



The association between fatigue and pain symptoms and decreased physical activity after cancer

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Abstract

Purpose Patients with cancer frequently experience symptoms such as fatigue and pain that can influence their ability to maintain their usual physical activity (PA). This study aimed to evaluate whether symptoms of fatigue and pain are associated with decreased PA among patients with cancer.

Methods We recruited patients with a cancer diagnosis from one academic medical center and 11 affiliated community hospitals to participate in a cross-sectional survey. Multivariate logistic regression models were used to examine the association between symptoms, demographics, and clinical characteristics and decreased PA since cancer diagnosis.

Results Among 629 participants, 499 (79%) reported a decreased level of PA since their cancer diagnosis. In the past 7 days from the time of the survey, 78% of participants reported moderate to very severe fatigue, and 68% reported a pain level 4 or greater on a scale of 0 to 10. Adjusted for covariates, patients with fatigue (Adjusted Odds Ratio, AOR 4.01, 95% CI 2.41–6.65) and pain (AOR 1.89, 95% CI 1.14–3.12) had higher odds of reporting decreased PA since diagnosis. Receipt of chemotherapy or currently receiving active cancer treatment was also associated with decreased PA ($p < 0.05$).

Conclusions Fatigue and pain are associated with decreased PA among patients with cancer, even after adjusting for cancer treatment. Interventions focused on managing these symptoms may help promote maintenance of PA throughout cancer treatment and beyond.

Keywords Physical activity · Fatigue · Pain · Cancer · Supportive care

Introduction

As of January 2016, 15.5 million Americans were living with a cancer diagnosis [1]; many of whom experience bothersome symptoms, such as fatigue and pain, after their cancer diagnosis [2–4]. Previous research has shown that physical activity is important for cancer prevention [5, 6]; in addition, emerging data from clinical trials highlight that exercise during and after

cancer treatment may improve cancer-related fatigue, quality of life, and other cancer-related outcomes [7–11]. Physical activity can be defined as any movement of the skeletal muscles that results in energy expenditure; whereas, exercise is a type of physical activity (PA) that is planned, structured and repetitive and has a set objective of improving or maintaining physical fitness [12]. Many professional clinical societies and cancer organizations, such as the American Cancer Society (ACS) and the American College of Sports Medicine, have made PA recommendations for cancer patients [7, 13]. Among these recommended guidelines, cancer patients are encouraged to engage in 150 min of moderate aerobic activity or 75 min of vigorous aerobic activity per week, including strength training exercises at least 2 days per week [7].

Despite the recognized benefits of PA, many cancer patients are not meeting recommended guidelines and are less likely than the general population to engage in PA [14–16]. Previous research in primarily breast and colorectal cancer populations has found that the majority of these patients decrease their PA levels after a cancer diagnosis [17–20]. Cancer

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and its related treatments are often accompanied by significant symptom burden, including fatigue [2, 21], pain [21, 22], and psychosocial distress [23, 24], which may influence PA levels among cancer patients. While growing research exists examining PA levels following a cancer diagnosis among cancer patients, this research has mainly focused on breast and colorectal cancer patients and is often limited to patients seen in academic centers or in the context of formal exercise intervention studies.

Much less is known about patients with diverse cancer types seen in community cancer care settings or outside the confines of an exercise clinical trial, which by its nature recruits already motivated patients to participate in PA. Using a health services perspective of PA as a desired health behavior, this study examines PA level after cancer among patients diagnosed with different cancer types in both academic and community cancer care settings. Specifically, the objectives of this study were (1) to evaluate the relationship between current symptoms (i.e., fatigue, pain, and emotional distress) and a self-reported decrease in PA level following cancer diagnosis, and (2) to identify other risk factors associated with decreased PA.

Materials and methods

Study design and population

We conducted a cross-sectional survey study among cancer patients treated at the Abramson Cancer Center (ACC) at the University of Pennsylvania in Philadelphia and 11 ACC-affiliated community hospitals in Pennsylvania and New Jersey. Eligible patients were 18 years of age or older, had a primary diagnosis of any cancer type, were ambulatory (Karnofsky functional score of ≥ 60), understood written English, and reported experiencing non-zero (> 0) pain (on a scale of 0 to 10) in the last 7 days. Trained research staff met with patients in clinic waiting rooms, obtained written informed consent, and administered the written paper survey. The institutional review board of the University of Pennsylvania and the Clinical Trials Scientific Review and Monitoring Committee of the ACC approved the study protocol and survey.

Questionnaire content

Patient demographics, cancer and treatment characteristics, current symptoms, and physical activity questions were included in the study questionnaire completed by the patients. Demographic data included the following: age at study enrollment, sex, race/ethnicity, relationship status, education, and body mass index (BMI) (calculated from patient-reported height and weight). Participants reported information about

cancer type, cancer treatments (e.g., radiation, surgery, chemotherapy), treatment status at time of the questionnaire (i.e., completed cancer treatments, currently receiving cancer treatments, or about to start cancer treatments), and year of cancer diagnosis. Cancer type was verified and cancer stage was determined from chart abstractions.

The PROMIS global health 10-item validated instrument assesses general domains of health and functioning including perceived quality of life, overall physical health, mental health, emotional distress, pain, and fatigue [25, 26]. This instrument has been shown to demonstrate adequate reliability with the item-scale correlations for the 10 items ranging from 0.53 to 0.80, and internal consistency reliability equal to 0.92 in community and clinical samples [25]. Specifically, three items from this instrument were used to assess current symptoms of fatigue, pain, and emotional distress in the past 7 days. For fatigue, participants were asked “How would you rate your fatigue on average?” on a five-point Likert scale from “none” to “very severe.” To assess pain, participants answered “How would you rate your pain on average?” on a scale of “0—no pain” to “10—worst pain imaginable.” For emotional distress, participants were asked to rate on five-point Likert scale “How often have you been bothered by emotional problems such as feeling anxious, depressed, or irritable?” with response choices ranging from “never” to “always.”

To assess level of PA since cancer diagnosis, participants were asked “Since my cancer diagnosis, I have...” with these three answer options “decreased my level of physical activity,” “maintained my level of physical activity,” or “increased my level of physical activity.” Participants were also asked to report if they had met the ACS physical activity recommendations of 150 min of moderate activity or 75 min of vigorous activity per week on average in the past month with answer choices of “yes” or “no.”

Statistical analysis

Descriptive statistics were calculated as frequencies and percentages. The primary outcome was level of physical activity since cancer diagnosis, for which we dichotomized responses as “decreased” or “maintained/increased” level of PA. Pearson chi-square tests were conducted examining demographic, clinical characteristics, and current symptoms associated with level of PA since cancer diagnosis. Explanatory variables associated with the primary outcome at $p < 0.20$ in the univariate analyses were included in the multivariate regression models.

Logistic regression models were used to estimate odds ratios (OR) for characteristics associated with decreased level of PA. For demographics, we dichotomized race as “White” and “non-White,” education as “high school or less” and “some college or above,” and relationship status as “partnered” or “not partnered.” For cancer characteristics, cancer type was dichotomized as “breast” versus “other” diagnosis, stage as

“metastatic” or “non-metastatic,” and cancer treatment status as “currently receiving treatment” or “completed treatment.” For current symptoms, pain was dichotomized as “level 0 (no pain) to 3” or “level 4 to 10 (worst pain),” fatigue as “none to mild” or “moderate to very severe,” and emotional distress as “never to rarely” or “sometimes to always.” Statistical significance for the multivariate regression models was set at $p < 0.05$. All statistical analyses were conducted using SPSS (Windows version 24.0, IBM Corporation, Armonk, NY) software.

Results

From September 2014 through September 2015, 706 patients with diverse cancer diagnoses were approached, and of these, 668 patients (95%) were consented and enrolled to participate in the survey. Of the 668 patients, 6 individuals withdrew from the study prior to completing the survey for the following reasons: changed mind ($n = 4$), time constraints ($n = 1$), and health issue ($n = 1$). Of the 662 participants who completed the survey, 33 (5%) chose not to report their level of physical activity since cancer diagnosis (primary outcome of interest) leaving 629 (89% of the overall sample) included in the analyses.

Characteristics of study participants

The mean age of participants was 60.4 ± 11.6 years (range 23–90), 66% were female, 83% were White, 68% had completed at least some college, and 66% were in a partnered relationship. Over half of the patients (52%) were seen in community hospitals. The most common cancer types reported were breast (32%), thoracic/lung (15%), and hematologic (15%), and 54% of the patients had a non-metastatic cancer diagnosis. Eighty percent of patients were currently receiving some form of active cancer treatment, and the most commonly reported cancer treatments received were chemotherapy (88%), surgery (53%), and radiation (53%). In terms of symptoms in the past 7 days, 78% reported moderate to very severe fatigue, 68% had a pain level 4 or greater on a scale of 0 to 10, and 63% reported experiencing emotional distress sometimes to always (see Table 1).

Physical activity level since cancer diagnosis

Since their cancer diagnosis, 499 (79%) reported that they had decreased their level of PA, whereas 17% maintained and 4% increased their level of PA. Of those who decreased their level of PA, 82% reported not having met the ACS physical activity recommendations of 150 min of moderate activity or 75 min of vigorous activity per week on average in the past month. In unadjusted analyses, patients with moderate to very severe fatigue compared to those with none to mild fatigue were more likely to report decreased PA (87 vs. 56%, $p < 0.001$) and not

meeting ACS recommendations (77 vs. 66%, $p = 0.010$). Similar findings were found for those experiencing emotional distress sometimes to always (decreased PA: 83 vs. 74%, $p = 0.007$; not meeting ACS recommendations: 78 vs. 70%, $p = 0.029$) compared to those who reported emotional distress never to rarely. Participants with a pain rating of 4 or greater compared to those with a rating of ≤ 3 were more likely to report decreased PA (84 vs. 72%, $p = 0.001$), yet no significant differences in meeting ACS recommendations were found (75 vs. 73%, $p = 0.574$).

Additionally, race, cancer type, cancer stage, cancer treatment status (currently receiving versus completed treatment), and receipt of chemotherapy were significantly associated with a decreased PA at $p < 0.05$ (Tables 1 and 2). When examining decreased PA level by cancer type, the highest percentages of decreased PA were reported by those with gastrointestinal (89%), gynecological (88%), and head/neck (87%) cancer (Fig. 1). Age, sex, body mass index, surgery, radiation treatment, or hospital treatment location were not significantly associated with decreased PA (Table 1).

Estimates from multivariable modeling of decreased level of PA since cancer diagnosis are shown in Table 2. In the fully adjusted model, participants who reported moderate to very severe fatigue had four times higher odds [Adjusted Odds Ratio (AOR) 4.01, 95% Confidence Interval (CI) 2.41, 6.65, $p < 0.001$] of reporting a decreased level of PA than those who did not report fatigue. Participants reporting pain levels ranging from 4 to 10 (worst pain) had a 1.89 times higher odds of decreased PA levels than those with pain levels ranging from 0 to 3 [AOR 1.89, 95% CI 1.14, 3.12, $p = 0.013$]. Participants who were currently receiving cancer treatment had almost three times the odds of decreased PA levels [AOR 2.71, 95% CI 1.55, 4.73, $p < 0.001$] and those who reported having received chemotherapy had 3.5 higher odds [AOR 3.54, 95% CI 1.77, 7.08, $p < 0.001$]. The fully adjusted logistic regression model (including symptoms) in Table 2 explained 26% of the variance in decreased level of PA (Nagelkerk $R^2 = 0.26$); whereas, the model that included only race and clinical characteristics explained 13% of the variance (Nagelkerk $R^2 = 0.13$).

Further, the results of sensitivity analyses (excluding participants who maintained their PA level) conducted among participants who reported a decreased PA level ($N = 499$) compared to those who increased PA level ($N = 24$) confirmed the association between fatigue and pain symptoms and level of PA (data not shown).

Discussion

Engaging in physical activity after a cancer diagnosis has numerous benefits for cancer patients [7–11]. Unfortunately, in this study of over 600 cancer patients seen in academic and community clinical settings, four out of five patients reported a decreased level of PA following their cancer diagnosis.

Table 1 Participant characteristics by change in physical activity (PA) level since cancer diagnosis

Characteristic	Overall <i>N</i> = 629 <i>N</i> (% of total)	Decreased PA <i>N</i> = 499 <i>N</i> (% within each category)	<i>p</i> value
Demographics			
Age			0.66
< 45	63 (10.0)	51 (79.7)	
45–54	120 (19.1)	100 (83.3)	
55–64	207 (32.9)	160 (77.7)	
≥ 65	239 (38.0)	188 (78.7)	
Sex			0.48
Male	215 (34.2)	174 (80.9)	
Female	414 (65.8)	325 (78.5)	
Race			0.008
White	519 (82.5)	422 (81.3)	
Non-White	110 (17.5)	77 (70.0)	
Body mass index (kg/m ²)			0.68
< 25	218 (34.8)	170 (78.0)	
25–29.9	215 (34.4)	169 (78.6)	
≥ 30	193 (30.8)	157 (81.3)	
Education			0.42
High school or less	199 (31.9)	154 (77.4)	
Some college or above	424 (68.1)	340 (80.2)	
Relationship status			0.27
Partnered	413 (65.7)	333 (80.6)	
Not partnered	216 (34.3)	166 (76.9)	
Cancer characteristics			
Cancer type			0.010
Breast	199 (31.6)	144 (72.4)	
Thoracic/lung	95 (15.1)	77 (81.1)	
Hematologic	92 (14.7)	71 (77.2)	
Other*	243 (38.6)	207 (85.2)	
Cancer stage			0.016
Non-metastatic	310 (53.7)	235 (75.8)	
Metastatic	267 (46.3)	224 (83.9)	
Cancer treatment status			< 0.001
Currently receiving treatment	480 (80.3)	404 (84.2)	
Completed treatment	104 (17.4)	65 (62.5)	
About to start treatment	14 (2.3)	9 (64.3)	
Cancer treatment received			< 0.001
Chemotherapy	552 (87.8)	455 (82.4)	
Radiation	336 (53.4)	266 (79.2)	0.91
Surgery	334 (53.1)	270 (80.8)	0.32
Hospital treatment location			0.21
Academic	302 (48.0)	246 (81.5)	
Community	327 (52.0)	253 (77.4)	
Symptoms in past 7 days			
Fatigue			< 0.001
None to mild	137 (22.2)	77 (56.2)	
Moderate to very severe	481 (77.8)	416 (86.5)	
Pain			0.001
Level of 0 (no pain) to 3	201 (32.5)	144 (71.6)	
Level of 4 to 10 (worst pain)	418 (67.5)	349 (83.5)	
Emotional distress			0.007
Never to rarely	227 (36.6)	168 (74.0)	
Sometimes to always	394 (63.4)	327 (83.0)	

Due to missing data, some variables do not add up to 629

*Other cancer type includes but is not limited to gastrointestinal, gynecological, genitourinary, head and neck, sarcoma, and skin

Italic emphasis (originally boldfaced) indicates statistical significance of *p* < 0.05

Fatigue and pain were significantly associated with reduced PA since cancer diagnosis. More research and clinical

innovations are needed to manage current symptoms and encourage maintenance of PA among cancer patients.

Table 2 Participant characteristics associated with decreased physical activity levels since cancer diagnosis ($N = 629$)

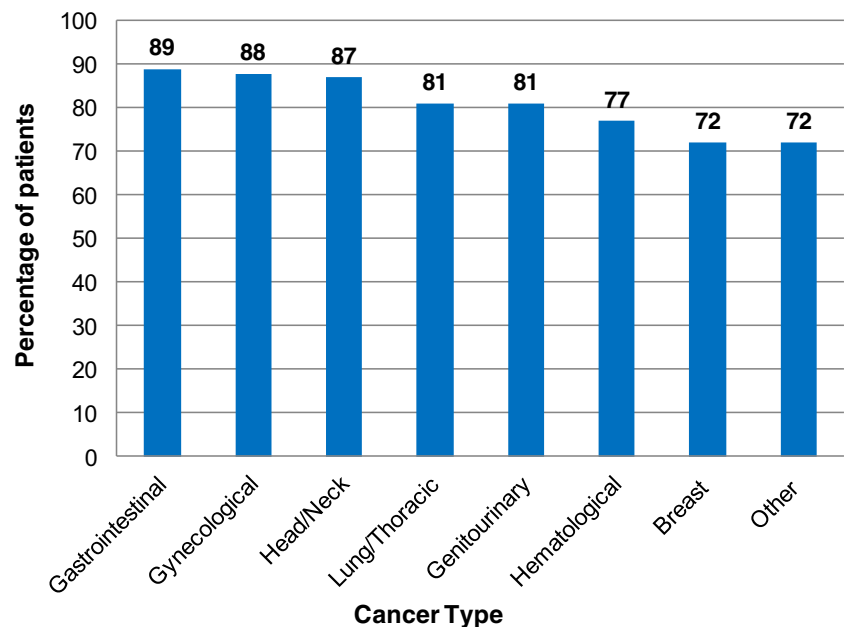
Characteristic	Unadjusted models			Multivariate model		
	Un-AOR	(95% CI)	<i>p</i> value	AOR	(95% CI)	<i>p</i> value
Fatigue (vs. none to mild)	4.99	(3.25–7.64)	< 0.001	4.01	(2.41–6.65)	< 0.001
Pain level 4 to 10 (vs. level 0 to 3)	2.00	(1.34–2.99)	0.001	1.89	(1.14–3.12)	0.013
Emotional distress (vs. never to rarely)	1.71	(1.15–2.55)	0.008	1.62	(0.99–2.65)	0.06
Race Non-White (vs. White)	0.54	(0.34–0.85)	0.008	0.58	(0.32–1.07)	0.08
Cancer type Breast (vs. other)	0.55	(0.37–0.82)	0.004	0.74	(0.44–1.23)	0.24
Cancer stage Metastatic (vs. non-metastatic)	1.66	(1.10–2.52)	0.017	1.17	(0.70–1.95)	0.55
Cancer treatment status Currently receiving (vs. completed)	3.19	(2.00–5.09)	< 0.001	2.71	(1.55–4.73)	< 0.001
Chemotherapy (vs. no chemotherapy)	3.52	(2.13–5.81)	< 0.001	3.54	(1.77–7.08)	< 0.001

The final logistic regression model was adjusted for all variables shown in the table

AOR adjusted odds ratio, CI confidence interval

Our study findings provide evidence that patients with fatigue or pain are more likely to report decreased PA since cancer diagnosis, after adjusting for covariates. By contrast, Schmidt and colleagues (2017) found that neither fatigue nor pain were significantly associated with physical inactivity among breast cancer survivors participating in exercise intervention trials [19]. These disparate findings may reflect that

patients who enroll in exercise clinical trials are more motivated and have fewer comorbidities and symptoms than patients in the general clinical population, such as those in our study [27, 28]. Another possible explanation is that these symptoms may not be associated with absolute levels of physical activity but rather changes in physical activity during cancer treatment and beyond. Because our analyses are cross-sectional, prospective

Fig. 1 Percentage of patients who reported decreased physical activity since cancer diagnosis by cancer type ($N = 629$)

studies are needed to elucidate the temporal relationship between fatigue and pain symptoms and PA.

While the mechanisms of how fatigue and pain influence PA are not fully understood, the observed decreased level of PA may be explained within the “sickness behavior” theoretical framework. This framework posits that the body will exhibit sickness behavior, such as fatigue, as a reaction to the body’s inflammatory response to fighting infection or a disease, such as cancer [29, 30]. This heightened inflammatory response can affect a variety of cellular pathways that can potentially influence neurotransmitter systems in the brain that regulate behavior [29]. For example, in animal models, rhesus monkeys with elevated inflammatory biomarkers will crouch into a depressive-like, huddled position and exhibit anhedonic behavior [31, 32]. In a recent population-based study in colorectal cancer survivors, Thong et al. report that survivors with fatigue and distress were more likely to experience anhedonia compared to survivors with no fatigue and distress [33]. Since cancer and its related treatments often trigger a heightened inflammatory response in the body [30], this “sickness behavior” reaction may explain how symptoms can contribute to decreased PA following a cancer diagnosis.

As postulated by the “sickness behavior” framework and shown by our study findings, patients experiencing fatigue or pain symptoms are the least likely to participate in PA, yet these patients potentially would benefit the most by engaging in PA. Many professional cancer organizations recommend PA as a non-pharmacological treatment intervention for fatigue and pain in cancer populations [2–4]. Additionally, a recent meta-analysis found that exercise, psychological, and combined exercise/psychological interventions were more effective at reducing cancer-related fatigue than pharmaceutical options [34]. Since many patients suffering from fatigue and pain symptoms are sedentary and not motivated to participate in exercise clinical trials, future research needs to focus on developing strategies to enroll sedentary cancer patients and to motivate them to engage in PA at home or in community treatment settings. Clinical care teams should consider referral of patients to cancer fitness specialists, physical therapists, or supervised exercise classes in order to help patients learn how to be more physically active, despite their symptoms or physical limitations [9].

Despite the ability of PA to improve cancer-related symptoms, many cancer patients rely on their health care providers for symptom management and advice regarding PA. The cancer care team can help patients effectively manage cancer-related symptoms by eliciting information about any symptoms their patients may be experiencing and develop symptom management solutions early in the cancer trajectory to help their patients stay physically active. Research has shown that cancer patients who received a health care provider’s recommendation to engage in PA were more likely to participate in PA than those who did not receive such a recommendation [35–37]. However, provider-patient communication regarding PA does not occur on a regular basis.

A recent study found that only 35% of 361 medical encounters between oncology providers and patients resulted in communication involving PA or exercise [38].

A few limitations to our study should be acknowledged. The primary limitation is the reliance on self-report for the main outcomes of interest, which may be subject to recall bias or social desirability bias and result in an over-report of PA levels. However, patients in our study who responded affirmatively to not meeting ACS guidelines also reported decreased PA levels since cancer diagnosis, which suggests that patients accurately reported their PA. Another limitation is that this study did not assess the patients’ level of PA prior to their cancer diagnosis or use an objective and validated measure of PA. Further, our cross-sectional design versus a longitudinal study design limits our ability to establish causal relationships between decreased PA level and the factors, such as fatigue and pain, identified in this study. Finally, while this study enrolled patients from both academic and community centers, the majority of patients were White and reported experiencing at least some pain; therefore, the results may not be generalizable to racial/ethnic minority patients or the larger population of cancer patients.

Conclusions

Our study included a large cohort of patients with diverse cancer types from both academic and community settings and provides evidence that fatigue and pain are associated with decreased PA among cancer patients, even after adjusting for cancer treatment. Future studies should be conducted to better understand how clinical care teams and patients can work together to manage fatigue and pain to promote maintenance of PA levels after cancer.

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Compliance with ethical standards

Conflict of interest The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Dr. Mao has full control of all primary data and agrees to allow the journal to review the data if requested. Research related to the development of this paper was supported in part by the National Cancer Institute grants to

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Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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