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Disease burden and pain in obese cancer patients with chemotherapy-induced peripheral neuropathy

Emily Cox-Martin¹, Lisa H. Trahan^{2,3}, Matthew G. Cox⁴, Patrick M. Dougherty⁵, Emily A. Lai⁶, and Diane M. Novy⁵

¹Division of Medical Oncology, Department of Medicine, School of Medicine, University of Colorado Anschutz Medical Campus, 12801 E 17th Ave, Aurora, CO 80045, USA

²Department of Behavioral Science, The University of Texas MD Anderson Cancer Center, 1155 Pressler Street, Unit 1330, Houston, TX 77030, USA

³Present address: Cedar Creek Associates, LLC, 631 Mill St., Ste. 101, San Marcos, TX 78666, USA

⁴Adult and Child Consortium for Health Outcomes Research and Delivery Science, School of Medicine, University of Colorado Anschutz Medical Campus, 13199 E. Montview Blvd, Suite 358, Aurora, CO 80045, USA

⁵Department of Pain Medicine, The University of Texas MD Anderson Cancer Center, 1400 Holcombe Boulevard, Unit 409, Houston, TX 77030, USA

⁶McGovern Medical School, University of Texas, 1885 El Paseo St, # 35303, Houston, TX 77054, USA

Abstract

Purpose—Chemotherapy-induced peripheral neuropathy (CIPN) and obesity are prevalent in cancer survivors and decrease quality of life; however, the impact of the co-occurrence of these conditions has garnered little attention. This study investigated differences between obese and non-obese cancer survivors with CIPN and predictors of symptom burden and pain.

Methods—Patients with CIPN were administered the MD Anderson Symptom Inventory and a modified version of pain descriptors from the McGill Pain Inventory. Independent *t* tests assessed group differences between obese and non-obese survivors, and linear regression analyses explored predictors of patient outcomes.

Results—Results indicated a significant difference in symptom severity scores for obese (M = 32.89, SD = 25.53) versus non-obese (M = 19.35, SD = 16.08) patients (t(37.86) = -2.49, p = .02). Significant differences were also found for a total number of pain descriptors endorsed by obese

Correspondence to: Emily Cox-Martin.

A portion of this work was conducted while the author was affiliated with the Department of Behavioral Science, The University of Texas MD Anderson Cancer Center.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

The authors have full control of all primary data and agree to allow the journal to review data if requested.

(M = 4.21, SD = 3.45) versus non-obese (M = 2.42, SD = 2.69) participants (t(74) = -2.53, p = .01). Obesity was a significant predictor of symptom severity and total pain descriptors endorsed. Other significant predictors included age and months since treatment.

Conclusions—Cancer survivors with CIPN and co-occurring obesity may be more at risk for decreased quality of life through increased symptom severity and pain compared to non-obese survivors. This paper identified risk factors, including obesity, age, and months since treatment, that can be clinically identified for monitoring distress in CIPN patients. Future research should focus on the longitudinal relationship between obesity and CIPN, and robust interventions to address the multifaceted issues faced by cancer survivors.

Keywords

Cancer; Obesity; Chemotherapy-induced peripheral neuropathy; Pain; Quality of life

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a known side effect of therapeutic drugs commonly used in the treatment of cancer, including platinum-based compounds, taxanes, vinca alkaloids, bortezomib, and thalidomide. Symptoms of CIPN include sensory, autonomic, and motor difficulties, the most prominent of which is a sensory pain characterized by burning, tingling, and numbness, occurring most often in the hands and feet. There are, at present, no established agents for prevention of CIPN [1, 2], and so dose reduction and cessation of treatment are often the only options for prevention of severe CIPN. The estimated prevalence of CIPN ranges from 30 to 68.1% based on a variety of factors, including the timing of measurement and the chemotherapy drug used [1, 3]. Chemotherapy-induced peripheral neuropathy can persist after treatment has ended, effectively becoming a chronic issue for many patients [4–6]. It is negatively associated with health-related quality of life (HRQoL) [1, 5, 7] and has been shown to have a detrimental impact on survivors' physical and mental health, as well as cognitive functioning, completion of activities of daily living, sleep, and social well-being [6, 8–10].

Obesity, defined as a body mass index (BMI) of 30.0 or greater, is another common risk factor for poor HRQoL in cancer survivors. This finding extends to a variety of cancer populations, including colorectal, breast, and prostate cancer survivors and in racial/ ethnically diverse samples [11–16]. In their study of prostate cancer survivors, Sanda and colleagues showed that obesity in patients who had undergone either a prostatectomy or radiotherapy was related to lower quality of life scores associated with vitality or hormonal function [14]. In addition to poorer quality of life in relation to physical outcomes, Connor and colleagues also found obesity to be significantly associated with decreased mental health in a sample of Hispanic and non-Hispanic white breast cancer survivors [13]. Across medical populations, obesity and pain are highly comorbid [17]. In addition, higher BMI is associated with poorer quality of life and functional capacity in individuals with chronic pain syndromes such as fibromyalgia, lower back pain, and arthritis [18]. Furthermore, obesity can complicate the pain experience through its relation to greater pain-related distress and pain sensitivity. When obesity and pain co-occur, HRQoL is impacted to a greater extent than when either occurs in isolation [19].

Although there has been a great deal of research on the co-occurrence of obesity and chronic pain syndromes and its impact on HRQoL, there is a dearth of information on the co-occurrence of obesity and CIPN in cancer survivors. Both obesity and CIPN have been shown to independently impact quality of life in this population, but it is unknown whether their co-occurrence leads to a greater risk for distress. This study seeks to address this question by exploring the extent to which obesity status is related to the experience of CIPN and overall symptom burden in cancer survivors. Understanding the cumulative effect these frequent comorbidities have on cancer survivors is important for identifying and targeting those survivors most at risk for poor HRQoL. The roles of other potentially relevant demographic, behavioral, and medical predictors with the co-occurrence of obesity and pain are also explored.

Methods

Study design and participants

The cross-sectional data used for this study were collected as part of a larger parent study examining the feasibility of using quantitative sensory testing procedures for CIPN. Other relevant demographic and medical data were collected via electronic chart review. Patients for the parent study were recruited through either the Pain Management Service or the Leukemia, Myeloma, Breast, Gastrointestinal, or Lung Clinics at the University of Texas MD Anderson Cancer Center. The sub-sample for this study included male and female participants with various cancer diagnoses who had developed neuropathic pain as a consequence of cancer therapy with either vinca alkaloids, taxanes, bortezomib, thalidomide, or platinum-based compounds. While all participants had CIPN, clinical diagnosis of this issue by a referring provider was not standardized. Data for this study were collected via self-report measures and clinical chart review.

Measures

Primary outcomes were patient reported and included symptom severity, symptom interference, and descriptors of pain experience.

MD Anderson Symptom Inventory—The MD Anderson Symptom Inventory (MDASI) is a patient-reported outcome measure which evaluates multiple cancer treatment-related symptoms. It includes a total of 19 items, 13 of which comprise a symptom severity subscale and 6 of which comprise a symptom interference subscale [20]. For the symptom severity sub-scale, patients are asked to rate how severe various cancer-related symptoms (e.g., fatigue, nausea, disturbed sleep) have been for them in the past 24 hours on a 0–10 numeric rating scale with 0 being "not present" and 10 being "as bad as you can imagine." For the symptom interference subscale, patients are asked to rate how much their symptoms have interfered with various domains of functioning (e.g., work, relations with other people) in the past 24 hours on a 0–10 numeric rating scale with 0 being "interfered completely." The mean interference items score can also be used to indicate overall symptom burden. Reliability, as evaluated through internal consistency, for the MDASI was shown to be high with Cronbach's alpha = 0.85 for the severity factor and

0.91 for the interference factor in the initial sample, and 0.87 and 0.94, respectively, in the cross-validation sample [20].

McGill Pain Questionnaire descriptive items—A modified list of pain descriptors derived from the McGill Pain Questionnaire [21] was used to evaluate the descriptive nature and extent of the participants' pain. Descriptors listed included drilling, stabbing, sharp, squeezing, tugging, tearing, dull, splitting, tingling, itching, hot, burning, cold, numb, spreading, flashing, flickering, throbbing, shooting, and electric. Participants were asked to circle all words listed that described their sensation of pain.

Analyses

Standardized forms and procedures were used to collect data, which were double entered into Microsoft Excel to ensure accuracy. The data were analyzed with R statistical software, version 3.3.1 [22] for all analyses, and listwise deletion was used for missing data. Independent two-sample *t* tests and Welch two-sample *t* tests (when variances were unequal) were used to assess mean differences between obese (BMI 30) and non-obese (BMI < 30) participants on the symptom severity and symptom interference factors of the MDASI as well as the sum score of pain descriptors endorsed. Linear ordinary least squares regression analyses (for continuous outcomes) and negative binomial regressions (for categorical outcomes) were then conducted to further explore demographic and behavioral predictors of the above outcomes.

Results

Participant characteristics

A total of 86 patients were included in this investigation, with an average age of 58.91 (range = 31-83). A majority of patients were female (58%) and white (72%). The average BMI was 28.98 (range = 19.47-51.12). Just over half of the samples fit the obese criterion. Most participants had a myeloma diagnosis. Full sample characteristics can be found in Table 1. On average, there was 1.86% of missing data with obesity having the largest amount of missing data (11.6%). *t* tests and chi-square tests comparing demographic characteristics between those with missing data and those without showed no significant differences.

t tests for obese versus non-obese participants

Welch two-sample *t* test results indicated a significant difference in the mean symptom severity score for obese (M = 32.89, SD = 25.53) versus non-obese (M = 19.35, SD = 16.08) patients (t(37.86) = -2.49, p = .02), but not for symptom interference. Independent two-sample *t* test results also showed a significant difference for a total number of pain descriptors endorsed, with obese participants reporting nearly double the number of descriptors (M = 4.21, SD = 3.45) as non-obese participants (M = 2.42, SD = 2.69) (t(74) = -2.53, p = .01).

Regression results for MDASI and pain constructs

Regression analysis results indicated that obesity was a significant predictor of symptom severity (B = 13.893, p < .01) as well as total pain descriptors endorsed (B = 1.680, p < .05), but not symptom interference. Age was a significant predictor for both symptom interference (B = -0.442, p < .01) and total pain descriptors endorsed (B = -0.068, p < .05), while months since treatment was a significant predictor of all three outcomes (B = 0.432, p < .01; B = 0.328, p < .01; and B = 0.059, p < .01). See Table 2 for full regression results for these outcomes. Unstandardized beta coefficients and standard errors have been provided for all analyses, but for this table, standardized beta coefficients have also been provided to increase interpretation across measures.

Regressions for predictors of individual items of the MDASI were investigated. Eleven out of the 19 items included on the MDASI were considered relevant for the current research objective. Full results from these regressions are shown in Tables 3 and 4. Obesity significantly predicted multiple items from the symptom severity subscale of the MDASI including lack of appetite (B = 1.230, p < .05), shortness of breath (B = 2.085, p < .001), and pain (B = 0.690, p < .05). Age significantly predicted items from both the symptom severity subscale, including pain (B = -0.031, p < .05), and the symptom interference subscale, including mood (B = -0.036, p < .01), relationship (B = -0.061, p < .01), walking (B = -0.029, p < .05), and work (B = -0.027, p < .05). Additionally, months since last chemotherapy treatment significantly predicted items from both the symptom severity subscale, including shortness of breath (B = 0.032, p < .01), numbness or tingling (B = 0.019, p < .05), sadness (B = 0.033, p < .01), and pain (B = 0.031, p < .001), and the symptom interference subscale, including shortness of breath (B = 0.032, p < .01), numbness or tingling (B = 0.019, p < .05), sadness (B = 0.033, p < .01), and pain (B = 0.031, p < .001), and the symptom interference subscale, including mood (B = 0.018, p < .05) and walking (B = 0.017, p < .05).

Regressions for predictors of pain descriptors thought to be most relevant to the sensory experience of CIPN were also assessed. Specific descriptors included as outcomes were tingling, burning, and numb. Months since treatment were found to be a significant predictor for all three descriptors (B = 0.939, p < .05; B = 0.088, p < .05; and B = 0.556, p < .01).

Discussion

Results from this study indicate that obese cancer patients with CIPN experience higher levels of disease burden in the form of symptom severity as well as pain. This may increase their risk for treatment-related distress as well as decreased quality of life. Age was found to negatively predict symptom interference and pain, such that younger patients were found to endorse greater symptom interference for mood, relationships, walking, and work. Although age was not a significant predictor for the MDASI symptom severity subscale, it was for the individual pain item included in this factor. These findings align with previous research showing that younger survivors often experience greater levels of symptom occurrence, severity, frequency, and distress as well as lower quality of life [23–25]. Researchers have hypothesized many reasons for this relationship. For example, it has been suggested that younger patients are more likely to receive more aggressive therapies associated with greater side effects [24, 25]. This choice may be related to younger patients having fewer comorbidities or better levels of overall health at the start of treatment as compared to older

patients. Additionally, disease- or age-related disability may be more normative in older populations; therefore, the disease-related burden and pain caused by cancer and its treatments may be perceived as more severe or interfering for younger survivors. This may be particularly felt in relation to social or vocational roles in which younger survivors are still active. Finally, older adults who have encountered other health-related difficulties prior to their cancer diagnosis may have more experience coping with disease-related symptoms and distress than younger patients [25].

The number of months since the patient's last chemotherapy treatment was also a significant predictor of both MDASI subscales, symptom interference, and symptom severity, as well as pain. While it is well known that cancer treatments can have long-term side effects, previous research has shown mixed findings for ongoing, post-treatment increases in disease-related symptom burden and distress [26-29]. In long-term lung cancer survivors, increases in symptoms of pain and dyspnea were found over a 7-year period, although overall HRQoL did not show a clinically meaningful decline [26]. The trajectory of symptom burden after treatment may depend on the type of treatment the patient received, their premorbid functioning, and the symptom of interest (i.e., physical vs. mental functioning). The positive relationship found in this study does highlight the ongoing nature of treatment-related burden, which some survivors face long after active treatment has ended. It also emphasizes the critical nature of understanding long-term survivorship issues and the impact that they have on day-to-day life for cancer survivors. It should be noted that neither smoking nor diabetic status was found to be a consistently significant predictor; however, sample size was low for both of these variables, and therefore, there might not have been enough power to detect possible effects.

This is the first study to look at the impact of comorbid CIPN and obesity in cancer survivors. While individually both of these factors have a negative effect on functioning and HRQoL in this population [5, 7, 13, 15], this study demonstrates the differential impact on symptom severity, symptom burden, and pain in obese versus non-obese CIPN patients. Despite this study's strengths, there were limitations. The cross-sectional design and lack of randomization prevents any claims of causality from these findings. Additionally, the relatively small sample size limits the generalizability of our findings. Studies using a longitudinal design would allow for the modeling of weight, pain, and HRQoL trajectories over time so that the dynamic nature of the constructs and their interactions could be better understood. A larger more diverse sample would improve the generalizability of the findings and allow for investigation of further group differences that may impact these relationships or disparities that might exist; that the majority of patients in this study are myeloma patients is a limitation of generalizability. Diagnoses of CIPN were made by referral physicians, and therefore, clinical measurement was not standardized in this sample. Overall, there is little consensus on the best clinical method for measuring CIPN, and this is therefore an overall limitation to this field of research [4, 30]. Other data collected, including symptom severity, symptom interference, and pain, were all self-reported and therefore subject to bias/ measurement error but currently represent the best practice for assessment of these constructs.

These findings have broad implications for clinical practice as well as future research. Results indicate that obese patients with CIPN may experience higher levels of symptom severity and pain, both of which can increase their risk for treatment-related distress as well as decreased quality of life. In addition to patients' obesity status, their age and months since last chemotherapy treatment were also shown to be important predictors in various patient outcome measures. These results indicate certain patient characteristics that may point to higher risk for distress and symptom burden. Monitoring these higher-risk groups may allow for targeted, more efficient intervention and symptom management, ameliorating negative outcomes often faced by survivors. Future research should utilize longitudinal designs so that the dynamic relationship between obesity, CIPN, and distress can be better understood. This research should then inform the development of interventions that can simultaneously target these comorbid factors. Specifically, researchers should focus on how the timing and extent of these conditions affects the co-occurrence and severity of future conditions. For example, are patients who are obese before they receive chemotherapy more likely to experience CIPN, HRQoL issues, and greater symptom burden? Understanding the timing of these relationships could help identify optimal time points for intervention (or preinterventions for chemotherapy) as well as delineate the potential iatrogenic effects of chemotherapy.

Research regarding the co-occurrence of other pain conditions and obesity has recommended robust, multitargeted interventions that can help to manage not only these particular outcomes but also the distress and disability that often accompany them [17–19]. Physical activity and lifestyle interventions with cancer survivors have been shown to be efficacious for both weight [31, 32] and pain management [33], as well as improving HRQoL [34–36]. Evidence is emerging that physical activity is effective in ameliorating CIPN symptoms in particular [37, 38]. Interventions using components of cognitive behavioral therapies have also been successful in targeting a range of issues pertinent to cancer survivorship [39, 40], including weight management [40], pain [41, 42], and HRQoL [43, 44]. Given the efficacy of these interventions for treating obesity and pain in cancer survivors, one potential intervention that could prove highly effective is a multicomponent CBT and physical activity intervention for obese cancer survivors with CIPN.

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References

- Hershman DL, Lacchetti C, Dworkin RH, Smith EML, Bleeker J, Cavaletti G, Paice J. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014; 32(18): 1941–1967. [PubMed: 24733808]
- Majithia N, Temkin SM, Ruddy KJ, Beutler AS, Hershman DL, Loprinzi CL. National Cancer Institute-supported chemotherapy-induced peripheral neuropathy trials: outcomes and lessons. Support Care Cancer. 2016; 24(3):1439–1447. [PubMed: 26686859]

- Seretny M, Currie GL, Sena ES, Ramnarine S, Grant R, MacLeod MR, Fallon M. Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. PAIN®. 2014; 155(12):2461–2470. [PubMed: 25261162]
- Park SB, Lin CS, Krishnan AV, Goldstein D, Friedlander ML, Kiernan MC. Long-term neuropathy after oxaliplatin treatment: challenging the dictum of reversibility. Oncologist. 2011; 16(5):708– 716. [PubMed: 21478275]
- 5. Mols F, Beijers T, Lemmens V, van den Hurk CJ, Vreugdenhil G, van de Poll-Franse LV. Chemotherapy-induced neuropathy and its association with quality of life among 2-to 11-year colorectal cancer survivors: results from the population-based PROFILES registry. J Clin Oncol. 2013; 31(21):2699–2707. [PubMed: 23775951]
- Ezendam NP, Pijlman B, Bhugwandass C, Pruijt JF, Mols F, Vos MC, van de Poll-Franse LV. Chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among ovarian cancer survivors: results from the population-based PROFILES registry. Gynecol Oncol. 2014; 135(3):510–517. [PubMed: 25281491]
- Mols F, Beijers T, Vreugdenhil G, van de Poll-Franse L. Chemotherapy-induced peripheral neuropathy and its association with quality of life: a systematic review. Support Care Cancer. 2014; 22(8):2261–2269. [PubMed: 24789421]
- Bakitas MA. Background noise: the experience of chemotherapy-induced peripheral neuropathy. Nurs Res. 2007; 56(5):323–331. [PubMed: 17846553]
- Tofthagen C. Surviving chemotherapy for colon cancer and living with the consequences. J Palliat Med. 2010; 13(11):1389–1391. [PubMed: 21091028]
- Tofthagen C, Donovan KA, Morgan MA, Shibata D, Yeh Y. Oxaliplatin-induced peripheral neuropathy's effects on health-related quality of life of colorectal cancer survivors. Support Care Cancer. 2013; 21(12):3307–3313. [PubMed: 23903798]
- Smits A, Lopes A, Bekkers R, Galaal K. Body mass index and the quality of life of endometrial cancer survivors—a systematic review and meta-analysis. Gynecol Oncol. 2015; 137(1):180–187. [PubMed: 25636459]
- Adams SV, Ceballos R, Newcomb PA. Quality of life and mortality of long-term colorectal cancer survivors in the Seattle Colorectal Cancer Family Registry. PLoS One. 2016; 11(6):e0156534. [PubMed: 27253385]
- 13. Connor AE, Baumgartner RN, Pinkston CM, Boone SD, Baumgartner KB. Obesity, ethnicity, and quality of life among breast cancer survivors and women without breast cancer: the long-term quality of life follow-up study. Cancer Cause Control. 2016; 27(1):115–124.
- Sanda MG, Dunn RL, Michalski J, Sandler HM, Northouse L, Hembroff L, Mahadevan A. Quality of life and satisfaction with outcome among prostate-cancer survivors. New Engl J Med. 2008; 358(12):1250–1261. [PubMed: 18354103]
- Paxton RJ, Phillips KL, Jones LA, Chang S, Taylor WC, Courneya KS, Pierce JP. Associations among physical activity, body mass index, and health-related quality of life by race/ethnicity in a diverse sample of breast cancer survivors. Cancer. 2012; 118(16):4024–4031. [PubMed: 22252966]
- Imayama I, Alfano CM, Neuhouser ML, George SM, Smith AW, Baumgartner RN, Ballard-Barbash R. Weight, inflammation, cancer-related symptoms and health-related quality of life among breast cancer survivors. Breast Cancer Res Tr. 2013; 140(1):159–176.
- Okifuji A, Hare BD. The association between chronic pain and obesity. J Pain Res. 2015; 8:399–408. [PubMed: 26203274]
- 18. Arranz LI, Rafecas M, Alegre C. Effects of obesity on function and quality of life in chronic pain conditions. Cuu Rheumatol Rep. 2014; 16(1):1–8.
- Janke EA, Collins A, Kozak AT. Overview of the relationship between pain and obesity: what do we know? Where do we go next? J Rehabil Res Dev. 2007; 44(2):245–262. [PubMed: 17551876]
- 20. Cleeland CS, Mendoza TR, Wang XS, Chou C, Harle MT, Morrissey M, Engstrom MC. Assessing symptom distress in cancer patients. Cancer. 2000; 89(7):1634–1646. [PubMed: 11013380]
- Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. Pain. 1975; 1(3):277–299. [PubMed: 1235985]

- 22. R Development Core Team. A language and environment for statistical computing. R Foundation for Statistical Computing; Vienna, Austria: 2016.
- 23. Wu HS, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. Cancer Nurs. 2015; 38(1):E29–E54. [PubMed: 24831042]
- Cataldo JK, Paul S, Cooper B, Skerman H, Alexander K, Aouizerat B, Yates P. Differences in the symptom experience of older versus younger oncology outpatients: a cross-sectional study. BMC Cancer. 2013; 13(6):1471–2407.
- Mao JJ, Armstrong K, Bowman MA, Xie SX, Kadakia R, Farrar JT. Symptom burden among cancer survivors: impact of age and comorbidity. The J Am Board Fam Med. 2007; 20(5):434– 443. [PubMed: 17823460]
- Yang P, Cheville AL, Wampfler JA, Garces YI, Jatoi A, Clark MM, Okuno SH. Quality of life and symptom burden among long-term lung cancer survivors. J Thorac Oncol. 2012; 7(1):64–70. [PubMed: 22134070]
- Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. Int J Psychiat Med. 2010; 40(2): 163–181.
- Resnick MJ, Koyama T, Fan KH, Albertsen PC, Goodman M, Hamilton AS, Van Horn RL. Longterm functional outcomes after treatment for localized prostate cancer. New Engl J Med. 2013; 368(5):436–445. [PubMed: 23363497]
- Koch L, Jansen L, Herrmann A, Stegmaier C, Holleczek B, Singer S, Arndt V. Quality of life in long-term breast cancer survivors—a 10-year longitudinal population-based study. Acta Oncol. 2013; 52(6):1119–1128. [PubMed: 23514583]
- Griffith KA, Merkies IS, Hill EE, Cornblath DR. Measures of chemotherapy-induced peripheral neuropathy: a systematic review of psychometric properties. J Peripher Nerv Syst. 2010; 15(4): 314–325. [PubMed: 21199103]
- Morey MC, Snyder DC, Sloane R, Cohen HJ, Peterson B, Hartman TJ, Demark-Wahnefried W. Effects of home-based diet and exercise on functional outcomes among older, overweight longterm cancer survivors: RENEW: a randomized controlled trial. JAMA. 2009; 301(18):1883–1891. [PubMed: 19436015]
- 32. Rock CL, Flatt SW, Byers TE, Colditz GA, Demark-Wahnefried W, Ganz PA, Naughton M. Results of the exercise and nutrition to enhance recovery and good health for you (ENERGY) trial: a behavioral weight loss intervention in overweight or obese breast cancer survivors. J Clin Oncol. 2015; 33(28):3169–3176. [PubMed: 26282657]
- Rajotte EJ, Jean CY, Baker KS, Gregerson L, Leiserowitz A, Syrjala KL. Community-based exercise program effectiveness and safety for cancer survivors. J Cancer Surviv. 2012; 6(2):219– 228. [PubMed: 22246463]
- 34. Rogers LQ, Courneya KS, Anton PM, Hopkins-Price P, Verhulst S, Vicari SK, McAuley E. Effects of the BEAT Cancer physical activity behavior change intervention on physical activity, aerobic fitness, and quality of life in breast cancer survivors: a multicenter randomized controlled trial. Breast Cancer Res Tr. 2015; 149(1):109–119.
- 35. Swisher AK, Abraham J, Bonner D, Gilleland D, Hobbs G, Kurian S, Vona-Davis L. Exercise and dietary advice intervention for survivors of triple-negative breast cancer: effects on body fat, physical function, quality of life, and adipokine profile. Support Care Cancer. 2015; 23(10):2995– 3003. [PubMed: 25724409]
- Mishra SI, Scherer RW, Snyder C, Geigle P, Gotay C. Are exercise programs effective for improving health-related quality of life among cancer survivors? A systematic review and metaanalysis. Oncol Nurs Forum. 2014; 41(6):E326–E342. [PubMed: 25355029]
- 37. Wonders KY. The effect of supervised exercise training on symptoms of chemotherapy-induced peripheral neuropathy. Int J Phys Med Rehabil. 2014; 2(4):1–5.
- Wonders KY, Whisler G, Loy H, Holt B, Bohachek K, Wise R. Ten weeks of home-based exercise attenuates symptoms of chemotherapy-induced peripheral neuropathy in breast cancer patients. Health Psychology Research. 2013; 1(3):149–152.

- Faller H, Schuler M, Richard M, Heckl U, Weis J, Küffner R. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. J Clin Oncol. 2013; 31(6):782–793. [PubMed: 23319686]
- Mefferd K, Nichols JF, Pakiz B, Rock CL. A cognitive behavioral therapy intervention to promote weight loss improves body composition and blood lipid profiles among overweight breast cancer survivors. Breast Cancer Res Tr. 2007; 104(2):145–152.
- Gorin SS, Krebs P, Badr H, Janke EA, Jim HS, Spring B, Jacobsen PB. Meta-analysis of psychosocial interventions to reduce pain in patients with cancer. J Clin Oncol. 2012; 30(5):539– 547. [PubMed: 22253460]
- 42. Somers TJ, Abernethy AP, Edmond SN, Kelleher SA, Wren AA, Samsa GP, Keefe FJ. A pilot study of a mobile health pain coping skills training protocol for patients with persistent cancer pain. J Pain Symptom Manag. 2015; 50(4):553–558.
- 43. Stagl JM, Bouchard LC, Lechner SC, Blomberg BB, Gudenkauf LM, Jutagir DR, Antoni MH. Long-term psychological benefits of cognitive-behavioral stress management for women with breast cancer: 11-year follow-up of a randomized controlled trial. Cancer. 2015; 121(11):1873– 1881. [PubMed: 25809235]
- 44. Andersen BL, Farrar WB, Golden-Kreutz DM, Glaser R, Emery CF, Crespin TR, Carson WE. Psychological, behavioral, and immune changes after a psychological intervention: a clinical trial. J Clin Oncol. 2004; 22(17):3570–3580. [PubMed: 15337807]

Table 1

Participant characteristics

Demographic characteristic	Participant data
Age, years (mean/SD)	58.91 (10.6)
Sex (n/%, female)	50 (58)
Race (<i>n</i> /%)	
White	62 (72)
African American	15 (17)
Hispanic	7 (8)
Other	2 (2)
BMI (kg/m ²) (mean/SD)	28.98 (6.5)
Obese (<i>n</i> /%)	48 (56)
Cancer Dx (<i>n</i> /%)	
Myeloma	60 (70)
Breast	12 (14)
Ovarian	4 (5)
Other	10(11)

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Unstandardized beta coefficients, standard errors, and standardized beta coefficients from respective OLS regression analyses with MDASI severity, MDASI interference and nain descriptor sum score as dependent variables

B (SE)			
1 840 13 6481	β	B (SE)	β
(040.0) 640.4	0.156	$1.680^{*}(0.731)$	0.265^{*}
$-0.442^{**}(0.165)$	-0.312	$-0.068^{*}(0.034)$	-0.229 *
-2.458 (3.466)	-0.081	-0.615 (0.706)	-0.099
0.099 (3.786)	0.003	0.913 (0.771)	0.133
5.521 (3.527)	0.179	-0.250 (0.715)	-0.039
-0.851 (6.861)	-0.014	0.118(1.404)	0.010
$0.328^{**}(0.104)$	0.337^{**}	$0.059^{**}(0.021)$	0.293^{**}
0.183		0.185	
73		75	
	5.521 (3.527) -0.851 (6.861) 0.328 ** (0.104) 0.183 73	5.521 (3.527) 0.179 -0.851 (6.861) -0.014 0.328 ** (0.104) 0.337 ** 0.183 73	$\begin{array}{llllllllllllllllllllllllllllllllllll$

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Table 3

Unstandardized beta coefficients and standard errors from respective negative binomial models with relevant MDASI severity items as dependent

Non-obese vs. obese $1.230^{*}(0.489)$ $2.085^{***}(0.480)$ $0.276(0.348)$ $0.525(0.327)$ $-0.326(0.456)$ $0.690^{*}(0.330)$ Age $-0.037(0.022)$ $-0.023(0.021)$ $-0.023(0.021)$ $-0.023(0.015)$ $-0.013(0.019)$ $-0.031^{*}(0.015)$ Female vs. male $-0.059(0.469)$ $-0.621(0.477)$ $-0.214(0.342)$ $-0.329(0.316)$ $-1.655^{***}(0.482)$ $-0.028(0.322)$ White vs. other race $-0.868(0.529)$ $-0.934(0.528)$ $-0.214(0.342)$ $-0.329(0.316)$ $-1.655^{***}(0.482)$ $-0.028(0.322)$ White vs. other race $-0.868(0.529)$ $-0.934(0.528)$ $-0.169(0.372)$ $0.186(0.340)$ $0.024(0.464)$ $0.479(0.338)$ Non-smoker vs. ever smoker $-0.479(0.482)$ $-0.372(0.467)$ $0.295(0.342)$ $-0.058(0.319)$ $0.939^{*}(0.433)$ $0.133(0.323)$ Diabetic vs. non-diabetic $0.292(0.900)$ $-0.372(0.467)$ $0.295(0.342)$ $-0.018(0.619)$ $0.033^{**}(0.010)$ $0.133(0.323)$ Last chemo Txt (months) $-0.007(0.017)$ $0.032^{**}(0.010)$ $0.014(0.009)$ $0.019^{*}(0.009)$ $0.033^{**}(0.010)$ $0.031^{***}(0.008)$ n7474747474747474	Non-obese vs. obese 1.230 Age –0.03 Female vs. male –0.05		Shortness of breath	Distress	Numbness or tingling	Sadness	Pain
Age $-0.037(0.022)$ $-0.023(0.021)$ $-0.022(0.016)$ $-0.003(0.015)$ $-0.013(0.019)$ $-0.031^*(0.015)$ Female vs. male $-0.059(0.469)$ $-0.621(0.477)$ $-0.224(0.342)$ $-0.239(0.316)$ $-1.655^{***}(0.482)$ $-0.028(0.322)$ White vs. other race $-0.868(0.529)$ $-0.934(0.528)$ $-0.169(0.372)$ $0.186(0.340)$ $0.024(0.464)$ $0.479(0.338)$ Non-smoker vs. ever smoker $-0.479(0.482)$ $-0.934(0.528)$ $-0.169(0.372)$ $0.186(0.340)$ $0.024(0.464)$ $0.479(0.338)$ Non-smoker vs. ever smoker $-0.479(0.482)$ $-0.321(0.938)$ $-0.169(0.372)$ $0.186(0.340)$ $0.024(0.464)$ $0.479(0.338)$ Diabetic vs. non-diabetic $0.292(0.900)$ $-0.321(0.938)$ $-1.957(1.158)$ $-0.018(0.619)$ $0.033^{**}(0.433)$ $-0.188(0.537)$ Last chemo Txt (months) $-0.007(0.017)$ $0.032^{**}(0.010)$ $0.014(0.009)$ $0.019^{*}(0.009)$ $0.033^{**}(0.010)$ $0.031^{***}(0.008)$ n7474747474747474	Age –0.03 Female vs. male –0.05	0*(0.489)	2.085 *** (0.480)	0.276 (0.348)	0.525 (0.327)	-0.326 (0.456)	$0.690^{*}(0.330)$
Female vs. male $-0.059 (0.469)$ $-0.621 (0.477)$ $-0.214 (0.342)$ $-0.329 (0.316)$ $-1.655^{***} (0.482)$ $-0.028 (0.322)$ White vs. other race $-0.868 (0.529)$ $-0.934 (0.528)$ $-0.024 (0.528)$ $0.024 (0.464)$ $0.479 (0.338)$ Won-smoker vs. ever smoker $-0.479 (0.482)$ $-0.934 (0.528)$ $-0.169 (0.372)$ $0.166 (0.340)$ $0.024 (0.464)$ $0.479 (0.338)$ Non-smoker vs. ever smoker $-0.479 (0.482)$ $-0.372 (0.467)$ $0.295 (0.342)$ $-0.058 (0.319)$ $0.939^{*} (0.433)$ $0.133 (0.323)$ Diabetic vs. non-diabetic $0.292 (0.900)$ $-0.321 (0.938)$ $-1.957 (1.158)$ $-0.018 (0.619)$ $0.003 (1.016)$ $-0.188 (0.637)$ Last chemo Txt (months) $-0.007 (0.017)$ $0.032^{**} (0.010)$ $0.014 (0.009)$ $0.019^{*} (0.009)$ $0.033^{**} (0.010)$ $0.031^{***} (0.008)$ n74747474747474	Female vs. male –0.05	137 (0.022)	-0.023 (0.021)	-0.022 (0.016)	-0.003 (0.015)	-0.013 (0.019)	-0.031 $^{*}(0.015)$
White vs. other race $-0.868 (0.529)$ $-0.934 (0.528)$ $-0.169 (0.372)$ $0.186 (0.340)$ $0.024 (0.464)$ $0.479 (0.338)$ Non-smoker vs. ever smoker $-0.479 (0.482)$ $-0.372 (0.467)$ $0.295 (0.342)$ $-0.058 (0.319)$ $0.939 * (0.433)$ $0.133 (0.323)$ Diabetic vs. non-diabetic $0.292 (0.900)$ $-0.321 (0.938)$ $-1.957 (1.158)$ $-0.018 (0.619)$ $0.003 (1.016)$ $-0.188 (0.637)$ Last chemo Txt (months) $-0.007 (0.017)$ $0.032 * * (0.010)$ $0.014 (0.009)$ $0.019 * (0.009)$ $0.033 * * (0.010)$ $0.031 * * * (0.008)$ n74747474747474		159 (0.469)	-0.621 (0.477)	-0.214 (0.342)	-0.329 (0.316)	$-1.655^{***}(0.482)$	-0.028 (0.322)
Non-smoker vs. ever smoker -0.479 (0.482) -0.372 (0.467) 0.295 (0.342) -0.058 (0.319) 0.939 *(0.433) 0.133 (0.323) Diabetic vs. non-diabetic 0.292 (0.900) -0.321 (0.938) -1.957 (1.158) -0.018 (0.619) 0.003 (1.016) -0.188 (0.637) Last chemo Txt (months) -0.007 (0.017) 0.032 ** (0.010) 0.014 (0.009) 0.019 *(0.009) 0.033 ** (0.010) 0.031 *** (0.008) n 74 74 74 74 74 74 74	White vs. other race -0.86	68 (0.529)	-0.934 (0.528)	-0.169 (0.372)	$0.186\ (0.340)$	0.024 (0.464)	0.479 (0.338)
Diabetic vs. non-diabetic $0.292 (0.900)$ $-0.321 (0.938)$ $-1.957 (1.158)$ $-0.018 (0.619)$ $0.003 (1.016)$ $-0.188 (0.637)$ Last chemo Txt (months) $-0.007 (0.017)$ $0.032^{**} (0.010)$ $0.014 (0.009)$ $0.019^{*} (0.009)$ $0.033^{***} (0.010)$ $0.031^{****} (0.008)$ n 74 74 74 74 74 74	Non-smoker vs. ever smoker -0.47	179 (0.482)	-0.372 (0.467)	0.295 (0.342)	-0.058 (0.319)	$0.939^{*}(0.433)$	0.133 (0.323)
Last chemo Txt (months) $-0.007 (0.017)$ $0.032 * (0.010)$ $0.014 (0.009)$ $0.019 * (0.009)$ $0.033 * (0.010)$ $0.031 * (0.008)$ n 74 74 74 74 74 74 74 74	Diabetic vs. non-diabetic 0.292	12 (0.900)	-0.321 (0.938)	-1.957 (1.158)	-0.018(0.619)	0.003 (1.016)	-0.188 (0.637)
<i>n</i> 74 74 74 74 74 74 74	Last chemo Txt (months) -0.00	07 (0.017)	$0.032^{**}(0.010)$	$0.014\ (0.009)$	0.019 $^{*}(0.009)$	0.033 ** (0.010)	$0.031^{***}(0.008)$
	<i>n</i> 74		74	74	74	74	74
	p < 0.01;						
p < 0.01;	2 < 0.05						

Table 4

Unstandardized beta coefficients and standard errors from respective negative binomial models with relevant MDASI interference items as dependent -1-1--

	I life Mood	Kelaulonsnips	Walking	Work
on-obese vs. obese 0.225 (0.330)	0.268 (0.313)	0.236 (0.501)	0.277 (0.269)	0.230 (0.261)
ge –0.026 (0.01:	$(-0.036^{**}(0.014))$	$-0.061^{**}(0.023)$	-0.029 $^{*}(0.012)$	-0.027 $^{*}(0.012)$
smale vs. male -0.059 (0.31'	7) -0.132 (0.307)	-0.043 (0.483)	-0.092 (0.258)	-0.203 (0.252)
hite vs. other race -0.037 (0.34)	0.127 (0.326)	0.237 (0.514)	0.174 (0.275)	0.170 (0.268)
on-smoker vs. ever smoker 0.356 (0.318)	0.249 (0.308)	0.439 (0.485)	0.132 (0.260)	0.309 (0.252)
iabetic vs. non-diabetic 0.349 (0.614)	-2.270 [*] (1.140)	-1.137 (1.161)	0.189 (0.505)	0.096(0.499)
ast chemo Txt (months) 0.014 (0.009)	$0.018 \ ^{*}(0.008)$	0.023 (0.013)	0.017 $^{*}(0.007)$	0.013 (0.007)
73	74	74	74	74