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Attribution of functional limitation to cancer decreases in the year following breast cancer diagnosis in older patients

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Abstract

Objectives—To examine the prevalence of self-reported functional limitations in a breast cancer population, identify whether these reported limitations are attributed to breast cancer versus other coexisting illnesses, and examine how this attribution changes over time from early in treatment to 9-months later.

Design—Longitudinal, observational study.

Setting—Community dwelling adults in Detroit metropolitan area.

Participants—2033 participants (1011 breast cancer patients, 1022 controls), aged 40–84 years.

Measurements—Participants were asked about each of 23 possible coexisting illnesses in addition to breast cancer and whether or not each illness, including breast cancer, caused any activity limitation.

Results—Of the 933 cancer patients who completed both baseline and follow up evaluations, 45% were aged 65 years and older. At baseline, 56% of patients 65 years and older reported functional limitation compared with 50% of patients younger than 65 years ($p=0.005$). Of those patients who reported limitation at baseline, 59% of older patients and 78% of younger patients attributed their limitation to breast cancer ($p<0.001$). At follow up, 53% of older and 37% of younger patients reported functional limitation ($p<0.001$), with 27% of older patients compared with 57% of younger patients ($p<0.001$) attributing limitation to breast cancer.

Conclusion—Self-reported functional limitations are common 3 months after breast cancer diagnosis, being attributed primarily to breast cancer. By 1 year after diagnosis, much of the limitation due to breast cancer resolves. Older women are less likely to have resolution of their limitations, which are most commonly due to other coexisting illnesses.

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Keywords

breast cancer; functional limitation; comorbidity

1. INTRODUCTION

The population of cancer patients over the age of 65 is markedly heterogeneous with respect to comorbidity, performance status, and functional status. There is a longstanding question in the field of geriatric oncology as to whether functional decline in patients with cancer is caused by underlying coexisting illnesses or the cancer itself.¹ Several studies have shown a significantly positive correlation between comorbidity and impaired functional status in elderly cancer patients.^{2,3,4}

Patient attribution of functional limitation to cancer versus other causes has recently been shown to be predictive of shorter survival in a large study derived from the Second Longitudinal Study on Aging (LSOA).⁵ Measuring patient attribution may thus potentially serve as a measure of severity of disease and a prognostic marker. To clarify the relationship between breast cancer and functional limitation, we used an existing cohort of breast cancer patients to determine 1) the prevalence of patient attribution of activity limitation to breast cancer versus other underlying coexisting illnesses, 2) changes in patient attribution of causes of limitation during the year following breast cancer diagnosis, and 3) differences in patient attribution of activity limitation to breast cancer versus other causes in younger (<65 years) versus older (65 years and older) age groups.

2. METHODS

2.1 Population

The data set used for this analysis has been previously described.⁴ Briefly, it is derived from a study that began in 1984 in the Detroit metropolitan area to assess the functional and psychosocial status of women after the diagnosis and treatment of breast cancer. Women aged 40 to 84 years, recently found to have a confirmed histology of invasive breast cancer, were identified through the Metropolitan Detroit Cancer Surveillance System (MDCSS) in the Division of Epidemiology at the Michigan Cancer Foundation, with identification of cases within 4 weeks of diagnosis. Patients were interviewed 2 to 4 months after diagnosis. Most of the interviews were performed in the participant's home; 5% were done by telephone.

In the first cohort, 571 eligible women ages 55 to 84 years were identified in a 7-month period between 1984 and 1985, and 463 (81.1%) were successfully interviewed. In the second cohort, 620 women were identified in a 7-month period between 1987 and 1988, and 548 (88.4%) of those women were interviewed. The second cohort was selected to broaden the age range from 40 to 84 years and to increase the representation of women ages 75 to 84 years. Because there were no substantial differences found between the two cohorts in treatment patterns or in the association between other variables and survival, the two cohorts were combined for all analyses.

A total of 1022 control participants, women residents of the Detroit metropolitan area, age-matched to the patient population (aged 40 to 84 years), were identified through telephone random-digit dialing, as previously described,⁶ and completed questionnaires, both baseline and 9 month follow up. The control group was used in the analysis reported here, in order to compare trends in self-reported activity limitation in breast cancer patients to controls.

Data on age, race, stage of breast cancer at diagnosis, and treatment status were obtained from MDCSS files and by contacting the physician on record. Race was coded as black or white. Stage of breast cancer at diagnosis was coded as a three-level variable (local, regional, or remote) according to criteria established by the National Cancer Institute's SEER program. Treatment status information included type of surgery and type of adjuvant therapy. Categories for type of surgery included 1) no surgery, 2) partial mastectomy, 3) modified radical mastectomy, while categories for type of adjuvant therapy included radiation, chemotherapy and hormone modulation therapy.

2.2 Questionnaire

Home interviews were conducted for both breast cancer patients and control participants. Patients were interviewed 2–4 months after diagnosis and again 8 to 10 months later (approximately one year after diagnosis). Controls were interviewed twice over the same period. The questionnaire included questions on physical functioning and health, and required 45–60 minutes to complete. During the interview, additional information was obtained on demographic data, body mass index, education, history of alcohol use, smoking history, and self-reported financial resources. In addition, participants were asked whether or not they had each of 23 coexisting illnesses,⁴ including breast cancer. Participants were asked “Are any of your regular activities currently limited because of (name of condition)” for each illness. If the participant answered ‘yes’ for any illness, the person was considered to have functional limitation.

2.3 Statistical Analysis

Figure 1 describes the derivation of the sample population included in our analysis. Of the 933 breast cancer patients who completed both baseline and follow-up surveys, 41 (4.4%) had remote disease. These patients were excluded from our analysis, because of the markedly different clinical course in patients with remote versus local and regional disease. The analysis was based on the 892 early stage breast cancer patients and 962 control participants who completed both the baseline and follow-up surveys.

The prevalence of each coexisting illness using self-reported data was calculated, as well as the percent of patients with each illness subjectively attributing activity limitation to the condition. Chi-square test statistics were used to test for statistical significance when comparing results for younger (age less than 65 years) to older (aged 65 years or more) groups, and breast cancer to control populations. Baseline results were also compared to follow-up results using chi-square test statistics. Statistical significance was defined as a p-value below 0.05. This analysis was performed using STATA/SE 8.0 (StataCorp LP, College Station, TX) statistical software.

3. RESULTS

3.1 Sample characteristics

The demographic, social and clinical characteristics of patients with breast cancer and control participants are described in Table 1. Mean age at baseline for breast cancer patients was similar for controls and cancer patients, with 44% of controls and 45% of cancer patients being aged 65 years and older. Patients were predominantly white in each group. Most of the patients with breast cancer had early stage (local and regional) breast cancer. Most of the patients were treated surgically with mastectomy (75% of patients), with 25% of patients receiving both mastectomy and adjuvant therapy (9% adjuvant chemotherapy alone, 2% adjuvant hormone modulation therapy alone, and 14% adjuvant chemotherapy and hormone modulation therapy). Only 11% of patients were treated with lumpectomy and radiation. In the entire sample,

including controls and breast cancer patients, 43% of women reported functional limitation at baseline and 39% reported limitation at 9 month follow up (12 months after diagnosis).

3.2 Prevalence of comorbidities and attribution of limitation

The prevalence of coexisting illnesses in breast cancer patients is listed in Table 2. The most common coexisting illnesses were hypertension (48%), arthritis (48%), and hemorrhoids (29%). For each coexisting illness, including breast cancer, the number and percentage of patients with that illness who attributed activity limitation to that illness at baseline is listed in Table 2. Of the 892 patients who completed both at baseline and follow up interviews, 455 (51%) attributed activity limitation to at least one illness. Of these, 309 (68% of those with attribution, 35% of breast cancer patients) attributed limitation to breast cancer, while 146 (32%) of patients attributed limitation to at least one other cause. The coexisting illnesses that caused activity limitation most frequently, included heart disease (38%), arthritis (38%), stroke (33%), and breast cancer itself (35%). At follow up, 44% of patients reported activity limitation and 40% of these patients attributed it to breast cancer, whereas 60% attributed it to another coexisting condition ($p < 0.001$ comparing attribution to cancer between baseline and follow up).

3.3 Comparison of older and younger populations

Self reported activity limitation was found to resolve at 9 months follow up in younger women, whereas in older persons, activity limitation persisted, as described in Table 3. At baseline, 55% of patients 65 years or older reported functional limitation compared with 47% of patients younger than 65 years ($p = 0.011$). Of those patients who reported limitation at baseline, 58% of older patients and 78% of younger patients attributed their limitation to breast cancer ($p < 0.001$). At follow up, 53% of older and 37% of younger patients reported functional limitation ($p < 0.001$), with 26% of older patients compared with 56% of younger patients ($p < 0.001$) attributing limitation to breast cancer. Among older patients, the conditions other than breast cancer that were most likely to be associated with limitation were heart disease (43%), arthritis (42%), colitis (31%), chronic nervous conditions (24%), pulmonary disease (19%), diabetes (17%), and cataracts (14%).

Attribution of activity limitation to coexisting illnesses for older and younger controls is also described in Table 3. In the control population, 25% of participants younger than 65 compared with 49% of participants aged 65 years or older reported activity limitation at baseline ($p < 0.001$ comparing young to old). At follow up, the percentages of control participants reporting activity limitation was similar to baseline for both young (25%) and old (47%) groups.

In participants younger than 65, activity limitation was significantly higher in the breast cancer population than in the control population, both at baseline (47% versus 25%; $p < 0.001$) and follow up (37% versus 25%; $p < 0.001$), whereas in participants 65 years of age and older, activity limitation was not significantly higher in breast cancer patients than in controls (55% versus 49%; $p = 0.08$) at baseline or at follow up (53% versus 47%; $p = 0.12$).

3.4 Comparison of treatment by age and limitation status

Of the 400 breast cancer patients aged 65 years and older, 236 (59%) received mastectomy alone, and 85 (21%) received mastectomy plus adjuvant therapy, with 21 (5%) receiving adjuvant chemotherapy alone, 52 (13%) adjuvant hormone modulation therapy alone and 12 (3%) receiving adjuvant chemotherapy plus hormone modulation therapy. Fewer older patients received lumpectomy plus radiation 27 (6%) or lumpectomy plus adjuvant therapy 13 (3%). The overall proportion of older patients receiving mastectomy was higher than in younger patients (80% vs. 75%, $p = 0.0024$), while the proportion receiving chemotherapy was lower

(9% vs. 40%; $p < 0.0001$), and the proportion receiving hormone modulation therapy was not significantly different (19.5% vs. 19.7%; $p = 0.85$).

Of the 455 breast cancer patients with activity limitation at baseline, 219 (48%) received mastectomy alone, and 120 (26%) received mastectomy plus adjuvant therapy; 52 (11%) received adjuvant chemotherapy alone, 48 (10%) received adjuvant hormone modulation therapy alone, and 20 (4%) received adjuvant chemotherapy and hormone modulation therapy. Lumpectomy plus radiation was administered in 41 (9%), and lumpectomy plus adjuvant therapy in 28 (6%) patients with activity limitation. Fewer women with activity limitation received mastectomy compared to those without limitations (64% vs. 95% $p < 0.0001$), and the proportion receiving chemotherapy was also significantly lower (19% vs. 34%, $p < 0.0001$), while the proportion receiving hormone modulation therapy was not significantly different among those with different activity limitations (20% vs. 18%; $p = 0.83$).

DISCUSSION

The findings of this study provide new insights into functional limitation in breast cancer patients. Three months after being diagnosed with breast cancer, over half of women report functional limitations; most of these limitations are attributed to breast cancer. Among younger women, these limitations resolve in about a third of cases and those that remain are usually attributable to breast cancer. Among older women, limitations persist but are attributed to other coexisting conditions rather than cancer. These results suggest that with increasing age, the presence of a greater number and severity of coexisting illnesses may play a larger role in perception of activity limitation than the diagnosis and treatment of the cancer itself. An alternative explanation is that older people have less reserve and once the breast cancer has precipitated a limitation, they cannot recover because of other conditions.

Of note, fewer older patients received chemotherapy compared to younger patients. This may account for the differences in attribution of limitation to cancer at baseline and the resolution of self-reported limitation in younger patients after chemotherapy is completed. Moreover, fewer women who reported limitation at baseline (3 months after diagnosis), received either mastectomy or adjuvant chemotherapy. This suggests that treating physicians may have recommended less aggressive therapy for women who have functional impairment or that these women opted for more conservative therapy.

The high prevalence of self-reported functional limitation among elderly cancer patients found in our study has been noted in previous studies. The percentages of older cancer patients reporting limitation in activities of daily living (ADL) range from 17%⁷ to 33%.⁵ Limitation in instrumental activities of daily living (IADL)^{2,7} and poor Eastern Cooperative Oncology Group (ECOG) performance status⁷ have also shown to be prevalent in elderly cancer patients, and to increase with advancing age. Self-reported functional difficulty has been shown to persist in older (age > 60 yrs) long-term (> 5 years) survivors of breast, prostate and colorectal cancer with 56% of patients scoring a 3 or higher on the Nagi Functional Difficulty Index.⁸

We found a higher prevalence of coexisting illness among older cancer patients, as has been shown previously.³ Hypertension, arthritis, digestive diseases, heart disease, respiratory disease, cataracts and diabetes were among the most prevalent coexisting illnesses in our study, in accordance with previous studies of comorbidity in elderly cancer patients.^{3,9-12} Despite its relatively low prevalence, stroke, when reported, was a major cause of limitation. In this study, approximately 1/3 of patients of all ages attributed activity limitation to breast cancer. This estimate is higher than that reported in a general cancer population. In an analysis of data derived from the Second Longitudinal Study on Aging, 33% of cancer patients reported limitation in ADLs and 14% of these patients subjectively attributed this limitation to the cancer

itself.⁵ Examining whether activity limitation is subjectively attributed to coexisting illnesses versus cancer itself may provide useful prognostic information for cancer patients, beyond information on number of coexisting illnesses and functional status measures. While perceived cause of disability has provided prognostic information on 3–4 year survival beyond medical conditions and functional status in patients over age 70 with various types of cancer,⁵ the predictive value of attribution of activity limitation to cancer for longer term (i.e., 10 to 15-year) survival is a topic for future research. Furthermore, targeting subgroups of patients with higher subjective attribution to cancer may be an indication for comprehensive geriatrics assessment, allowing for early intervention for these patients, with the intention of limiting symptoms and preventing functional decline.

One important limitation in our study is that the majority of patients in the time period of the study were treated with simple mastectomy, which is no longer the standard of care for early stage breast cancer. Usually, the combined modality of radiation and segmental mastectomy or lumpectomy can be used in this population and may have less impact on function. Modern surgical techniques utilizing sentinel lymph node biopsy may also decrease the functional impact of breast cancer surgery. Additionally, in this study, relatively few patients received adjuvant chemotherapy or hormone therapy whereas patients with early stage breast cancer today might be offered adjuvant chemotherapy. With a larger number of women receiving adjuvant therapy, different patterns of functional limitation might be observed. Finally, another limitation of our study is that self-reported activity limitation is a subjective rating, in which the participant attributes limitation or not to each coexisting illness. Self-reported functional limitation has been shown to be correlated with performance-based measures¹³ and is commonly used in measuring functional status. However, it is not possible to establish a precise disease-limitation link objectively.

This study also suggests that a direction for future research is to better characterize the relationship between cancer, coexisting illnesses and transitions in functional status in elderly cancer patients. Allostatic load has been described as a manifestation of cumulative physiologic burden, which may include subclinical physiologic disturbances as well as comorbidity.¹⁴ There is a complex interactive relationship between cancer and comorbidity, potentially related to common pathophysiologic mechanisms.^{12,15} Allostatic load has been shown to predict functional decline.¹⁶ Physiologic reserve, as measured by allostatic load, may be able to contribute information about the interface of comorbidity, functional status and tumor burden.¹⁷ It will be worthwhile to examine the prognostic value of a comorbidity index that includes information on attribution of functional limitation to each illness, both in predicting survival and transitions in functional status in older cancer patients.

In conclusion, self-reported activity limitation tends to be transient following diagnosis in younger patients with breast cancer, while it usually persists in patients older than 65 years. There is a significant shift in attribution over the year following diagnosis from predominantly attributing limitation to breast cancer to other coexisting illnesses and this shift is more prominent in the elderly population. Further research on the attribution of activity limitation to cancer and coexisting illnesses is warranted as a means of clarifying the complex relationship between cancer, comorbidity and functional limitation.

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Biography

Mary E. Sehl, M.D., is a fellow in Geriatric Oncology at the University of California, Los Angeles, where she was awarded a Specialty Training and Advanced Research (STAR) Fellowship to combine clinical fellowship training with Ph.D. graduate studies in Biomathematics. Her research interests include identifying predictors of functional decline in older cancer patients, and mathematical and statistical models of cancer genetics and frailty. Arash Naeim, M.D., Ph.D. is the director of the Geriatric Oncology Research Initiative at the University of California, Los Angeles. He is a recipient of a Young Investigator Award from the American Society of Clinical Oncology in 2002, and a current NIH K23 awardee for his work on cost-effectiveness and optimization of delivery of cancer treatment to elderly patients, by taking into account preferences, comorbidity, and functional status.

Figure 1.
Participant selection.

Table 1

Participant population characteristics

	Cancer patients (N=892)		Controls (N=962)
Age (years) *	62.6 ± 12		62.8 ± 12
Ethnicity (% white)	83		80
Education (years) *	11.6 ± 3.1		11.7 ± 3.0
Stage (%)			
Local	57		
Regional	43		
Treatment received, N (%)	<u>< 65 years</u>	<u>≥ 65 years</u>	
No therapy	5 (0.75)	2 (0.90)	
Hormone modulation alone	1 (0.15)	1 (0.45)	
Lumpectomy alone	19 (2.8)	15 (6.7)	
Lumpectomy and radiation †	86 (13)	10 (4.5)	
Lumpectomy and adjuvant chemotherapy	6 (0.90)	7 (3.1)	
Lumpectomy and adjuvant hormone modulation	9 (1.3)	2 (0.90)	
Lumpectomy and adjuvant chemotherapy plus hormone modulation therapy †	22 (3.3)	0 (0)	
Mastectomy alone †	326 (49)	121 (54)	
Mastectomy and radiation **	28 (4.2)	10 (4.5)	
Mastectomy and adjuvant chemotherapy	50 (7.5)	32 (14)	
Mastectomy and adjuvant hormone modulation †	1 (0.15)	17 (7.6)	
Mastectomy and adjuvant chemotherapy plus hormone modulation therapy †	114 (17)	6 (2.7)	

* Values are mean ± standard deviation.

** p-values comparing young to old age groups were significant at 0.05 level.

† p-values comparing young to old age groups were significant at 0.0001 level.

Table 2
Self-reported activity limitation attributed to breast cancer and coexisting illnesses at baseline and follow-up

	Breast cancer patients			Control participants		
	Prevalence (%) [*]	No. of patients attributing limitation to illness (%) [†]	No. of controls attributing limitation to illness (%) [†]	Prevalence (%) [*]	No. of controls attributing limitation to illness (%) [†]	No. of controls attributing limitation to illness (%) [†]
	baseline	follow-up	baseline	baseline	follow-up	baseline
Breast cancer	892 (100)	892 (100)	309 (35)	-	-	-
Other Coexisting illnesses						
Hypertension	431 (48)	446 (50)	41 (9)	449 (47)	461 (48)	65 (14)
Arthritis	426 (48)	470 (53)	161 (38)	485 (50)	505 (52)	209 (43)
Hemorrhoids	264 (29)	275 (31)	11 (5)	265 (27)	272 (28)	9 (3)
Cataracts	159 (18)	181 (20)	33 (21)	178 (19)	199 (21)	37 (21)
Thyroid disease	148 (16)	160 (18)	10 (7)	168 (18)	178 (19)	9 (5)
Diabetes mellitus	120 (13)	127 (14)	13 (11)	113 (12)	122 (13)	32 (28)
Heart disease	120 (13)	130 (14)	46 (38)	155 (16)	171 (18)	69 (45)
Ulcer	114 (13)	120 (13)	15 (13)	129 (13)	135 (14)	15 (12)
Pulmonary disease	118 (13)	129 (15)	26 (22)	156 (16)	170 (18)	38 (24)
Gall bladder	145 (16)	152 (17)	8 (5)	167 (17)	177 (18)	10 (6)
Hernia	103 (12)	111 (12)	17 (17)	142 (15)	153 (16)	26 (18)
Chronic nervous condition	98 (11)	113 (13)	19 (19)	120 (12)	136 (14)	29 (24)
Diverticulosis	87 (6)	94 (10)	13 (15)	86 (9)	87 (9)	13 (15)
Colitis	53 (6)	50 (6)	15 (28)	52 (5)	53 (6)	9 (17)
Kidney disease	42 (5)	52 (6)	2 (5)	58 (6)	63 (7)	12 (21)
Stroke	30 (3)	37 (4)	10 (33)	49 (5)	54 (6)	21 (43)
Cancers (other than breast)	32 (4)	32 (4)	3 (9)	32 (3)	34 (4)	3 (9)
Glaucoma	25 (3)	30 (3)	6 (24)	37 (4)	41 (4)	5 (14)
Liver	16 (2)	17 (2)	2 (13)	14 (1)	19 (2)	1 (7)
Total attribution to conditions other than breast cancer	-		146			343
Total no. patients attributing activity limitation to >= 1 illness (including breast and other cancers)	-		455 (51)			343 (36)

* = % of patients with breast cancer (N=892)

[†] = % of participants with condition reporting limitation due to this condition
[‡] = % of control participants (N=962)

Table 3
Percent of patients with self-reported activity limitation at baseline and follow up surveys.

	Age < 65 years		Age ≥ 65 years		p-values comparing younger vs. older populations	
	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up
Control participants						
No. of patients reporting activity limitation (%) [†]	136/535 (25%)	132/535 (25%)	211/427 (49%)	202/427 (47%)	<0.001	<0.001
Breast cancer patients						
No. of patients reporting activity limitation (%) [†]	232/492 (47%)	181/492 (37%)	223/400 (55%)	212/400 (53%)	0.011	<0.001
% attributing to breast cancer [*]	78%	56%	58%	26%	<0.001	<0.001

[†] p-values comparing baseline to follow up were <0.00001 for patients aged < 65 years, p=0.43 for patients aged ≥ 65 years.
^{*} p-values comparing baseline to follow up in control populations were not significant (p = 0.78, young; p = 0.54, old)
^{*} p-values comparing baseline to follow up % attributing limitation to breast cancer were p<0.00001 for both age groups of cancer patients.