HHS Public Access

Author manuscript

J Am Geriatr Soc. Author manuscript; available in PMC 2020 May 01.

Published in final edited form as:

J Am Geriatr Soc. 2019 May ; 67(5): 920–927. doi:10.1111/jgs.15493.

Functional Decline and Resilience among Older Women Receiving Adjuvant Chemotherapy for Breast Cancer

Arti Hurria, MD[#1], **Enrique Soto-Perez-de-Celis, MD**[#1,2], **Jacob B. Allred, MS**[3], **Harvey Jay Cohen, MD**[4], **Anait Arsenyan, MPH**[1], **Karla Ballman, PhD**[5], **Jennifer Le-Rademacher, PhD**[6], **Aminah Jatoi, MD**[3], **Julie Filo, BS**[1], **Jeanne Mandelblatt, MD, MPH**[7], **Jacqueline M. Lafky, MS**[3], **Gretchen Kimmick, MD, MS**[4], **Heidi D. Klepin, MD, MS**[8], **Rachel A. Freedman, MD, MPH**[9], **Harold Burstein, MD, PhD**[9], **Julie Gralow, MD**[10], **Antonio C. Wolff, MD**[11], **Gustav Magrinat, MD**[12], **Myra Barginear, MD**[13], and **Hyman Muss, MD**[14]

[1.]City of Hope Comprehensive Cancer Center and Beckman Research Institute, Duarte, CA, USA

[2.]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Mexico City, Mexico

[3.]Mayo Clinic, Rochester, MN, USA

[4.]Duke Cancer Institute, Duke University Medical Center, Durham, NC, USA

[5.]Weill Medical College of Cornell University, New York, NY, USA

[6.]Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA

[7.]MedStar Georgetown University Hospital, Washington, D.C., USA

[8.]Wake Forest University Health Sciences, Winston Salem, NC, USA

[9.]Dana-Farber Cancer Institute, Boston, MA, USA

[10.]University of Washington Seattle Cancer Care Alliance, Seattle, WA, USA

[11.]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA

[12.]Cone Health Cancer Center, Greensboro, NC, USA

[13.]Northwell Health-North Shore Long Island Jewish Medical Center, New Hyde Park, NY, USA

Correspondence: Arti Hurria, MD. City of Hope, 1500 E. Duarte Road; Duarte, CA 91010. ahurria@coh.org. Phone: 626-256-4673 x84467; Fax: 626-301-8898.

Author Contributions: Conception and Design: AH, HM; Collection and Assembly of Data: JBA, KB, HM; Data Analysis and Interpretation: ES, JBA, HJC, AA, KB, JLR, AJ, JF, JM, JML, GK, HDK, RAF, HB, JG, ACW, GM, MB, HM. All authors meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

ClinicalTrials.gov Identifier: NCT00024102 (49907)

Conflict of Interest: Arti Hurria reports research funding from Celgene, Novartis, and GlaxoSmithKlein, as well as has served as a consultant for Boehringer Ingelheim Pharmaceuticals, Carevive, Sanofi, GTx, Inc., Pierian Biosciences, and MJH Healthcare Holdings, LLC outside the submitted work. Karla Ballman reports research funding from the National Cancer Institute. Gretchen Kimmick reports research funding from Roche, Genentech, Abraxis BioScience, Bristol-Meyers Squibb, Puma Biotechnology, Wyeth, Novartis, GlaxoSmithKlein, Johnson & Johnson, Travel, Accommodations, Expenses: Genomic Health. Rachel A. Freedman reports research funding from Puma Biotechnology, Genentech, and Eisai. Julie Gralow reports consulting for Novartis, Genentech, Bayer, Pfizer, Merck, Puma Biotechnology, and AstraZeneca. Antonio Wolff reports research funding from Myriad Genetics, Pfizer. Antonio Wolff also reports patents, royalties, other intellectual property: he has been named as inventor on one or more issued patents or pending patent applications relating to methylation in breast cancer, and has assigned his rights to JHU, and participates in a royalty sharing agreement with JHU. Enrique Soto Perez de Celis, Anait Arsenyan, Jennifer Le-Rademacher, Julie Filo, Jacqueline M. Lafky, Heidi D. Klepin, Harold Burstein, Jake Allred, Harvey J. Cohen, Gustav Magrinat, Hyman Muss, Jeanne Mandelblatt, and Myra Barginear have no conflicts of interest to disclose.

[14.]University of North Carolina at Chapel Hill, Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

[#] These authors contributed equally to this work.

Abstract

Objectives—To analyze self-reported changes in physical function among older women with breast cancer receiving adjuvant chemotherapy.

Design—Secondary analysis of the Cancer and Leukemia Group B 49907 prospective randomized clinical trial.

Setting—CALGB institutions in the United States

Participants—Women aged 65 and older with stage I-III breast cancer enrolled in CALGB 49907 who had physical function data before and after adjuvant chemotherapy (n = 256)

Measurements—Patients completed the physical function subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire pre-chemotherapy, end-chemotherapy and 12 months from chemotherapy initiation. Functional decline was defined as a >10-point decrease from baseline at each time point. Resilience was defined as return to within 10 points of baseline. Multivariable regression was used to examine pre-treatment characteristics associated with physical function changes.

Results—Mean age was 71.9 (range 65–85). Forty-two percent had physical function decline from pre- to end-chemotherapy and 47% of these recovered (were resilient) by 12 months. Almost one-third experienced functional decline from pre-chemotherapy to 12 months later. Pre-treatment fatigue was a risk factor for functional decline from pre- to end-chemotherapy (P=0.024). Risk factors for functional decline at 12 months included pre-treatment dyspnea (P=0.007) and being unmarried (P = 0.015).

Conclusions—Functional decline was common among older women receiving adjuvant chemotherapy for breast cancer in a clinical trial. Although half recovered their physical function, a third had a clinically meaningful decline at 12 months. Strategies are needed to prevent functional decline in older patients receiving chemotherapy.

Keywords

Breast Neoplasms; Quality of Life; Resilience; Older Adults

INTRODUCTION

The risk of developing breast cancer increases with age. Almost half of breast cancer diagnoses and most breast cancer deaths occur in women age 65 and older.[1] However, there are limited data on the impact of cancer and its treatments on functional outcomes of older survivors.[2,3] The impact of chemotherapy on functional status can be critical for older adults, especially if it affects their ability to live independently. Understanding which women are at risk for functional decline could inform treatment discussions and interventions aimed at maintaining function.

The Cancer and Leukemia Group B (CALGB) study 49907, "A Randomized Trial of Adjuvant Chemotherapy with Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or Node-Negative Breast Cancer" focused on the adjuvant treatment of older adults with breast cancer.[4]

The goals of this secondary analysis were to describe self-reported changes in physical function among older adults receiving adjuvant chemotherapy during the first year after chemotherapy initiation, as well as to understand factors associated with decline in physical function vs. return to baseline ("resilience", or the ability to recover to baseline functional level). Ultimately, such findings might help identify survivors at risk of physical function decline as well as inform future interventions to decrease this risk.

PATIENTS AND METHODS

Patients

This is an unplanned secondary analysis of a prospective clinical trial which enrolled 633 patients age ≥65 years with stage I-III breast cancer. The primary objective of the parent study was to evaluate the efficacy of standard adjuvant chemotherapy (AC or CMF) in comparison with capecitabine.[4] The study found capecitabine was associated with inferior disease-free and overall survival compared with standard chemotherapy. Each participant signed an IRB-approved, protocol-specific informed consent in accordance with federal and institutional guidelines.

Participation in a QOL companion study (CALGB 361002) was offered to consecutive patients included in CALGB 49907 until the required number of 350 evaluable patients were accrued.[5] Of these, 323 had baseline physical function data. This study included 256 of those patients who had physical function data for the pre-chemotherapy (baseline), end-chemotherapy (within one month of the completion of the planned chemotherapy), and 12-month follow-up time points (Supplemental Figure).

Outcome Variables

Measures of Functional Status—Self-reported functional status was evaluated utilizing the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) pre-chemotherapy, end-chemotherapy, and 12 months post-chemotherapy initiation. The questionnaire contains 30 items including subscales whose sum is transformed into a 0–100 score, with higher scores indicating better function.[6] A 10-point change in the scale was considered as meaningful since it represented a 0.5 standard deviations change on the 0 – 100 QLQ-C30 physical function subscale score and was determined to be clinically significant.[7] The physical function subscale included the following items: "1) Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?; 2) Do you have any trouble taking a long walk?; 3) Do you have any trouble taking a short walk outside of the house?; 4) Do you need to stay in bed or a chair during the day?; and 5) Do you need help with eating, dressing, washing yourself or using the toilet?"

There were 4 measures of interest: 1) Decline in physical function from pre-chemotherapy to end-chemotherapy (defined by a ≥ 10 point decrease in the QLQ-C30 physical function subscale from pre-chemotherapy to end-chemotherapy); 2) Resilience: recovery of physical function (limited to those patients that had a decline from pre-chemotherapy to end-chemotherapy; patients who returned to within 10 points of their pre-chemotherapy QLQ-C30 physical function subscale result at the 12 month timepoint were considered resilient); 3) Decline in physical function from pre-chemotherapy to 12 months later (defined by a ≥ 10 point decrease in the QLQ-C30 physical function subscale from pre-chemotherapy to 12 months later); 4) Resistance to decline in physical function (defined as a <10 point decrease in the QLQ-C30 physical function subscale from pre-chemotherapy to both the end-chemotherapy and the 12 month timepoint).

Independent Variables—Independent variables included patient, tumor (size, nodal status, hormone receptor status), and treatment (type of surgical intervention, chemotherapy received, receipt of radiation) characteristics which could impact functional decline. Pre-treatment patient characteristics included: age, socioeconomic factors, and geriatric assessment variables. The geriatric assessment variables included aspects of daily function (role, emotional, cognitive, and social [EORTC QLQ-C30]), comorbidities (Physical Health Section – Subscale of the Older American Resources and Services[8]), social support (Medical Outcomes Study [MOS] Social Support Survey[9]), and psychological state (Hospital Anxiety and Depression Scale [HADS][10,13]), and cognition (Blessed Orientation-Memory-Concentration [BOMC] test[11]). Patient symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss) captured in the EORTC QLQ-C30 were also evaluated.[12]

Statistical Analysis

Our primary endpoint was the change in physical function at the end of chemotherapy as measured using the EORTC QLQ-C30 subscale. The association between pre-chemotherapy independent variables and physical function decline was evaluated using logistic regression.

Due to potential collinearity among baseline characteristics, the correlations between variables were explored. The risk factors associated with a decline in physical function from pre-chemotherapy to end-chemotherapy, resilience, decline in physical function from pre-chemotherapy to the 12 month timepoint, and resistance to physical function decline were identified using a backward model selection procedure at the significance level of 0.05. The final models were confirmed using the forward and stepwise procedure. PROC LOGISTIC in SAS v9.2 was utilized, and treatment arm and baseline physical function were included as stratification factors for all models. All baseline QOL scores were considered in the analysis as dichotomous variables categorized as “perfect vs. “not perfect”. Although the primary analysis was a complete-case analysis, which included all patients who had physical function data at three time points (baseline, end-chemotherapy, and 12-month follow-up), additional analyses were conducted to evaluate the potential bias caused by missing data. The distributions of baseline characteristics between patients with missing physical function data versus those with complete data were compared. Missing physical function data were imputed using various techniques. Results from sensitivity analyses using these imputation methods confirmed the primary analysis results. Additionally, there were four patients who

progressed by the 12 month timepoint. Results for sensitivity analysis excluding these four patients were similar to those of the primary analysis.

RESULTS

Patient and Treatment Characteristics

Baseline characteristics of the patients are shown in Table 1. Mean age was 71.9 years (standard deviation [SD] 4.7, range 65–85). Patients were predominantly white (88%), not employed (69%), married (58%), and living with at least one person (67%). Most patients had at least a high school education (89%). The majority of patients had node positive disease (71%), tumor size ≥ 2.0 cm (56%) and hormone receptor positive tumors (68%). Sixty-seven patients (21%) had missing physical function data at either post-chemotherapy or the 12 month visit. We found no significant differences in baseline characteristics between those 67 patients and the 256 that had physical function data at all 3 time points other than patients with missing data were less likely to be married (45% vs. 58%; P=0.05) (Table 1). Ninety-three percent of included patients (n = 238) completed the planned adjuvant chemotherapy according to the planned protocol (84% for CMF; 99% for AC and 93% for capecitabine).

Pre-Chemotherapy Physical Function and Patient Characteristics

Table 2 displays the EORTC QLQ-C30 scores and other assessment items (social support and comorbid conditions). This group was highly functional, with a mean pre-chemotherapy physical function score of 86.4 (SD 15.9). At baseline, most individuals were independent in their activities of daily living (only 1.6% needed help with eating, dressing, bathing or using the toilet), 44% reported no trouble doing strenuous activities, 51% had no trouble taking a long walk, and 86% had no trouble taking a short walk.

The most commonly reported pre-chemotherapy symptoms were fatigue (82%) and pain (65%). The group reported high levels of emotional support (mean score 86.1; SD 16.8). Twenty-two percent of patients met the HADS criteria for anxiety, 7% met criteria for depression and 11.4% had a high global HADS score (15+) indicative of depression and/or anxiety. The median number of comorbid conditions was two (range 0–8), most commonly arthritis, rheumatism, or other connective tissue disorders (60%); hypertension (54%); and osteoporosis (24%).

Decline in Physical Function from Pre-Chemotherapy to End-Chemotherapy

The median time from pre- to end-chemotherapy questionnaires was 5.1 months (range 2.2–6.4) for patients who received CMF (n = 55), 2.2 months (range 0.9–5.1) for patients who received AC (n = 80), and 4.2 months (range 3.6–9) for patients who received capecitabine (n = 121). Almost half of the patients (42%, 108/256) had a decline in physical function at end-chemotherapy (median decline = −20 points; range −73.3 to −11.7) (Figure 1). In multivariable analysis (adjusting for treatment arm and baseline physical function as stratification factors), only baseline fatigue was associated with decline in physical function from pre-chemotherapy to end-chemotherapy. Women with some fatigue at baseline had a

higher odds of decline than those without (odds ratio [OR]: 2.37; 95% Confidence Interval [CI]: 1.12–5.02; $P = 0.024$).

Resilience: Recovery of Physical Function

Of the 108 patients who experienced a decline in physical function from pre-to end-chemotherapy and had 12 month physical function data, approximately half (N=51, 47%) recovered (were resilient) to within 10 points of their baseline values by 12 months after chemotherapy initiation, while 57 (53%) did not recover (Figure 1). The median recovery was 20 points (range 6.7 to 66.7 points). After adjusting for treatment arm and baseline physical function, being married (OR = 2.52; 95% CI: 1.06, 6.03; $P = 0.037$), having fewer than 4 positive nodes (OR = 3.57; 95% CI: 1.01, 12.60; P= 0.048) and experiencing no pre-treatment appetite loss (OR = 3.65; 95% CI: 1.20, 11.11; $P = 0.022$) remained significantly associated with resilience in physical function (Table 3).

Decline in Physical Function from Pre-Chemotherapy to 12 Months Later

Of the 256 patients, regardless of whether they had experienced a decline in physical function by the end of chemotherapy, approximately one-third (30%, 78/256), showed a decline in physical function 12 months after chemotherapy initiation (median decline = −20 points; range −53.3 to −13.3) (Figure 1). After adjusting for treatment arm and baseline physical function, being unmarried (OR = 1.98; 95% CI: 1.14–3.44; $P = 0.015$) and having some pre-chemotherapy dyspnea (OR = 2.37; 95% CI: 1.26–4.46; $P = 0.007$) remained significantly associated with a decline in physical function from pre-chemotherapy to 12 months later (Table 3).

Resistance to Decline in Physical Function

Approximately half of the patients (49.6%, 127/256) showed resistance to functional decline (i.e. never had a 10 point or larger decline in physical function). Factors associated with resistance to functional decline (after adjusting for treatment arm and baseline physical function) were absence of pre-treatment fatigue (OR = 2.49; 95% CI: 1.20–5.19; P=.015) and absence of pretreatment dyspnea (OR = 1.94; 95% CI: 1.07–3.54; P=.030).

DISCUSSION

In this cohort of older adults receiving adjuvant chemotherapy for breast cancer in a clinical trial setting, short-term physical function decline was common, with almost half (42%) experiencing functional decline from pre- to end-chemotherapy, and almost a third (30%) experiencing functional decline from pre-chemotherapy to 12 months later. Among patients who experienced physical function decline from pre- to end of chemotherapy, approximately half (47%) were resilient, recovering to their baseline status by 12 months after initiation of treatment.

The impact of treatment on physical function is an important consideration for all patients, but it is particularly important for older adults.[14,15] Functional decline is associated with loss of independence, an increased risk of hospitalization, nursing home placement, and poorer OS.[16–18] A study of 2202 women ages 21–79 demonstrated that 39% of women reported

one or more functional limitation(s) following a breast cancer diagnosis (between 9 and 39 months post diagnosis [average 21 months]). In that study, functional limitations increased with age, and were associated with poorer overall survival, independent of lifestyle, clinical, or sociodemographic factors.[19] Furthermore, a prospective longitudinal study of patients with breast cancer aged ≥65 years demonstrated that a decline in physical function in the first two years after diagnosis was associated with a poorer ten-year survival.[20]

Interestingly, some older adults experiencing functional limitations after cancer treatment are able to return to their baseline function. This dynamic process of recovery and adaptation, or resilience, is considered a central aspect of successful aging,[21] and may be a latent characteristic in some individuals which allows them to resist functional decline or recover physical health following a stressor such as chemotherapy.[22] In our study, about half of the patients who experienced functional decline were able to return to baseline physical function and were thus considered physically resilient. However, it is important to mention that half of the patients were resistant to decline, and maintained their functional status throughout treatment. The differences between patients who resist functional decline and those who "bounce back" have not been fully elucidated and represent one of the main gaps in research on resilience.[22] However, data are available regarding long-term older survivors of breast, prostate and colorectal cancer (≥5 years from diagnosis) who enrolled in a randomized trial of a behavioral intervention over a two-year period of time.[23] In this study, 49% were resistant to functional decline and of those who did decline, 57% recovered. These data suggest that interventions aimed to increase functional recovery may improve outcomes for patients with cancer who receive chemotherapy.

Understanding risk factors for functional decline, and for lack of resilience, could guide the need for further evaluation and interventions. In our study, pre-treatment fatigue was associated with functional decline, highlighting the importance of conducting a thorough evaluation of patients who report fatigue.[24] Other risk factors for functional decline one year after chemotherapy included having baseline dyspnea, potentially reflecting decreased cardiopulmonary reserve. Unmarried patients were at higher risk of functional decline and lack of resilience, highlighting the potential importance of that form of social support in the maintenance of function in older adults with breast cancer. Moreover, in our study, resilience was associated with social support, in particular being married. The importance of social support among older adults has also been demonstrated, with a lack of friends or smaller social networks being associated with poorer survival.[25,26] The importance of social support among patients with breast cancer has also been reported in observational research suggesting its association with improved survival.[27–29] Some studies have suggested that this benefit is from the social network itself, and not necessarily linked to marital status.[27,29,30] Patients with a lower nodal burden were also more likely to be resilient, which could be related to the extent of axillary dissection. Previous studies have shown that patients who undergo less aggressive axillary procedures have earlier recoveries and improved QOL.[31,32] Finally, patients reporting appetite loss at baseline were less likely to be resilient. Poor appetite could be a marker of both malnutrition risk and depression, which in turn have been found to be associated with worse functional status and quality of life in older adults.[33–35]

The significance of functional limitations and lack of resilience in older adults highlights the importance of designing and evaluating interventions for those at risk. Randomized studies in older (≥65 years) cancer survivors have focused on the benefits of home-based diet and exercise programs. One study demonstrated that a diet and exercise program initiated within 18 months of diagnosis was associated with an improvement in self-reported physical function.[36] The aforementioned randomized study of a home-based diet and exercise program in long-term survivors of breast, colorectal, and prostate cancer also demonstrated the intervention could slow functional decline.[37] Overall, lifestyle interventions appear to be beneficial for patients with cancer; however, further research is needed to understand the optimal timing of interventions and the specific type and extent of exercise that is feasible and efficacious for older adults.

There are limitations to this research. This is a healthier group of older adults, with a low burden of comorbidities, high educational level, and good social support, who were eligible and fit enough to enroll in a clinical trial. However, we believe that detecting a high prevalence of decline in this healthier study cohort suggests even higher levels may be present in unselected populations. Furthermore, this highlights the importance of modernizing clinical trial design and eligibility criteria in order to include vulnerable and frail older adults, who represent a significant part of older patients seen in everyday clinical practice and for whom there is a lack of data regarding treatment outcomes.[38] Physical function was obtained via self-report using a brief 5-item scale rather than objectively measured or assessed using more detailed questionnaires and may be subject to bias, although one could argue that how patients subjectively feel about their functional status may be equally important to any objective finding. In addition, only patients with longitudinal data were included in the analysis, and all available data were used. While statistical modeling of physical function could have utilized techniques for repeated measures or longitudinal data analysis, the development of dichotomous outcomes for each of the timepoints of interest was chosen to aid in the clinical interpretation and application of the results. As with any QOL study, patients who withdrew may have had increased symptoms or functional decline and therefore we may be underestimating the degree of functional decline experienced. Additionally, we reported on a 12 month follow-up period after the initiation of treatment. Longer follow-up would be needed to understand the trajectory of recovery beyond this point. Furthermore, given the exploratory nature of the study, no corrections were made for multiple comparisons.

This study provides insight into the incidence of functional decline in older patients with breast cancer receiving adjuvant chemotherapy, a group that has been under-studied to date. It also provides insight into potential risk factors for functional decline and lack of resilience that can be targeted for interventions. Future research is needed to confirm if these findings are generalizable to diverse and under-served patients with breast cancer who did not enroll on this clinical trial, as well as to identify interventions that will avoid the loss of physical function and maximize resilience in this vulnerable population over the course of their cancer care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

Financial Disclosure: Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under the Award Number UG1CA189823 (Alliance for Clinical Trials in Oncology NCORP Grant), U10CA003927, U10CA007968, U10CA032291, U10CA033601, U10CA047559, U10CA047577, U10CA077406, U10CA077597, U10CA077651, U10CA180790, CA180802, CA180820, CA180863, U10CA180867, U10CA180857, U10CA180838, U10CA180888, 2U10CA077202, and P30-AG-028716 from the National Institute on Aging to the Duke Claude Pepper Older Americans Independence Center, U10CA85850. This research was supported in part by NCI grant U10CA084131, K05CA096940, R01CA129769, R01CA127617, and R35CA197289 to JSM. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References:

1. Howlader NNA, Krapcho M, Garshell J, et al. SEER Cancer Statistics Review, 1975–2012. In. Bethesda, MD: National Cancer Institute.
2. Weaver KE, Leach CR, Leng X, et al. Physical Functioning among Women 80 Years of Age and Older With and Without a Cancer History. J Gerontol A Biol Sci Med Sci 2016;71 Suppl 1:S23–30. [PubMed: 26858321]
3. Durá-Ferrandis E, Mandelblatt JS, Clapp J, et al. Personality, coping, and social support as predictors of long-term quality-of-life trajectories in older breast cancer survivors: CALGB protocol 369901 (Alliance). Psychooncology. 2017 2 20. doi: 10.1002/pon.4404.
4. Muss HB, Berry DA, Cirrincione CT, et al. Adjuvant chemotherapy in older women with early-stage breast cancer. N Engl J Med 2009;360(20):2055–65. [PubMed: 19439741]
5. Kornblith AB, Lan L, Archer L, et al. Quality of life of older patients with early-stage breast cancer receiving adjuvant chemotherapy: a companion study to Cancer and Leukemia Group B 49907. J Clin Oncol 2011;29(8):1022–8. [PubMed: 21300923]
6. Sprangers MA, Cull A, Bjordal K, et al. The European Organization for Research and Treatment of Cancer. Approach to quality of life assessment: guidelines for developing questionnaire modules. EORTC Study Group on Quality of Life. Qual Life Res 1993;2(4):287–95.
7. Sloan JA, Vargas-Chanes D, Kamath CC, et al. Detecting worms, ducks and elephants: a simple approach for defining clinically relevant effects in qualty-of-life measures. J Cancer Integr Med. 2003; 1 :41–7. In.
8. Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. J Gerontol 1981;36(4):428–34. [PubMed: 7252074]
9. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32(6):705–14. [PubMed: 2035047]
10. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67(6):361–70. [PubMed: 6880820]
11. Katzman R, Brown T, Fuld P, et al. Validation of a short Orientation-Memory-Concentration Test of cognitive impairment. Am J Psychiatry 1983;140(6):734–9. [PubMed: 6846631]
12. Scott N, Fayers P, Aaronson N, et al. EORTC QLQ-C30 Reference Values. In: EORTC, (ed). Brussels: EORTC; 2008.
13. Spinhoven P, Ormel J, Sloekers PP, et al. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol Med 1997;27(2):363–70. [PubMed: 9089829]
14. Klepin HD, Tooze JA, Pardee TS, et al. Effect of Intensive Chemotherapy on Physical, Cognitive, and Emotional Health of Older Adults with Acute Myeloid Leukemia. J Am Geriatr Soc 2016;64(10):1988–1995. [PubMed: 27627675]

15. Hoppe S, Rainfray M, Fonck M, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol 2013;31(31):3877–82. [PubMed: 24062399]
16. Boyd CM, Ricks M, Fried LP, et al. Functional Decline and Recovery of Activities of Daily Living in Hospitalized, Disabled Older Women: The Women's Health and Aging Study I. J Am Geriatr Soc 2009;57(10):1757–1766. [PubMed: 19694869]
17. Mor V, Wilcox V, Rakowski W, et al. Functional Transitions among the Elderly - Patterns, Predictors, and Related Hospital Use. Am J Public Health 1994;84(8):1274–1280. [PubMed: 8059885]
18. Marinac C, Patterson RE, Villasenor A, et al. Mechanisms of association between physical functioning and breast cancer mortality: evidence from the Women's Healthy Eating and Living Study. J Cancer Surviv 2014;8(3):402–409. [PubMed: 24570214]
19. Braithwaite D, Satariano WA, Sternfeld B, et al. Long-term prognostic role of functional limitations among women with breast cancer. J Natl Cancer Inst 2010;102(19):1468–77. [PubMed: 20861456]
20. Sehl M, Lu X, Silliman R, et al. Decline in physical functioning in first 2 years after breast cancer diagnosis predicts 10-year survival in older women. J Cancer Surviv 2013;7(1):20–31. [PubMed: 23232922]
21. Windle G, Bennett KM, Noyes J. A methodological review of resilience measurement scales. Health Qual Life Outcomes 2011;9:8. [PubMed: 21294858]
22. Whitson HE, Duan-Porter W, Schmader KE, et al. Physical Resilience in Older Adults: Systematic Review and Development of an Emerging Construct. J Gerontol A Biol Sci Med Sci 2016;71(4): 489–95. [PubMed: 26718984]
23. Duan-Porter W, Cohen HJ, Demark-Wahnefried W, et al. Physical resilience of older cancer survivors: An emerging concept. J Geriatr Oncol 2016;7(6):471–478. [PubMed: 27478133]
24. Brown LF, Kroenke K. Cancer-related fatigue and its associations with depression and anxiety: a systematic review. Psychosomatics 2009;50(5):440–7. [PubMed: 19855028]
25. Seeman TE, Kaplan GA, Knudsen L, et al. Social network ties and mortality among the elderly in the Alameda County Study. Am J Epidemiol 1987;126(4):714–23. [PubMed: 3631060]
26. Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. Am J Epidemiol. 2 1979;109(2):186–204. [PubMed: 425958]
27. Kroenke CH, Kubzansky LD, Schernhammer ES, et al. Social networks, social support, and survival after breast cancer diagnosis. J Clin Oncol 2006;24(7):1105–11. [PubMed: 16505430]
28. Waxler-Morrison N, Hislop TG, Mears B, et al. Effects of social relationships on survival for women with breast cancer: a prospective study. Soc Sci Med 1991;33(2):177–83. [PubMed: 1887281]
29. Maunsell E, Brisson J, Deschenes L. Social support and survival among women with breast cancer. Cancer 1995;76(4):631–7. [PubMed: 8625157]
30. Ell K, Nishimoto R, Mediansky L, et al. Social relations, social support and survival among patients with cancer. J Psychosom Res 1992;36(6):531–41. [PubMed: 1640391]
31. Belmonte R, Garin O, Segura M, et al. Quality-of-life impact of sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer patients. Value Health 2012;15(6):907–15. [PubMed: 22999141]
32. Peintinger F, Reitsamer R, Stranzl H, et al. Comparison of quality of life and arm complaints after axillary lymph node dissection vs sentinel lymph node biopsy in breast cancer patients. Br J Cancer 2003;89(4):648–52. [PubMed: 12915872]
33. Presley CJ, Dotan E, Soto-Perez-de-Celis E, et al. Gaps in nutritional research among older adults with cancer. J Geriatr Oncol 2016;7(4):281–92. [PubMed: 27197919]
34. van Bokhorst-de van der Schueren MA, Lonterman-Monasch S, de Vries OJ, et al. Prevalence and determinants for malnutrition in geriatric outpatients. Clin Nutr 2013;32(6):1007–11. [PubMed: 23755842]
35. Sanford AM. Anorexia of aging and its role for frailty. Curr Opin Clin Nutr Metab Care 2017;20(1):54–60. [PubMed: 27749690]

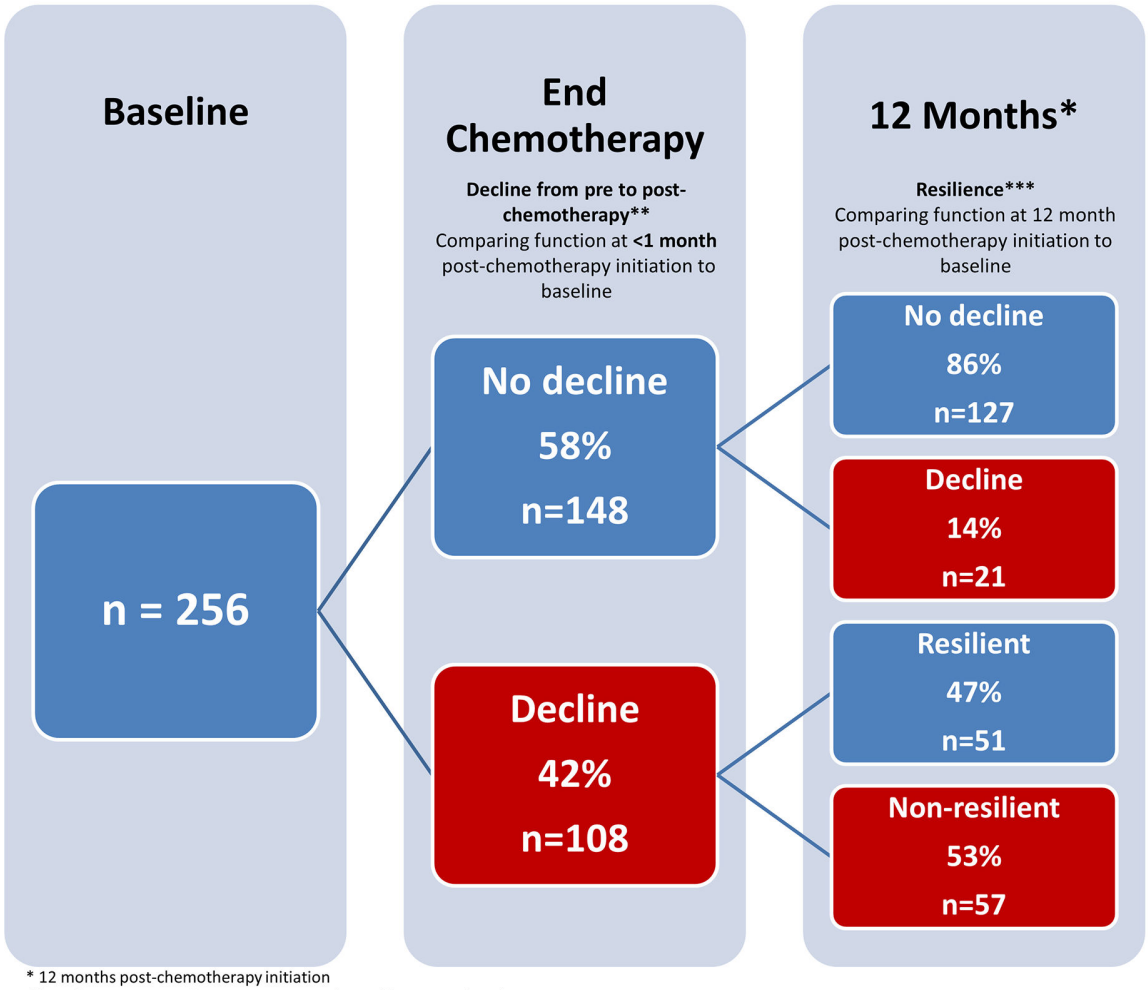
36. Demark-Wahnefried W, Clipp EC, Morey MC, et al. Lifestyle intervention development study to improve physical function in older adults with cancer: outcomes from Project LEAD. J Clin Oncol 2006;24(21):3465–73. [PubMed: 16849763]

37. Morey MC, Snyder DC, Sloane R, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. JAMA 2009;301(18):1883–91. [PubMed: 19436015]

38. Hurria A, Levit LA, Dale W, et al. Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement. J Clin Oncol 2015;33(32):3826–3833. [PubMed: 26195697]

Impact Statement:

1. We certify that this work is novel or confirmatory of recent novel clinical research
2. The potential impact of this research on clinical care or health policy includes the following: This research provides insight into potential risk factors for functional decline and lack of resilience in older women receiving chemotherapy, and could help in identifying patients at higher risk who could be targeted for interventions aimed at ameliorating or preventing such decline.



* 12 months post-chemotherapy initiation
** **Decline**: ≥ 10 point decrease in EORTC physical function subscale
*** **Resilience**: Return to within 10 points of pre-chemotherapy EORTC physical function subscale result at the 12 month post-chemotherapy initiation timepoint. Only patients with a decline in physical function from pre to post-chemotherapy were included in this analysis.

Figure 1:
Changes in physical function for patients with physical function assessments at all timepoints (N=256).

Table 1:

Baseline patient Demographics and Characteristics

	Patients without missing physical function data (N=256)	Patients with missing physical function data (N=67)	p value
Age			
Mean (SD)	71.9 (4.7)	72.7 (5.2)	0.3542
Median	71.5	72.7	
Range	(65.1–85.2)	(65.0–89.8)	
Race			
White	224 (87.5%)	55 (83.3%)	0.6739
African American	26 (10.2%)	9 (13.6%)	
Other	6 (2.3%)	2 (3.0%)	
Missing	0	1	
Employment Status			
Employed/Homemaker	77 (30.8%)	20 (30.8%)	0.9962
Not employed	173 (69.2%)	45 (69.2%)	
Missing	6	2	
Home Setting			
Lives with at least 1 person	170 (67.2%)	36 (55.4%)	0.0754
Lives alone	83 (32.8%)	29 (44.6%)	
Missing	3	2	
Marriage Status			
Married	147 (58.1%)	29 (44.6%)	0.0511
Not Married	106 (41.9%)	36 (55.4%)	
Missing	3	2	
Education Level			
Less than high school	28 (11.1%)	13 (20.0%)	0.1926
High school graduate	99 (39.3%)	27 (41.5%)	
Some undergraduate work	95 (37.7%)	18 (27.7%)	
Some graduate work	30 (11.9%)	7 (10.8%)	
Missing	4	2	
Nodal Disease			
Negative	75 (29.4%)	21 (31.3%)	0.7584
Positive	180 (70.6%)	46 (68.7%)	
Missing	1	0	
Tumor Size			
0–2cm	111 (43.5%)	28 (41.8%)	0.7982
≥ 2cm	144 (56.5%)	39 (58.2%)	
Missing	1	0	
Hormone Receptor Status			0.3786

	Patients without missing physical function data (N=256)	Patients with missing physical function data (N=67)	p value
Negative	81 (31.6%)	25 (37.3%)	
Positive	175 (68.4%)	42 (62.7%)	
Regimen			
CMF	55 (21.5%)	15 (22.4%)	0.6368
AC	80 (31.3%)	17 (25.4%)	
Capecitabine	121 (47.3%)	35 (52.2%)	

Abbreviations: CMF = Cyclophosphamide, Methotrexate and Fluorouracil; AC=Doxorubicin and Cyclophosphamide.

Table 2:

EORTC QLQ-C30 Functional Status and Physical Function Measures at Baseline (n=256)

Scales/Symptoms	Items	Range of Scores	Mean score (SD)	% with Perfect Score
EORTC QLQ-C30 Functional Scales				
Physical Function	5	0–100 (100=perfect physical function)	86.4 (15.9)	35.9%
Role Function	2	0–100 (100=perfect role function)	84.8 (21.0)	53.9%
Emotional Function	4	0–100 (100=perfect emotional function)	78.7 (17.8)	20.7%
Cognitive Function	2	0–100(100=perfect cognitive function)	87.8 (14.5)	48.4%
Social Function	2	0–100 (100=perfect social function)	87.3 (18.8)	60.4%
EORTC QLQ-C30 Symptom Scales				
Fatigue	3	0–100 (0=no fatigue)	23.7 (17.7)	17.6%
Nausea and Vomiting	2	0–100 (0=no nausea/vomiting)	2.4 (6.9)	87.5%
Pain	2	0–100 (0=no pain)	18.8 (19.4)	35.2%
Dyspnea	1	0–100 (0=no dyspnea)	11.1 (19.7)	71.9%
Insomnia	1	0–100 (0=no insomnia)	24.7 (25.6)	43.7%
Appetite Loss	1	0–100 (0=no appetite loss)	7.7 (15.3)	78.4%
Financial Difficulties	1	0–100 (0=no financial difficulties)	10.1 (21.9)	78.7%
Medical Outcomes Survey (MOS)				
Emotional Support	8	0–100 (100=perfect emotional support)	86.1 (16.8)	35.5%
Affectionate Support	3	0–100 (100=perfect affectionate support)	91.5 (15.6)	64.9%
Tangible Support	4	0–100 (100=perfect tangible support)	84.2 (20.3)	40.1%
Positive Social Interaction	3	0–100 (100=perfect positive social interaction)	85.9 (18.5)	50.6%
MOS Total	19	0–100 (100=perfect social support)	86.3 (15.8)	24.3%
Hospital Anxiety and Depression Scale (HADS)				
Anxiety	7	0–21 (8+=anxiety)	5.1 (3.5)	21.6% anxiety
Depression	7	0–21 (8+=depression)	2.4 (2.7)	6.7% depression
HADS Total	14	0–42 (15+anxiety/depression)	7.5 (5.5)	11.4% anxiety/depression
Other Measures				
Comorbid Conditions *	12	0–12 (number of conditions)	2.2 (1.5)	-

* (1) other cancers or leukemia, (2) arthritis, rheumatism, or other connective tissue disorders, (3) glaucoma, (4) emphysema or chronic bronchitis, (5) high blood pressure, (6) heart disease, (7) circulation trouble in arms or legs, (8) diabetes, (9) stomach or intestinal disorders, (10) osteoporosis, (11) chronic liver or kidney disease, (12) stroke. **Abbreviations**: EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30.[6]

Table 3.

Univariable and Multivariable Analysis of Variables Associated With Decline in Physical Function and Resilience (Recovery of Physical Function)

Physical Function Logistic Regression Models				
	Univariable		Multivariable	
Variable (at baseline)	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Decline in Physical Function Pre- to End-Chemotherapy (N=256)				
Fatigue (vs. none)	2.37 (1.12,5.02)	.024	2.37 (1.12,5.02)	.024
2+ Comorbid conditions (vs. 0–1)	1.82 (1.04,3.20)	.037		
Resilience (Recovery of Physical Function) (N=108)				
Positive nodes (0–3 vs 4+)	3.83 (1.15,12.72)	.029	3.57 (1.01,12.60)	.048
Married (vs. not married)	2.32 (1.04,5.17)	.040	2.52 (1.06,6.03)	.037
No appetite loss (vs appetite loss)	2.76 (1.01,7.56)	.049	3.65 (1.20,11.11)	.022
Decline in Physical Function Pre-Chemotherapy to 12 months later (N=256)				
Dyspnea (vs. none)	2.47 (1.33,4.59)	.004	2.37 (1.26,4.46)	.007
Not married (vs. married)	2.01 (1.17,3.44)	.011	1.98 (1.14,3.44)	.015
Fatigue (vs. none)	2.48 (1.07,5.74)	.035		
Positive nodes (4+ vs 0–3)	2.04 (1.02,4.10)	.045		
≥75 y.o. (vs. younger)	1.82 (1.01,3.29)	.048		
Resistance to Decline (N=256)				
No Fatigue (vs. some)	2.67 (1.29,5.53)	.008	2.49 (1.20,5.19)	.015
No Dyspnea (vs. some)	2.07 (1.15,3.75)	.016	1.94 (1.07,3.54)	.030
0–1 Comorbid Conditions (vs. 2+)	1.87 (1.08,3.22)	.025		

Footnote: all models are adjusted for baseline physical function and treatment arm