determination of this interaction changed significantly. Based on a simple slope analysis that visualized the interaction between the two variables, the daily PA of patients with faster walking speeds was more strongly associated with depressive symptoms than those of patients with slower walking speeds.

Most studies showing the association between depressive symptoms and physical inactivity have been conducted in individuals with no significant decline or impairment in physical function [12, 13, 42]. Furthermore, even studies indicating an association between depressive symptoms and PA in patients on HD included relatively healthy patients in their analysis [20, 21, 35]. Therefore, our results, which indicated a greater association of depressive symptoms with PA in patients with a fast walking speed (i.e., relatively good physical function) compared to patients with a slow walking speed, confirm the aforementioned reports. The reason for the lack of association of depressive symptoms with PA in patients on HD with slow walking speeds may be that it was masked by the association of the former with physical dysfunction. This suggests an independent association of physical function decline with PA.

The results of the present study may aid in the identification of causes of PA decline in patients on HD. To determine the cause of the decline in PA, we should first investigate whether there is a decrease in physical function, such as walking speed. If this is confirmed, we should identify the factors that cause a decline in walking speed (lower limb muscle strength or balance). On the other hand, if there is no deterioration in physical functioning, it is necessary to evaluate the mental or psychological functions, such as depressive symptoms (two-step screening). The two-step screening may also be useful to develop effective treatment guidelines for the prevention of decline in PA.

The present study had some notable strengths and limitations. First, an accelerometer was used to assess PA, which objectively and accurately assesses daily PA. Self-reported PA assessed using questionnaires may be affected by social desirability or recall bias. However, our results may not be generalizable due to the small sample size and single-center study design, which included only Japanese patients on HD. Furthermore, we used a cross-sectional study design. Studies have suggested that physical dysfunction, depressive symptoms, and physical inactivity have bidirectional relationships [17, 43]. Therefore, a longitudinal study is required to identify changes in physical function and depressive symptoms to determine the factors that affect PA in patients on HD. Finally, depressive symptoms were evaluated using the 10-item version of the CES-D scale. An in-depth assessment of anxiety, apathy, and cognitive function is required in the future.

In conclusion, physical function (walking speed) and depressive symptoms were interactively associated with PA in patients on HD who could walk independently. Our results suggest that a two-step screening, primarily based on physical function and then depressive symptoms, can be useful to evaluate factors related to physical inactivity in patients on HD.

Abbreviations

HD	Hemodialysis
PA	Physical activity
CES-D	Center for Epidemiologic Studies for Depression

Acknowledgements

We thank the study participants and supporting medical staff. We also thank Editage (www.editage.com) for English language editing.

Author contributions

YM, YS, SY, MH, TK, KK, AY, KI, YF, NM, HT, and AM analyzed and interpreted the patient data for physical activity and depressive symptoms and contributed to the preparation of the manuscript. KI and SY performed physical activity and depressive symptom measurements. All authors read and approved the final manuscript.

Funding

This research was supported by JSPS KAKENHI (Grant Number 19K11372).

Availability of data and materials

We decided not to share the data in our study because all data are thoroughly described and reflected in the accompanying tables and figures (all relevant data are within the paper).

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards of the 1975 Declaration of Helsinki, as revised in 2013, and was approved by the Research Ethics Committee of Kitasato University (2015-033). All patients provided written informed consent for their participation in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 12 February 2023 Accepted: 30 May 2023
Published online: 15 June 2023

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