Function in Elderly Cancer Survivors Depends on Comorbidities

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Background. Factors associated with functional status in elderly cancer survivors, in particular, comorbidity, have been inadequately studied.

Methods. Of 4162 participants aged 65 and older enrolled in the Duke Established Populations for Epidemiologic Studies of the Elderly study in 1986, 376 of the participants self-reported a diagnosis of cancer. Participants were divided into 2 comorbidity groups and 4 cancer groups. Cancer groups included 132 participants diagnosed 0–4 years ago, 117 diagnosed 5–15 years ago, 127 diagnosed >15 years ago, and 3784 participants who had never been diagnosed with cancer. Comorbidity (self-reported stroke, diabetes, hypertension, and myocardial infarction) was classified as presence of 1 or no comorbidities (n = 3089) or 2 or more comorbidities (n = 1073). Function was assessed by Katz Activities of Daily Living, Rosow-Breslau, Nagi, and Instrumental Activities of Daily Living scales at the time of interview.

Results. In a two-way analysis of covariance model of comorbidity and cancer group controlling for age, race, sex, education, marital status, depression, and cognitive status, duration of cancer survivorship does not influence most measures of function. In the subset of 376 cancer survivors, comorbidity significantly correlates with the functional status of these older cancer survivors (<0.02, for all 4 measures of function).

Conclusions. In the older cancer survivor, regardless of duration following diagnosis, the presence of comorbidity rather than the history of cancer per se correlates with impaired functional status.

Patients with cancer are increasingly surviving initial diagnosis and treatment for substantial periods of time either cured of, or living with, cancer (1). With this increase in long-term survivorship, concerns have arisen about residual effects of the disease and its treatment (2,3). Such long-term sequelae have been demonstrated predominantly in survivors of childhood cancer into young adulthood. However, adult survivors of cancer have also been found to have sequelae, including effects on cardiovascular, pulmonary, gastroenterologic, neurologic, and endocrine function (4). The incidence and prevalence of cancer increases with increasing age and, as the population ages, it is expected that there will be increasing numbers of people surviving into older age following diagnosis and treatment of their cancer (5). The impact of surviving a diagnosis of cancer into old age, however, has been largely unexamined (6).

Aging is associated with increasing functional dependency and increasing comorbidity. It has been suggested that one characteristic of long-term cancer survivorship could be the premature expression of otherwise usual age-related changes, including functional decline (4). In previous work, we have demonstrated that there is little association between previous cancer and the prevalence of other comorbidities in the older cancer survivor (7). However, there has been no direct study of the interrelationships between the potential late effects of cancer and the effects of other age-related changes such as comorbidity on the functional status of older cancer survivors.

In order to explore these relationships, we present analyses using data from the Duke Established Populations for Epidemiologic Studies of the Elderly (EPESE), a population-based cohort study within which there is a diverse group of elderly participants who have survived cancer for varying periods of time.

Methods

Our participants were from the Duke component of the National Institute on Aging-funded study of EPESE. The populations of both the overall 4-site study and the Duke study have been described in detail (8–10). The Duke EPESE used a 4-stage stratified household sampling design to generate a probability sample of community residents aged 65 years and older living in a 5-county urban and rural area of the Piedmont region of North Carolina. The sample was stratified for race with blacks accounting for over half of the participants. This study utilizes information from the initial Duke EPESE interviews, conducted in 1986 (8–11). The Duke EPESE was approved by the Institutional Review Board at Duke University Medical Center. Informed consent was obtained from study participants after explanation of the project and prior to entry in the study.

In addition to cancer, self-reported information on stroke, diabetes mellitus, hypertension, and myocardial infarction was collected and reported here as comorbidities as in previous publications from this database (7,12,13). We compared those with 1 or more of these comorbidities with those with 2–4. Age, sex, race, marital status, and years of education were all reported by the participants as part of the EPESE questionnaire. Age and education were included in all analyses as continuous variables, while marital status and race were included as dichotomies.
Depression was measured using the 20-item Center for Epidemiologic Studies Depression (CES-D) scale, a self-report index of depressive symptoms developed by the Center for Epidemiologic Studies of the National Institute of Mental Health (14). For each question on the CES-D scale, study participants were asked whether they had felt that way during the past week. A total score was generated from the mean number of questions that received positive responses. Higher scores on this continuum indicate more depressive symptoms.

Cognitive impairment was measured using the 10-item Short Portable Mental Status Questionnaire scale (15). The number of incorrect responses is summed for a total score, and analyzed as a continuous variable, with a higher score indicating a greater level of impairment. Mean scores were obtained for each group.

Functional status was assessed using 4 different measures of function including the Katz Activities of Daily Living (ADL) (16,17), Nagi (18), and Rosow-Breslau (19) functional scales and the Instrumental Activities of Daily Living (IADL) scale (20). Study participants completed the questions of all 4 measures during a home interview. For each measure, the total number of reported deficits were tallied, thus resulting in a total score, and were analyzed as a continuous variable with a higher score indicating more functional impairment.

ADLs represent the most basic processes involved in everyday independent function. The Katz ADL questions cover basic functions including bathing, dressing, toileting, moving around the house, eating, and incontinence (16,21, 22). Two other measures of function used in this study include the Rosow-Breslau Health Scale and the Nagi. The Rosow-Breslau Health Scale was developed in 1966 specifically to measure function in the elderly population (19). It includes questions on ability to do heavy housework, to walk up and down stairs, and to walk a half mile. The Rosow-Breslau Health Scale contains some unique items, which may be especially relevant to a patient’s life at home. The types of tasks contained in the Rosow-Breslau Health Scale questions are generally amenable to intervention. The Nagi scale assesses changes in function caused by pathology and includes specifically physical movements such as standing, lifting, stairs, walking, stooping, bending, kneeling, using hands, and reaching. It was not designed specifically for use in assessing older people, but scores tend to decline with age, and older people typically show the most impairment (20).

The IADL questions are often combined with the ADL questions to give a more complete idea of a person’s level of function. The IADL scale, analyzed as a continuous variable, assesses activities that involve interaction with the environment such as handling finances, shopping, food preparation, housekeeping, using the telephone, doing laundry, using transportation, and taking medication (20).

Presence of cancer, cancer type, and year of cancer diagnosis were determined via self-report during the EPESE interview. Participants were divided into 4 groups based on cancer status: those who self-reported never to have had cancer (n = 3784), those who reported having had cancer diagnosed in the past 0–4 years (n = 132), cancer diagnosed in the past 5–15 years (n = 117), and cancer diagnosed more than 15 years ago (n = 127) to create approximately equal groups. Participants who had only reported having had skin cancer other than melanoma were not included in any of the groups with cancer. Participants who reported having had hysterectomy specifically for cancer were included in the gynecologic malignancies group. Participants who reported hysterectomy for fibroids were not.

Analysis of variance and Goodness-of-Fit chi-square statistics were employed to investigate bivariate differences between groups for the continuous and dichotomous covariates. To analyze the effect of comorbidity and cancer group on the various outcome measures of function, participants were divided into 2 comorbidity groups (high and low) and 4 groups describing survivorship from cancer diagnosis. A two-way analysis of covariance (ANCOVA) controlling for age, sex, race, education, marital status, depression, and cognitive status was performed. To control the overall or family-wise type I error rate in the study of multiple corrected outcomes, we analyzed the results by using the multivariate ANCOVA, employing Wilks’ lambda (23) as the test statistic. Only if this multivariate test was rejected were subsequent follow-up individual separate tests performed for each of the outcomes for cancer and comorbidity group differences. In these follow-up analyses, the same set of covariates were employed.

RESULTS

At the inception of the EPESE study in 1986, there were a total of 4162 participants. Of these, 3784 had never had cancer or had only had skin cancer (nonmelanoma), whereas 376 of the participants had a previous diagnosis of cancer (2 missing). Age ranged from 65–105 years, with a mean age of 73.6 years.

The most frequently reported cancer type in the recently diagnosed group and in the 5–15 years since diagnosis group was breast cancer. In the group that reported having been diagnosed with cancer more than 15 years ago, endometrial or uterine cancer was the most frequently reported cancer, followed by breast cancer (see Table 1).

### Table 1. Distribution of Cancer Type by Years Since Diagnosis

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>0–4 Years</th>
<th>5–15 Years</th>
<th>&gt;15 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>135 (100)</td>
<td>124 (100)</td>
<td>136 (100)</td>
</tr>
<tr>
<td>Colon</td>
<td>29 (21.5)</td>
<td>32 (25.8)</td>
<td>29 (21.3)</td>
</tr>
<tr>
<td>Lung</td>
<td>16 (11.9)</td>
<td>8 (6.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Prostate</td>
<td>12 (8.9)</td>
<td>11 (8.9)</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>12 (8.9)</td>
<td>3 (2.4)</td>
<td>6 (4.4)</td>
</tr>
<tr>
<td>Lymphoma/leukemia</td>
<td>1 (0.7)</td>
<td>4 (3.2)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>2 (1.5)</td>
<td>5 (4.0)</td>
<td>5 (3.7)</td>
</tr>
<tr>
<td>Esophageal, stomach, small bowel, liver</td>
<td>9 (6.7)</td>
<td>1 (0.8)</td>
<td>13 (9.6)</td>
</tr>
<tr>
<td>Renal/urologic</td>
<td>7 (5.2)</td>
<td>9 (7.3)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Uterine, ovarian, cervical, vaginal</td>
<td>8 (5.9)</td>
<td>11 (8.9)</td>
<td>38 (27.9)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>10 (7.4)</td>
<td>7 (5.6)</td>
<td>9 (6.6)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1 (0.7)</td>
<td>1 (0.8)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Diseased kidney missing</td>
<td>2 (1.5)</td>
<td>1 (0.8)</td>
<td>6 (4.4)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2 (1.5)</td>
<td>2 (1.6)</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>

Note: Dx = diagnosis.
Those participants who had never been diagnosed with cancer and the 3 groups of cancer survivors did not differ with respect to sex, presence of individual comorbidities (stroke, diabetes, hypertension, and myocardial infarction), or marital status. The groups did have significant differences in the distribution of age, race, education, total comorbidity, depression, and cognitive impairment. A higher proportion of white participants had previous cancer diagnoses (58% of the cancer group vs 44% of the no-cancer group ($p=.001$). Those participants who never had cancer were less educated than those who did report a cancer diagnosis ($p=.007$). Those participants who had been diagnosed with cancer more than 15 years ago tended to be older ($p=.02$), more depressed ($p=.003$), and more cognitively impaired than the other groups ($p=.0001$) (Table 2).

Function was measured by several indicators including the Katz ADL, Rosow-Breslau, Nagi, and IADL scales. The level of functional deficits from our controlled model (described below) is shown for each of the 3 cancer survivor groups and for the group without cancer in Table 3. Across the 4 functional status measures, there was no difference in the surviving cohorts (Wilks’ lambda, $p=.4404$) indicating no generalized effect of cancer status across the functional measures. In both the multivariate test and in follow-up separate models for each measure of function, controlling for age, race, sex, education, marital status, depression, and cognitive status by two-way ANCOVA, neither the previous diagnosis of cancer nor the duration of survivorship were associated with function (Table 3). The one seemingly significant association, Nagi, would not be declared significant since the multivariate test was not declared significant. In another controlled model, which included only the participants with cancer, the controlled values for level of functional deficit and the corresponding $p$ values were nearly identical to the model that included the participants who had never had cancer.

For the 3 cancer groups, multivariate analysis of comorbidity status (0–1, 2–4) indicated a generalized effect on functional status measures (Wilks’ lambda, $p=.0033$). Across all measures of function, the higher comorbidity group of cancer survivors had more-impaired function relative to the lower comorbidity group of cancer survivors (Table 4). In follow-up controlled analysis performed separately for each measure of function, all $p$ values were less than .05. In addition, all $p$ values from the interactions between comorbidity and cancer groups were greater than 0.3611, indicating no interaction between cancer group and comorbidity as it relates to function. Thus, we conclude that comorbidity, but not survivorship of cancer group per se, relates to functional status.

**DISCUSSION**

Functional status assessments such as the Karnofsky Performance Status have long been a part of the evaluation of cancer patients and have long been used as prognostic indicators. Such assessments capture a gestalt impression of function, but fall short of reflecting the issues of older cancer patients. Indeed, the Karnofsky (24) and Eastern Cooperative Oncology Group (ECOG) (25) performance status scales are not always helpful for assessing elderly cancer patients; 80% of elderly cancer patients score a 0 or 1 on the ECOG (indicating good performance status) despite the fact that elderly cancer patients often have comorbidities and functional deficits (26). In the context of the long-term follow-up of older cancer survivors, functional status has a broader importance and represents the essential life skills that need to be accomplished on a daily basis. Inability to complete functional skills may have dire ramifications on health such as poor hygiene, weight loss, and poor nutritional status.

Other types of functional assessment, such as the evaluation of Katz ADL, Rosow-Breslau Health Scale, Nagi, and IADL scales, may be more conducive to detecting clinically relevant functional deficits in older cancer patients and older cancer survivors. In a study by Siu and colleagues, the validity of the self-report measures of function was assessed by comparing scores on self-report measures with scores on performance-based measures in a group of 155 very old people with a mean age of 84.3 years, evaluated at the time of admission to a nursing home. Self-report of lower-extremity function correlated well with performance-based gait and balance (27). Short multidimensional health measures are appropriate for use in assessing function in the very old who have normal to mildly impaired cognition (27). Despite the importance of functional status in older people, performance-based measures have not yet been validated for those who are demented.
adults, little is known about the factors that influence functional status in older cancer survivors.

Though there has been considerable concern about the late effects of cancer and its treatment on both psychosocial and physical functional outcomes, most previous work has concentrated on survivors of childhood cancer into young adulthood and of adult cancer survivors into middle age (8). In these studies, substantial impact has been demonstrated (6). A recent study followed middle-aged breast cancer survivors an average of 6.3 years postdiagnosis and noted high levels of function and quality of life, though those who had received adjuvant chemotherapy had significantly worse quality of life, including physical function, than those who had not (28).

Our study indicates that, for older cancer survivors, neither the previous diagnosis of cancer nor the length of time since diagnosis is associated with the level of functional status. On the other hand, the presence of comorbidity does affect function. It is well established that in the general population, the presence of comorbid conditions is associated with a decrease in function (29,30), but the specific influence on function in cancer survivors has not been well established.

Previous studies assessing the function of older cancer patients in relation to comorbidity have done so in the context of cancer under active treatment (30–34). For example, in a sample of 203 older cancer patients, Extermann found that comorbidity correlated poorly with functional status and concluded that functional status and comorbidity both need to be assessed in older cancer patients, not substituted one for the other (34). Satariano demonstrated that, while women aged 55–64 with breast cancer had more trouble in the 3 months after diagnosis with upper body activities such as pushing, lifting, and reaching, the 75–84-year-olds did not have any more trouble with upper body tasks than did the controls in their age group. The researchers attributed this to a preexisting level of disability in the older women. These results demonstrate that a diagnosis of cancer may not actually confer as much disability to older women as to younger women (35). However, the older women both with and without cancer may have had disability conferred by some preexisting illness that may nevertheless have been amenable to treatment. Moreover, in older breast cancer patients, comorbidities appeared to act synergistically with the cancer to adversely affect survival (35).

Our study expands on prior knowledge of functional status in older cancer patients by demonstrating a clear correlation between comorbidity and function in older cancer survivors who participated in a large population-based study. We have demonstrated that the association between comorbidity and function is the same for older cancer survivors as it is for the general older population. In our study, the group of participants who had been diagnosed with cancer more than 15 years ago were older than any other group, which made it important to control for factors such as age and cognitive impairment in our analyses.

There are some limitations to our study. One is that cancer type and time of diagnosis were determined by self-report at the time of the in-person interview. In a study of 170 hospital inpatients age 50 and over, Katz and colleagues found that determining comorbidity by questionnaire is a reliable and valid alternative to chart review (37). Bergmann and colleagues demonstrated that self-report accuracy for diagnoses leading to hospitalization was not generally age dependent, and that for breast cancer and heart disease, self-reporting accuracy was high, whereas for stroke, prostate, lung, and colon cancer, it was moderate (38). Estimates of sensitivity of self-report of cancer in a registry-documented cancer from a study of the 63,582 participants of the Cancer Prevention Study II Nutrition Survey ranged from 0.79 for exact matches of type to 0.93 for positive report of cancer regardless of type (39). Participants with breast, prostate, lung, and colon cancer had a high sensitivity of exact matches between self-reported cancer type and presence in the registry; these 4 were the most commonly reported cancers in our study. While self-report may not be the ideal form of ascertaining cancer diagnosis, these other studies indicate that self-report of cancer is valid, especially for determining if cancer was present or not.
In general, our participants reported a broad variety of cancer types, but the numbers in each individual group were too small to analyze how function might differ according to cancer type. Given and colleagues have demonstrated differences in function based on cancer type and treatment type in active cancer patients (33). Patients with lung cancer had the lowest level of physical function, while patients with breast and colon cancer had intermediate levels of function, and patients with prostate cancer had the highest average level of physical functioning. In general, patients who underwent surgery or received chemotherapy reported lower levels of physical functioning than those who did not receive these treatments.

Our cross-sectional study includes people who have survived cancer for varying lengths of time and does not capture people with severe advanced cancer. This study contains only those who have lived with their cancer. Thus, there is a survivor bias, since we cannot provide information on those people who died and what their functional impairments may have been (e.g., perhaps those who died had experienced a combined effect of cancer and comorbidity on function). Another limitation is that we are limited to analyzing only a small number of comorbidities that were specifically asked about in the EPESE questionnaire.

Our finding that the level of functional impairment experienced by elderly cancer survivors depends on the level of comorbidity present reminds us that despite, or perhaps because of, surviving cancer into older age, such patients require continued, careful assessment for the impact of common medical problems and functional issues that occur in that setting. Management of these issues remains an important consideration for the older cancer survivor (40).

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