Falls and Physical Inactivity in Patients with Gastrointestinal Cancer and Hand–Foot Syndrome

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ABSTRACT

Objective: This study aims to ascertain the incidence and association of falls and physical inactivity in patients with gastrointestinal cancer and hand–foot syndrome (HFS) after receiving chemotherapy or targeted therapy. **Methods:** The present cross-sectional study was conducted on 50 outpatients with HFS of Grade 1 or above, according to the National Cancer Institute Common Terminology Criteria for Adverse Events, following the receipt of chemotherapy or targeted therapy for gastrointestinal cancer in Japan between November 2016 and February 2017. For measurement, Dermatology Life Quality Index (DLQI) and the International Physical Activity Questionnaire were used. Data were analyzed by logistic regression analysis. **Results:** Of the participants, 18% experienced falls and 60% reported physical inactivity. Multivariate logistic regression revealed that the DLQI treatment domain score was the only factor associated with falls (odds ratio [OR] =8.01, 95% confidence interval [CI] =1.27–50.63, P = 0.027). Physical inactivity was associated with DLQI symptom and feeling domain scores (OR = 5.54, 95% CI = 1.26–24.33, P = 0.023) and the with-oxaliplatin or paclitaxel regimen (OR = 3.71, 95% CI = 1.06–13.03, P = 0.041). **Conclusions:** The results of the present study suggest patients should be informed that HFS is a risk factor for physical inactivity and falls.

Key words: Falls, gastrointestinal cancer, hand–foot skin reaction, hand–foot syndrome, physical activity

Introduction

Hand–foot syndrome (HFS) is a common adverse event of chemotherapy and causes palmar and plantar erythema, edema, and dysesthesia, with pain, swelling, and vesiculation. HFS is classified into two groups:

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chemotherapy-related HFS following treatment with 5-fluorouracil, pegylated liposomal doxorubicin, and capecitabine and multikinase inhibitor-related HFS (also referred to as hand–foot skin reaction) following treatment with sorafenib and sunitinib.[1]

HFS is not life-threatening; however, it restricts daily activities,[2] which causes serious impairment of patients' social functioning and quality of life.[3] Typical HFS symptoms, such as paresthesia, tingling, burning, or painful sensations on the palms of the hands and soles of the feet interfere considerably with even the simplest everyday activities such as walking.[4] Moreover, patients could become physically inactive because of the recommendation to avoid traumatic activity to prevent the manifestation of HFS.[3,5]

Recent studies have reported that chemotherapy-induced peripheral neuropathy (CIPN) symptoms are associated with the risk of falls[6,7] and physical inactivity.[8] Although HFS affects daily activities, the nature of falls and physical inactivity associated with HFS have not been explored thoroughly. Most anticancer agents, including those that lead to HFS, are administered orally at outpatient clinics; therefore, patients have to cope with difficulties in daily living alone during cancer treatment. Falls and physical inactivity have also been associated with reduced quality of life,[9,10] psychological distress,[11,12] and increased health-care costs.[13] Moreover, patients are required to manage not only the side effects of chemotherapy but also the risk of falls and physical inactivity.

We aimed to ascertain the incidence and association of falls and physical inactivity in patients with gastrointestinal cancer and HFS after receiving chemotherapy or targeted therapy.

Methods

Participants and study design

A cross-sectional study design was adopted, and convenience sampling was used to recruit patients from Keio University Hospital in Tokyo, Japan, which has approximately 1000 beds. The attending physician selected potential participants from their medical records based on the inclusion and exclusion criteria. The researcher explained the research overview and methods to participants during their clinic visit using a written document and obtained their consent. Recruitment began in November 2016 and follow-up assessment was performed in February 2017. The inclusion criteria were as follows: (1) age of 20 years or older; (2) HFS of Grade 1 or above, according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE version 4.0),[14] following the receipt of chemotherapy or targeted therapy (i.e. monotherapy

or combination therapy) for gastrointestinal cancer between November 2016 and February 2017; and (3) the ability to provide written informed consent in Japanese. The exclusion criteria were as follows: (1) being deemed unsuitable for participation in the study by an attending physician because of a cognitive or mental disorder present at the time of recruitment; (2) an Eastern Cooperative Oncology Group performance status of Grade 3 or higher; and (3) registered in a clinical trial. Based on the previous studies, the following 6 risk factors for falls in cancer patients were extracted: age, diabetes status, time since last chemotherapy, CIPN symptom, functional impairment, anxiety, and depression.[7,15,16] HFS symptom and grade were added to these variables, and the sample size was calculated as follows: the number of variables (7) ×10 = 70 participants. However, the study was conducted in only one research site, and consequently, failed to include 70 participants. Of the 56 potential participants recruited, six were excluded (i.e., three whose HFS had improved, two with a performance status >3, and one who was already registered in a clinical trial). Fifty patients received written and oral explanations regarding the objectives of the study and provided informed consent. Ethical approval was obtained from the Internal Review Boards at the Faculty of Nursing and Medical Care, Keio University (no. 252), and Keio University School of Medicine (no. 20160181). Trial Registration: no. UMIN000024569.

Instruments for measurement

Hand–foot syndrome severity

The severity of HFS resulting from chemotherapy or targeted therapy was defined according to the clinical grades based on the NCI-CTCAE version 4.0.[14]

Patient-reported hand–foot syndrome outcomes

The Dermatology Life Quality Index (DLQI) is a simple, practical scale that was developed in the United Kingdom by Finlay and Khan[17] to measure dermatology-specific health-related quality of life. The questionnaire includes 10 items pertaining to the impact of the disease on the patient over the preceding week, which are divided between the following six domains: symptoms and feelings, daily activities, leisure, work or school, personal relationships, and treatment.[17] The reliability and validity of the Japanese version of the DLQI have been established in patients with acne.[18,19] The phrase, "your skin problem" in the DLQI can be replaced by another phrase based on the target disease; therefore, the present study used the Japanese version of DLQ1 and included the phrase, "your hand and foot problems." License ID CUQoL1369 was obtained to use DLQI. Permission was obtained to use the Japanese version of DLQI Institute for Health Outcomes and Process Evaluation research.

Incidence of falls

The participants were asked whether they had experienced any falls since the onset of HFS, and if so, they were instructed to describe the reasons for falls related to HFS. The patients were also asked whether they had experienced any injuries since the onset of HFS.

Physical activity

Physical activity during the preceding week was assessed using the International Physical Activity Questionnaire-Short Form (IPAQ-SF). The Japanese version of IPAQ-SF is in the public domain, and its reliability and validity have been established in Japanese people aged 20 years and older.[20] The IPAQ-SF, which was developed by the International Consensus Group for cross-national assessment, is a seven-item questionnaire that includes the following four activity-related domains: vigorous-intensity physical activity, moderate-intensity physical activity, walking, and sitting.[21] In accordance with the IPAQ guidelines,[22] total Metabolic Equivalent of Task minutes per week was calculated using the following equation: $3.3 \times$ walking $+ 4.0 \times$ moderate-intensity physical activity $+ 8.0 \times$ vigorous-intensity physical activity. Overall physical activity was also evaluated as a categorical variable (i.e. low, moderate, and high) per IPAQ classification.[22] In the current study, participants in the low-IPAQ category were classified as inactive and participants in the moderate- or high-IPAQ categories were classified as active.

Psychological distress

The present study used the Japanese version of the Kessler 6 (K6), which is the public domain and has demonstrated its reliability and validity in Japanese people aged 20 years and older in assessing psychological distress.[23] The K6, which was developed by Kessler *et al.*,[24] is a widely used screening scale and consists of six items on mental health problems. Respondents' indicate the extent to which they have experienced the following emotions during the preceding 30 days: sadness, nervousness, restlessness, hopelessness, worthlessness, and feeling that everything was an effort. Responses are provided using a five-point scale ranging from 0 (none of the time) to 4 (all of the time), and total scores range from 0 to 24. The optimal cutoff point for K6 is 13 or above for serious mental illness.[25]

Data analysis

Descriptive statistics were performed to analyze the following: history of falls, demographic characteristics, cancer type and treatment, physical activity (measured via the IPAQ-SF), patient-reported HFS outcomes (measured via the DLQI), and psychological distress (measured via the K6). Mann–Whitney U-test and Fisher's exact tests were used for continuous and categorical data, respectively, to compare demographic characteristics, cancer type and treatment, and health status between participants who had and had not fallen and participants in the IPAQ low (i.e. inactive) and moderate/high (i.e. active) activity categories. Multiple logistic regression was performed to identify factors associated with falls and physical inactivity. A simultaneous variable selection was used in logistic regression. Statistical tests were two-tailed, and the significance level was set to $P < 0.05$. Statistical analyses were performed using SPSS (Version 22.0. IBM Corp., Armonk, NY, USA).

Results

Participant characteristics

In total, 50 patients participated in the study. Participants' demographic and clinical characteristics at the time of the survey are shown in Table 1. Their mean age was 63.0 (standard deviation [SD] = 12.8) years. Of the 50 participants, 29 (58.0%) were men, 31 (62.0%) had been educated to college level or higher, and approximately half were employed. Twenty (40.0%), 18 (36.0%), and 12 (24.0%) participants were diagnosed with colon and rectal cancer, gastric cancer, and other types of cancer, respectively; of these, 34 (68.0%) participants had Stage IV cancer. In addition, combination therapy was common (37 participants; 74.0%).

Of 13 (26.0%) patients undergoing monotherapy, 8 (16.0%) and 5 (10.0%) received chemotherapeutic drugs (i.e. capecitabine, TS-1 [Tegafur, Gimeracil, Oteracil Potassium], fluorouracil) and targeted therapy (e.g., regorafenib, sunitinib, imatinib), respectively. Of 37 (74.0%) patients undergoing combination therapy, 23 (46.0%) received chemotherapeutic drugs (e.g., XELOX [capecitabine + oxaliplatin], SOX [TS-1 + oxaliplatin], and FOLFOX [leucovorin calcium + fluorouracil + oxaliplatin]), whereas 14 (28.0%) received chemotherapy and targeted therapy (e. g., XELOX + BV [bevacizumab], FOLFIRI [leucovorin calcium + fluorouracil + irinotecan hydrochloride] + BV). Regarding the combination of drugs for peripheral neuropathy, 32 participants (64.0%) followed a with-oxaliplatin or paclitaxel regimen, while 18 (36.0%) followed a without-oxaliplatin or paclitaxel regimen.

Hand–foot syndrome status

Overall, 32 (64.0%) and 18 (36.0%) participants were diagnosed with Grade 1 and Grade 2 HFS, respectively [Table 1]. Participants' mean (SD) total DLQI score was 4.43 (6.03). Among the six individual DLQI domains, "the effect of disease" was reported as ≥1 by

Table 1: Participants' characteristics and associations between cancer-related factors and physical inactivity and falls in cancer patients with hand-foot syndrome, *n* (%)

Variable	Total (*n*=50)	Inactive[a]	Active[b]	P	Falls	No falls	P
Age (years)							
<65	27 (54.0)	19 (63.3)	8 (40.0)	0.149	4 (44.4)	23 (56.1)	0.715
≥65	23 (46.0)	11 (36.7)	12 (60.0)		5 (55.6)	18 (43.9)	
Gender							
Male	29 (58.0)	16 (53.3)	13 (65.0)	0.560	3 (33.3)	26 (63.4)	0.140
Female	21 (42.0)	14 (46.7)	7 (35.0)		6 (66.7)	15 (36.6)	
Educational level							
High school or lower	19 (38.0)	12 (40.0)	7 (35.0)	0.774	4 (44.4)	15 (36.6)	0.715
College or higher	31 (62.0)	18 (60.0)	13 (65.0)		5 (55.6)	26 (63.4)	
Employment							
Employed	23 (46.0)	13 (43.3)	10 (50.0)	0.774	4 (44.4)	19 (46.3)	>0.999
Unemployed	27 (54.0)	17 (56.7)	10 (50.0)		5 (55.6)	22 (53.7)	
Diabetes							
Yes	10 (20.0)	6 (20.0)	4 (20.0)	>0.999	2 (22.2)	8 (19.5)	>0.999
No	40 (80.0)	24 (80.0)	16 (80.0)		7 (77.8)	33 (80.5)	
Cancer type							
Colon and rectum	20 (40.0)	14 (46.7)	6 (30.0)	0.084	5 (55.6)	15 (36.6)	0.229
Gastric	18 (36.0)	7 (23.3)	11 (55.0)		1 (11.1)	17 (41.5)	
Other	12 (24.0)	9 (30.0)	3 (15.0)		3 (33.3)	9 (22.0)	
Cancer stage							
II/III	9 (18.0)	4 (13.3)	5 (25.0)	0.569	0 (0.0)	9 (22.0)	0.285
IV	34 (68.0)	22 (73.3)	12 (60.0)		7 (77.8)	27 (65.9)	
Unknown	7 (14.0)	4 (13.3)	3 (15.0)		2 (22.2)	5 (12.2)	
Regimen							
With-oxaliplatin or paclitaxel	32 (64.0)	23 (76.7)	9 (45.0)	0.035	5 (55.6)	27 (65.9)	0.705
Without-oxaliplatin or paclitaxel	18 (36.0)	7 (23.3)	11 (55.0)		4 (44.4)	14 (34.2)	
NCI-CTCAE version 4.0 HFS grade							
1	32 (64.0)	18 (60.0)	14 (70.0)	0.556	6 (66.7)	26 (63.4)	>0.999
2	18 (36.0)	12 (40.0)	6 (30.0)		3 (33.3)	15 (36.6)	
DLQI							
Symptoms and feelings score (≥1)	36 (72.0)	25 (86.2)	11 (55.0)	0.022	8 (88.9)	28 (70.0)	0.412
Daily activities score (≥1)	22 (44.0)	14 (48.3)	8 (40.0)	0.771	7 (77.8)	15 (37.5)	0.060
Leisure score (≥1)	15 (30.0)	9 (31.0)	6 (30.0)	>0.999	5 (55.6)	10 (25.0)	0.110
Work or school score (≥1)	15 (30.0)	8 (28.6)	7 (35.0)	0.755	4 (44.4)	11 (28.2)	0.432
Personal relationships score (≥1)	7 (14.0)	4 (13.8)	3 (15.0)	>0.999	2 (22.2)	5 (12.5)	0.598
Treatment score (≥1)	10 (20.0)	7 (24.1)	3 (15.0)	0.496	5 (55.6)	5 (12.5)	0.011
Total, mean (SD) (*n*=49)	4.43 (6.03)	4.72 (6.24)	4.00 (6.01)	0.687	0.00 (3.17)	3.98 (6.52)	0.277
Depression (K6)							
Moderate or severe (≥13)	4 (8.0)	3 (10.0)	1 (5.0)	0.641	1 (11.1)	3 (7.3)	0.560
None or mild (<13)	46 (92.0)	27 (90.0)	19 (95.0)		8 (88.9)	38 (92.7)	

DLQI: Dermatology Life Quality Index, HFS: Hand-foot syndrome, NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events, SD: Standard deviation

almost two-thirds (36, 72.0%) of the participants in the symptoms and feelings domain and almost half (22, 44.0%) of the participants in the daily activities domain.

Incidence of falls

Of the 50 participants, nine (18.0%) had experienced falls since the onset of HFS. Five participants reported falling once, and four, more than three times. The reasons for falls included "because my feet were numb, it was hard to walk," "I could not hold a handrail (at home)," "I could not lift my feet up," and "I lost my balance." None of the participants who fell were injured.

Physical activity

Thirty (60.0%), 15 (30.0%), and 5 (10.0%) participants were classified into the low-, moderate-, and high-IPQA physical activity categories, respectively. Therefore, 60.0% of the participants were physically inactive.

Factors affecting falls and physical inactivity

Table 1 shows the associations between cancer-related factors and physical inactivity and falls in cancer patients with HFS. CTCAE grading for HFS was not associated with falls or physical inactivity (Grade 2: falls: 33.3% vs. no falls: 36.6%, *P* > 0.999; 40.0% of inactive participants vs. 30.0%

of active participants, $P = 0.556$). DLQI scores ≥ 1 in the symptom and feeling domains were significantly associated with inactivity (86.2% of inactive participants vs. 55.0% of active participants, $P < 0.022$), while DLQI treatment domain score >1 was significantly associated with falls (55.6% of fall participants vs. 12.5% of no fall participants, $P < 0.011$). After adjusting for age (<65 years = 0, >65 years = 1) and sex (man = 0, woman = 1), logistic regression analysis showed that scores of >1 in the DLQI symptoms and feelings domain were significantly associated with physical inactivity (odds ratio [OR] = 5.54, 95% confidence interval [CI] = 1.26–24.33, $P = 0.023$). In addition, the with-oxaliplatin or paclitaxel regimen was significantly associated with inactivity [OR = 3.71, 95% CI = 1.06–13.03, $P = 0.041$; Table 2]. DLQI treatment domain score was the only variable significantly associated with having fallen [OR = 8.01, 95% CI = 1.27–50.63, $P = 0.027$; Table 3].

Discussion

For patients with HFS symptoms, such as erythema, erosion, and edema, day-to-day activities could contribute to symptom exacerbation, and avoidance of exposure of the hands and feet to heat, trauma, and pressure is essential.[5] Consequently, patients are likely to be physically inactive. The DLQI symptoms and feelings domain includes items on

symptoms as well as embarrassment and self-consciousness related to body image. Moreover, the results suggested that patients with HFS were likely to be physically inactive if they were physically and emotionally concerned about skin problems.

Furthermore, physical inactivity was significantly associated with the with-oxaliplatin or paclitaxel regimen. Platinum-based chemotherapies, including oxaliplatin, tend to lead to sensory peripheral neuropathy consisting of numbness, tingling, and paresthesia in the hands and feet, whereas taxane-based chemotherapies, including paclitaxel, cause sensory neuropathy such as paresthesia, numbness, and neuropathic pain in the hands and feet.[26] Mols *et al.*[8] examined the association between physical activity and CIPN in colorectal cancer survivors and found that failure to follow the physical activity guidelines was associated with CIPN. As patients who follow a with-oxaliplatin or paclitaxel regimen could be vulnerable to both neurological and dermatological symptoms in the hands and feet, they could be at increased risk of physical inactivity.

In the current study, 18.0% of the 50 participants had experienced falls. This result was unable to be compared with data from previous research because few studies have focused on the incidence of HFS-related falls. The participants in the current study lost their balance because of numbness, hyperesthesia in the soles of their feet, and inability to hold handrails because of symptoms in the hands, which led to HFS-related falls. As dysesthesia develops not only insoles of the feet but also the palms and fingers,[27] patients could experience difficulty in holding handrails, which are intended to prevent falls.

Moreover, the DLQI treatment domain score was significantly associated with having fallen. Patients who reported that skin treatment caused a lot of problems (e.g., creating a mess at home or taking up time) were at a high risk of falls. In the prevention and management of HFS, different skin care approaches are required for different symptoms and grades of toxicity.[28] Peripheral neuropathy may underlie the difficulty in the management of patients with HFS. A cohort study using random sampling by regimen is needed to determine the incidence of peripheral neuropathy and assess the confounding factors of HFS and falls, taking into account peripheral neuropathy in falls and physical inactivity among patients with cancer and HFS.

The current study suggests that HFS is a risk factor for physical inactivity and falls, and patient education regarding HFS is important in the prevention of falls and physical inactivity. Ideally, patients should be educated before initiating anticancer therapy (e.g., advised that patients with numbness and dysesthesia are likely to lose their balance,

Table 2: Multivariate associations between physical inactivity and Dermatology Life Quality Index scores, demographic characteristics, and cancer-related factors in cancer patients with hand-foot syndrome

Predictor	Estimated adjusted odds ratio (adjusted for age[a] and sex[b])		
	OR	95% CI	P
Age (≥65 years vs. <65 years)	0.37	0.12-1.21	0.102
Gender (female vs. male)	1.72	0.52-5.73	0.377
Educational level (high school or lower vs. college or higher)	2.68	0.54-13.40	0.229
Employment (unemployed vs. employed)	1.94	0.43-8.81	0.389
Cancer stage (IV vs. others)	2.01	0.57-7.14	0.280
Regimen (with-oxaliplatin or paclitaxel vs. without-oxaliplatin or paclitaxel)	3.71	1.06-13.03	0.041
NCI-CTCAE version 4.0 grade (2 vs. 1)	1.25	0.35-4.42	0.730
DLQI			
Symptoms and feelings score (≥1 vs. 0)	5.54	1.26-24.3	0.023
Daily activities score (≥1 vs. 0)	0.99	0.28-3.54	0.983
Leisure score (≥1 vs. 0)	1.10	0.30-3.98	0.885
Work or school score (≥1 vs. 0)	0.51	0.13-1.99	0.334
Personal relationships score (≥1 vs. 0)	0.97	0.18-5.31	0.973
Treatment score (≥1 vs. 0)	1.34	0.25-7.03	0.733
Total	1.10	0.91-1.12	0.869
Depression (K6; <13 vs. ≥13)	0.80	0.07-9.32	0.862

[a]≥65 years=1, <65 years=0, [b]Male=0, female=1. CI: Confidence interval, NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events, OR: Odds ratio, DLQI: Dermatology Life Quality Index

Table 3: Multivariate associations between falls and Dermatology Life Quality Index, demographic characteristics, and cancer-related factors in cancer patients with hand-foot syndrome

Predictor	Estimated adjusted odds ratio (adjusted for age[a] and sex[b])		
	OR	95% CI	P
Age (≥65 years vs. <65 years)	1.59	0.36-7.05	0.546
Gender (female vs. male)	3.46	0.75-15.96	0.112
Educational level (high school or lower vs. college or higher)	0.66	0.09-4.67	0.679
Employment (unemployed vs. employed)	0.30	0.04-2.36	0.250
Cancer stage (IV vs. others)	1.85	0.32-10.63	0.492
Regimen (with-oxaliplatin or paclitaxel vs. without-oxaliplatin or paclitaxel)	0.62	0.13-2.90	0.548
NCI-CTCAE version 4.0 grade (2 vs. 1)	0.82	0.16-4.24	0.813
DLQI			
Symptoms and feelings score (≥1 vs. 0)	2.79	0.30-25.96	0.367
Daily activities score (≥1 vs. 0)	5.63	0.91-34.94	0.064
Leisure score (≥1 vs. 0)	4.28	0.87-21.03	0.073
Work or school score (≥1 vs. 0)	2.03	0.42-9.87	0.379
Personal relationships score (≥1 vs. 0)	2.74	0.38-19.75	0.317
Treatment score (≥1 vs. 0)	8.01	1.27-50.63	0.027
Total	1.05	0.94-1.17	0.406
Depression (K6) (<13 vs. ≥13)	0.49	0.04-6.97	0.601
Physical activity (IPAQ low vs. moderate/high)	1.34	0.27-6.58	0.721

[a]≥65 years=1, <65 years=0, [b]Male=0, female=1. CI: Confidence interval, IPAQ: International Physical Activity Questionnaire, NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events, OR: Odds ratio, DLQI: Dermatology Life Quality Index

which results in falling). In addition, the increased incidence and severity of adverse drug events resulting from novel therapy, such as HFS, has emphasized the significance of dermatological evaluation in patients with cancer.[29] Patient-reported outcome instruments, such as the DLQI, should be used in outpatient visits or telephone counseling conducted to assess difficulties involving dermatological problems affecting patients' daily lives and the continuation of treatment, which are not reflected in the objective assessment of HFS severity, and determine whether these difficulties are risk factors for falls. Moreover, it is important to understand changes in HFS-related body image and determine whether they are associated with physical inactivity. Frequent communication between patients and health-care professionals helps them to understand patients' recognition of HFS and encourage patients to manage HFS proactively.

Conclusion

The results of this study showed that physical inactivity and falls occurred in 60.0% and 18.0%, respectively, of patients with gastrointestinal cancer and HFS Grade 1 or above according to the CTCAE. DLQI symptoms and feelings domain score was significantly associated with physical inactivity, while treatment domain score was significantly associated with falls. In addition, the impact of combination therapy should not be overlooked, as the with-oxaliplatin or paclitaxel regimen was also significantly associated with physical inactivity. Moreover, patients should be informed that HFS is a risk factor for

physical inability and falls before initiating anticancer therapy.

This study has limitations. The study was conducted at only one research site; hence, the desired sample size was not included. Therefore, the present study could not establish causality in the relationship between physical inactivity and falls in patients with HFS. In addition, recall bias could have occurred in self-reported fall history. Moreover, the generalizability of the results is limited because the participants were cancer patients at a single hospital in Japan. Future studies with prospective study designs should be conducted to determine the causes of physical inactivity and falls while considering various cancer types and therapy regimens.

Conflicts of interest

There are no conflicts of interest.

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