RESEARCH ARTICLE

Physical Functions, Health-Related Outcomes, Nutritional Status, and Blood Markers in Community-Dwelling Cancer Survivors Aged 75 Years and Older

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Abstract

Background: A cancer survivor is defined as anyone who has been diagnosed with cancer, from the time of diagnosis through the rest of their life. The purpose of this study was to examine whether physical functions, health-related outcomes, nutritional status and blood markers in community-dwelling cancer survivors aged 75 years and older are different from those who do not have cancer Materials and Methods: Two hundred seventy-five participants were asked by physicians, nurses, and physical therapists, questions regarding cancer history in a face-to-face interview. Data were collected for demographic information, physical functions, such as handgrip strength, knee extension power, abdominal muscle strength, static standing balance, walking speed and the timed-up-and-go test, health-related outcomes, nutritional status, and blood markers. The measured parameters of survivor diagnosed with cancer were compared with those without a history of cancer. Results: Thirty-seven older adults were previously diagnosed with cancer. Female cancer survivors had lower knee extension power ($p<0.05$), abdominal muscle strength ($p<0.05$), walking speed ($p<0.05$), timed-up-and-go test score ($p<0.05$), and time to spend on walking per day ($p<0.05$) than older women without a history of cancer. In men, none of the measured parameters were significantly different between cancer survivors and older men with no history of cancer. Conclusions: The present study shows that partial physical function of women cancer survivors aged 75 years and older differs from that in women with no history of cancer.

Keywords: Cancer survivor - health-related quality of life - older women - physical function

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Introduction

The Japan Cancer Surveillance Research Group estimated the incidence of cancer in 2006 as part of the Monitoring of Cancer Incidence in Japan project. In their report, the total incidence of cancer in Japan for 2006 was estimated as 664,398, and the incidence of cancer continues to increase (Matsuda et al., 2012). Since the early 2000s, the age-standardized incidence rates in all cancer sites have slightly increased, whereas they remained unchanged in the 1990s. Although malignant tumors occur at all ages, cancer disproportionately strikes individuals in the age group of 65 years and older (Yancik, 2005). A cancer survivor is defined as anyone who has been diagnosed with cancer, from the time of diagnosis through the rest of their life (Rock et al., 2012). Older adults are more likely to experience age-related comorbid conditions, which may impact the prognosis of cancer, quality of life, and survival. Older adults may also be more susceptible to toxicities of cancer treatments, which contribute to the emergence of new comorbidities and to an increased risk of mortality (Balducci and Corcoran, 2000; Ahern et al., 2009).

When older cancer survivors finish medical treatment and return to home life, fundamental physical functions deteriorate because of the effect of surgical treatment, chemotherapy, and radiotherapy. Furthermore, older cancer survivors need to face ageing and disease-related functional deterioration simultaneously, which can affect their quality of life. For example, older cancer survivors report more health problems and reduced health-related quality of life compared with cancer-free controls (Baker et al., 2003). Studies have suggested that older cancer survivors are at increased risk for functional limitations compared with similarly aged individuals with no history of cancer (Kurtz et al., 1997; Given et al., 2000; 2001; Chirikos et al., 2002; Keating et al., 2005; Sweeney et al., 2006).

Some reports have suggested that physical function of cancer survivors returns to normal over time (Watters et

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al., 2003). However, it is expected that cancer survivors who are aged 75 years and older will have difficulty in recovering their functional capacity because of aging. Little is known about the characteristics of cancer survivors who are aged 75 years and older after medical treatment. Therefore, we examined whether physical functions, health-related outcomes, nutritional status and blood markers in community-dwelling cancer survivors aged 75 years and older are different from persons aged 75 years and older who do not have cancer.

Materials and Methods

Participants

This study was first wave of the "Population-based and Inspiring Potential Activity for Old-old Inhabitants (PIPAOI)" study. The ethical aspects of the study were approved by the Sapporo Medical University Hospital Ethics Committee. We obtained written informed consent from each patient before study initiation. For this cross-sectional study, the 1312 potential community-dwelling older adults aged 75 years and older were sent an introductory letter. Of the original 1312 potential participants who were mailed surveys, 316 participants replied that they would take the survey. Among the participants who sent replies, 275 replied that they would take the survey, but 41 did not attend. Eligible participants for PIPAOI included men and women aged 75 years and older who were able to walk in their home. Participants were excluded if they were hospitalized for longer than 1 week because of high blood pressure, stroke, cardiovascular disease, respiratory disease, diabetes, joint pain, and osteoporosis, 3 months before the study. Participants were also excluded if they were diagnosed with dementia, depression, and schizophrenia.

Data collection

All participants were asked by physicians, nurses, and physical therapist by face-to-face interview, "Have you ever been diagnosed with cancer or a malignancy of any kind by a doctor or other health professional?" If the respondents reported a history of cancer, they were asked about the site of the cancer and the age when they were first diagnosed. In analyses of this study, cancer survivors included respondents who reported ever having a diagnosis of cancer, regardless of whether they had symptoms of cancer at the time of the present survey.

Physical function

Measures of handgrip strength were taken twice from the dominant hand, and the best of these was used for analysis. Handgrip strength regarded to a valid indicator of general health status was measured using a Smedley-type handheld dynamometer (Matsumiya Medical Industry, Tokyo, Japan) (Nordenskiold and Grimby, 1993). Isometric knee extension strength was tested once using a dynamometer (μTas F-1; Anima Corp., Tokyo, Japan). Knee extension was measured while the participant was sitting on a chair with a backrest and the knee was flexed to 90˚C. A testing pad was attached to the front lower leg of the participant and strapped to the leg of the chair (Shimada et al., 2010). Maximal isometric knee extension torque was normalized against arm moment and body mass (Nm/kg) in the data analysis. The partial curl-up test of the Canadian Standardized Test of Fitness was used to assess abdominal muscle strength (Moreland et al., 1997). This test started from a supine position with the knee at 90˚C and the hands crossing in front of chest. Participants were instructed to flex the trunk as far as possible. Abdominal muscle strength was evaluated with a score of 1-5: *i*) cannot raise the occipital protuberance from the start position; *ii*) can raise the occipital protuberance from the start position; *iii*) can raise the inferior angle of the scapula from the start position; *iv*) cannot raise the whole upper body but can raise the posterior superior iliac spine from the start position and; *v*) can raise the whole upper body. Licensed and well-trained physical therapists confirmed compensatory movement, and assessed knee and abdominal muscle strength. For balance assessment of postural stability, postural sway during quiet standing was measured with a force plate (ECG-1500A, Kyowa, Japan). Signals were sampled at 50 Hz and registered for a period of 20s. The root mean squared was calculated for the test trial as the deviation from the average COP value. Higher root mean squared values indicate greater variability, traditionally interpreted as greater postural instability (Redfern et al., 2001). The maximum walking speed of the participants was measured. We asked subjects to walk on a straight walkway 11m in length on a flat floor at twice their maximum speed. Walking speed was measured over a 5m distance between 3 and 8m from the start of the walkway (Shinkai et al., 2000). The TUG test was performed according to the ordinary method that measures the time taken to rise from a chair, walk 3m, turn, and return to a sitting position (Podsiadlo and Richardson, 1991). Participants were instructed to complete the task at their maximal walking pace in the TUG test.

Health-related outcomes

Self-reported questionnaires were used to access the health-related outcomes. We assessed self-related health by asking respondents on a 4-point scale (very good, good, poor, very poor). Participants were asked self-rated physical and cognitive ages by: "How old are your physical and cognitive ages?" The fall history was assessed by questionnaire as follows (Lamb et al., 2005): "In the past month, have you had any falls, including slipping or tripping in which you lost your balance and landed on the floor, ground, or lower level?" The Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC) includes 13 items, which are used to measure high level functional capacity (Koyano et al., 1991). WHO-5 was originally designed by the World Health Organization for the assessment of well-being among diabetic patients (Bech et al., 1996). In the present study, the latest version of the WHO-5 was used. Items are rated on a 6-point scale ranging from "all of the time" (5) to "at no time" (0), resulting in a maximum sum score of 25. To estimate activity outside the home, participants were asked, "How frequently do you go outdoors in a week?" Participants responded by questionnaire on 8-point scale ranging from "Seven days per week" (7) to "Less than once per week" (0). Participants were also asked "Approximately how many minutes per day do you usually walk outside, including work, shopping, and exercise?"

Nutritional status

Food intake was also assessed using a questionnaire on food intake frequency covering 1 week and the 10 main food groups (meat, fish and shellfish, eggs, milk, soybean products, green and yellow vegetables, potatoes, fruits, seaweed, and fats and oils) in the Japanese diet (Kimura et al., 2013). There were four choices for food intake frequency for each food group: I) eat almost every day (3 points), II) eat 3 or 4 days a week (2 points), III) eat 1 or 2 days a week (1 point), and IV) hardly ever eat (0 points). We then calculated a food frequency score (FFS) as the sum of scores for each of the 10 food groups to evaluate dietary habits (range, 0-30). We also assessed appetite using a questionnaire.

Blood markers

Determinations of serum total protein (biuret assay), albumin (BCG assay), total cholesterol (cholesterol oxidase assay), aspartate aminotransferase (AST) (enzyme assay), alanine aminotransferase (ALT) (enzyme assay), C-reactive protein (latex agglutination assay), white blood cells (WBC) and red blood cells (RBC) were measured using an auto-analyzer (Hitachi 7700; Hitachi, Ltd., Japan). Blood samples were collected in EDTA tubes. All biochemical markers were measured by contract arrangement with Health Sciences Research Institute, Inc. (Sapporo, Japan).

Statistical analysis

Physical functions, health-related outcomes, nutritional status, and blood markers of cancer survivors were compared with those without history of cancer. Differences between cancer survivors and those with no cancer groups were evaluated using the Mann-Whitney U test for ordered variables, and t-tests were used for examining differences between these groups for continuous variables. Differences between three groups of cancer history (no cancer history, cancer survivor within 5 years, and cancer survivor who was diagnosed 5 years ago or longer) were assessed using analysis of covariance (ANCOVA), with age and body mass index (BMI) entered as covariates. Tukey's post hoc analysis was used to identify group differences. The threshold for statistical significance was defined as $p<0.05$. Statictical analysis was performed using SPSS (version 19.0, IBM Japan Ltd., Tokyo, Japan).

Results

In this study, 37 older adults (mean age, 79.8; SD, 3.8; range, 75-89 years) were previously diagnosed with cancer, and 238 older adults (mean age, 80.0; SD, 4.1; range, 75-96 years) did not have a history of cancer (Table 1). The mean duration of cancer history in cancer survivors was 8.9±7.6 years and ranged from 1 to 30 years. There were no significant differences in age, sex, body weight, body height, body mass index, and educational years in cancer survivors compared with older adults with no history of cancer.

In men, none of the measured parameters were significantly different between cancer survivors and older men with no history of cancer. However, female cancer survivors had a lower physical function, such as knee extension power, abdominal muscle strength, walking speed, and TUG test score than older women with no history of cancer (all $p<0.05$). In addition, female cancer survivors had little time to spend on walking per day ($p<0.05$) than older women without a history of cancer. Among blood markers, higher albumin levels were detected in female cancer survivors than older women without a history of cancer ($p<0.05$). There was no significant difference in nutritional status between cancer survivors and those without cancer (Table 2).

Figure 1 shows the mean differences in walking speed,

Table 1. Demographic Characteristics of Cancer Survivors and Without History of Cancer

		Cancer survivors (n=37)	Without history of cancer (n=238)	p value
Characteristics [Mean (SD)]				
Age, years		79.8 (3.8)	80.0(4.1)	0.77
Sex, male/female		18/19	94/144	0.37
Weight, kg		57.9 (11.2)	56.2(9.8)	0.39
Height, cm		153.6 (8.3)	152.2(9.3)	0.32
BMI		24.6 (3.9)	24.1(3.1)	0.63
Education, years		9.8 (2.2)	9.6(2.2)	0.69
History of cancer, years		8.9 (7.6)		
Cancer type [N (%)]	Breast	3 (8.2)		
	Lung	1 (2.7)		
	Lymphoma	2 (5.4)		
	Gastrointestinal	13 (35.1)		
	Genitourinary	9 (24.3)		
	Gynecologic	4 (10.8)		
	Skin	1 (2.7)		
	Brain tumor	1 (2.7)		
	Hepatic	1 (2.7)		
	Other	2 (5.4)		

*p values based on chi-square test of association for categorical variables and t-test for continuous variables. SD=standard deviation; BMI=body mass index

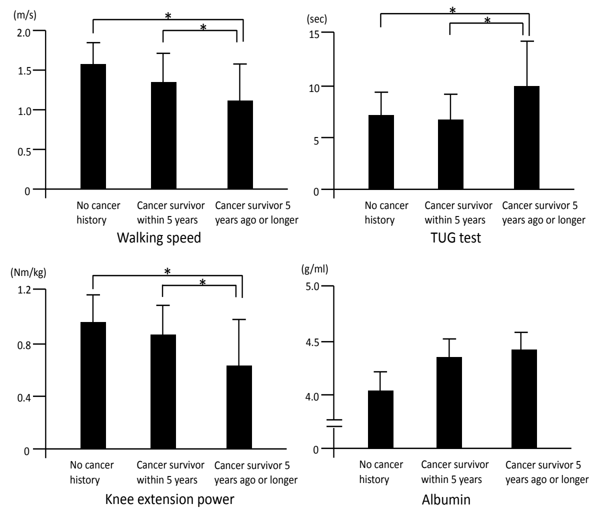

Figure 1. Walking Speed, Knee Extension Power, TUG and Serum Albumin Levels between the Three Groups (i.e., No Cancer History, Cancer Survivor Within 5 Years, and Cancer Survivor Who was Diagnosed 5 Years Ago or Longer)

Table 2. The Comparison of Physical Function, Health-Related Outcome, Nutritional Status and Blood Marker Between Cancer Survivors and Without History of Cancer

		Male		Female	
		Cancer survivors (n=18) Mean (SD)	Without history of cancer (n=94) Mean (SD)	Cancer survivors (n=19) Mean (SD)	Without history of cancer (n=144) Mean (SD)
Physical function	Grip power, kg	31.3 (7.5)	31.9 (6.3)	19.4 (4.9)	20.6 (4.7)
	Knee extension power, Nm/kg	1.2 (0.3)	1.2 (0.4)	0.7 (0.3)	0.9 (0.3)*
	Abdominal muscle strength, score	3.2 (0.8)	3.6 (1.0)	2.5 (0.8)	2.9 (1.0)*
	Postural sway area, mm^2	228.7 (127.2)	240.9 (151.4)	200.1 (100.6)	232.1 (193.6)
	Walking speed, m/s	1.7 (0.3)	1.7 (0.3)	1.3 (0.4)	1.5 (0.3)*
	TUG test, s	6.6 (2.0)	6.4 (1.7)	8.6 (4.0)	7.4 (2.5)*
Helth-related outcome	Self-rated health, score	2.4 (0.6)	2.2 (0.6)	2.6 (0.9)	2.4 (0.8)
	Self-rated physical age, years	76.4 (6.2)	75.3 (6.3)	77.7 (5.7)	78.3 (5.7)
	Self-rated cognitive age, years	76.6 (5.8)	75.8 (6.5)	76.1 (5.5)	77.3 (10.7)
	Fall history, yes/no	4/14	23/71	7/12	57/87
	TMIG, score	12.4 (1.0)	11.4 (2.5)	11.3 (1.9)	11.5 (2.1)
	WHO-5, score	18.0 (5.6)	16.5 (5.4)	14.6 (4.2)	16.4 (5.6)
	Frequency of going outdoors, day	4.3 (1.6)	4.5 (2.1)	3.4 (1.8)	3.8 (2.0)
	Walking times per day, min	44.4 (39.4)	49.2 (56.4)	22.3 (16.2)	34.0 (47.2)*
Nutritional status	Fish and shellfis, points	2.3 (0.8)	1.8 (0.8)	1.8 (0.7)	1.8 (0.8)
	Meat, points	2.6 (0.8)	2.4 (0.8)	2.5 (0.7)	2.5 (0.8)
	Eggs, points	2.2 (0.9)	2.3 (0.9)	2.1 (0.6)	2.1 (0.6)
	Milk, points	2.6 (1.4)	2.5 (1.2)	2.4 (1.1)	2.1 (1.2)
	Soybean products, points	2.1 (0.9)	1.9 (0.9)	1.6 (0.7)	1.6 (0.8)
	Green and yellow vegetables	1.8 (0.9)	1.7 (0.8)	1.7 (0.7)	1.4 (0.7)
	Seaweed, points	2.3 (1.0)	2.4 (0.9)	2.5 (0.8)	2.2 (0.9)
	Potatoes, points	2.2 (0.9)	2.3 (0.9)	2.3 (0.9)	2.1 (0.8)
	Fruits, points	1.5 (0.8)	1.8 (0.9)	1.5 (0.8)	1.5 (0.8)
	Fats and oil, points	2.3 (0.9)	2.1 (0.9)	2.0 (0.7)	2.0 (0.9)
	FFS, points	21.3 (5.0)	21.2 (4.9)	20.3 (4.4)	19.6 (4.3)
	Appetite, score	1.8 (0.4)	1.6 (0.5)	1.5 (0.6)	1.7 (0.5)
Blood marker	TP, g/dl	7.0 (0.5)	7.0 (0.5)	7.1 (0.4)	7.0 (0.4)
	Alb, g/dl	4.3 (0.2)	4.2 (0.2)	4.4 (0.2)	4.2 (0.2)*
	Total cholesterol, mg/dl	199.9 (29.0)	199.5 (37.1)	183.9 (21.0)	184.7 (38.0)
	AST, IU/L	23.2 (5.0)	25.4 (7.8)	25.4 (7.8)	25.4 (9.1)
	ALT, IU/L	18.7 (7.1)	20.4 (9.9)	26.3 (5.2)	20.0 (9.9)
	CRP, mg/dl	0.10 (0.15)	0.14 (0.26)	0.07 (0.06)	0.12 (0.17)
	WBC, ul	5617.7 (1161.0)	5848.4 (1524.3)	5705.3(1322.7)	5739.9(1449.8)
	RBC, $\times 10^4/\mu L$	437.1 (40.5	432.2 (45.6)	423.9 (28.6)	414.1 (46.5)

*p<0.05, p values based on Mann-Whitney's U test for ordered variables and t-test for continuous variables; SD=standard deviation; TUG=timed and up go; TMIG=Tokyo Metropolitan Institute of Gerontology; FFS=food frequency score, TP=total protein, Alb=albumin, AST=aspartate aminotransferase; ALT=alanine aminotransferase, CRP=C-reactive protein, WBC=white blood cell, RBC=red blood cell

knee extension power, TUG test, and serum albumin levels between the three groups (i.e., no cancer history, cancer survivor within 5 years, and cancer survivor who was diagnosed 5 years ago or longer). Analysis of covariance (age and BMI as covariates) for walking speed showed significant main effect of group divided into the duration from previously diagnosing cancer ($F=9.0$, $p<0.05$). Similar results were obtained for knee extension power ($F=3.8$, $p<0.05$) and the TUG test ($F=5.5$, $p<0.05$), whereas serum albumin was increased ($F=4.5$, $p<0.05$).

Discussion

In the present study, we measured physical functions, health-related outcomes, nutritional status, and blood markers to determine the characteristics of cancer survivors aged 75 years and older. We showed that walking speed, knee extension power, abdominal muscle strength, and the TUG score of female cancer survivors aged 75 years and older were significantly lower than those in older women with no history of cancer. There are two reasons for this finding. First, cancer survivors enrolled in this study could have been affected by cancer cachexia. Cancer cachexia, also known as muscle wasting, is a multifactorial syndrome characterized by continuing loss of skeletal muscle mass (Dobs et al., 2013). Approximately 30% of patients with cancer are estimated to be affected by cachexia (Morley et al., 2006). Muscle wasting according to cancer cachexia begins early in the disease process (Prado et al., 2008), resulting in decreased physical function, such as knee extension power and abdominal muscle strength. Patients with muscle wasting commonly also present with fatigue and reduced physical function, which can contribute to disability of mobility assessed by walking speed and the TUG test. Second, cancer survivors are likely to be sedentary. Because cancer survivors have limited activity owing to various side effects, such as fever, neuropathy, and edema during cancer treatment, their physical function deteriorates (Valenti et al., 2008). Moreover, psychosocial problems among cancer survivors are common and may include fear of recurrence and death, anxiety and depression, feelings of alienation or isolation, and problems with interpersonal relationships (Gotay et al., 1998). For these reasons, cancer survivors are likely to be inactive physically and psychologically. In addition, in the current study, the low activity of cancer survivors was accompanied by the finding that female cancer survivors had little time to spend on walking per day than those without history of cancer.

However, male cancer survivors showed no significant differences in any of the items studied compared with men with a history of cancer. Inoue et al reported that there was a stronger effect in women than in men on total physical activity among those who engaged in regular leisure-time sports or physical exercise than among those who did not (Inoue et al., 2008). Shephard and Shek also suggested that differences between the sexes associated with regular physical activity are due to the differences in hormonal conditions, which may lead to failure to adapt activity questionnaires to traditional patterns of physical activity in women (Shephard and Shek, 1998). Men are more likely to be physically active in their jobs and women are more likely to be involved in housework (Blair et al., 2001). There is a consensus that physical function of men is higher than that of women, as supported by the results of the present study. Therefore, we consider that a decline in physical functions is greater among female cancer survivors than those of male cancer survivors because low physical function in women and inactivity according to treatment and side effects overlap. Results of analysis of covariance, we found that cancer survivors who were diagnosed 5 years ago or longer had less deterioration in knee extension power, walking speed, and TUG scores than those who were diagnosed within 5 years. Previous studies have shown that approximately 50% of patients with cancer have significant weight and muscle loss at the time of cancer diagnosis, and that this weight or muscle loss continues throughout the course of malignant disease, affecting approximately 80% of patients at the time of death (Baracos et al., 2010). For this reason, it can be assumed that physical function in female cancer survivors is not fully recovered even if a long period of time has passed

Serum albumin is one of the most commonly used indices to measure nutritional status (McIntosh and Laurent, 1983). Physical function of community-dwelling older adults is associated with serum albumin levels and tends to decrease at low serum albumin levels (Kwon et al., 2005; Schalk et al., 2005). It is reported that cancer survivors is also similar to that (Maltoni and Amadori, 2002). In contrast, Takata et al. reported that lower serum albumin levels were an independent predictor of total mortality, but not mortality due to cancer in adults aged 70 years and older in Japanese people (Takata et al., 2012). In the present study, high serum albumin levels were detected in female cancer survivors. However, the reason for this finding is unclear. Limitations of this study include the cross-sectional design, self-reported measures of health-related outcome and nutritional status, and limited generalizability. In addition, the generalizability of our findings is constrained because the small sample size could be deemed a potential limitation of the present study cohort.

In conclusion, the present findings show that female cancer survivors aged 75 years and older have some lower physical functions compared with older women with no history of cancer. Results from this study also suggest that physical function of long-term cancer survivors is more deteriorated than in recent cancer survivors. Future research should determine whether exercise interventions that improve physical function or activity level, such as the frequency of going outdoors and walking time of outdoor interventions, have an impact on patterns of decline in physical functioning in cancer survivors aged 75 years and older.

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