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Motivation and mortality in older women with early stage breast cancer: A longitudinal study with ten years of follow-up

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ABSTRACT

Objectives: The Getting Out of Bed Scale (GOB) was validated as a health-related quality of life (HRQoL) variable in older women with early stage breast cancer, suggesting its potential as a concise yet powerful measure of motivation. The aim of our project was to assess the association between GOB and mortality over 10 years of follow-up.

Materials and Methods: We studied 660 women ≥ 65 -years old diagnosed with stage I–IIIA primary breast cancer. Data were collected over 10 years of follow-up from interviews, medical records, and death indexes.

Results: Compared to women with lower GOB scores, women with higher GOB had an unadjusted hazard ratio (HR) of all-cause mortality of 0.78 at 5 years, 95% confidence interval (CI) (0.52, 1.19) and 0.77 at 10 years, 95%CI (0.59, 1.00). These associations diminished after adjusting for age and stage of breast cancer, and further after adjusting for other HRQoL variables including physical function, mental health, emotional health, psychosocial function, and social support. Unadjusted HRs of breast cancer-specific mortality were 0.92, 95%CI (0.49, 1.74), at 5 years, and 0.82, 95%CI (0.52, 1.32), at 10 years. These associations also decreased in adjusted models.

Conclusion: Women with higher GOB scores had a lower hazard of all-cause mortality in unadjusted analysis. This effect diminished after adjusting for confounding clinical and HRQoL variables. GOB is a measure of motivation that may not be independently associated with cancer mortality, but reflects other HRQoL variables making it a potential outcome to monitor in older patients with cancer.

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1. Introduction

The number of cancer survivors is expected to grow to 19 million by January 2024, contributed by advances in detection and treatment as well as an aging population [1]. About 40% of new breast cancer diagnoses occur in those ≥ 65 years old, and these patients comprise the majority of breast cancer deaths and current breast cancer survivors [2]. Among the challenges of caring for older patients with cancer is appropriately balancing treatment outcomes, such as survival, with health-related quality of life (HRQoL) [3]. There is growing evidence that HRQoL in patients with cancer of all ages is not only an important outcome in itself but also a predictor of mortality [4–7].

Motivation plays an important role in an older patient's ability to overcome illness and stay engaged with healthy behaviors. Clough-Gorr et al. developed and validated a measure of motivation called the "Getting-Out-of-Bed (GOB) Scale" in a large cohort of older patients

with early stage breast cancer [8]. GOB was shown to correlate with several other HRQoL measures such as mental health and physical functioning, however GOB predicted certain outcomes and behaviors, such as participating in regular exercise, that were not predicted by HRQoL. Their results suggested that GOB reflects aspects of motivation potentially relevant to health behaviors and outcomes that overlap conceptually with, but are not entirely captured by, HRQoL. Measures similar to motivation, such as optimism and hope, have been linked to both disease-specific and all-cause mortality [9–11]. However, GOB's ability to predict mortality, either independently or in association with HRQoL, has yet to be studied.

In this secondary analysis of the same cohort of older women with early stage breast cancer studied by Clough-Gorr et al., we assessed the association between GOB and 5- and 10-year mortality, both all-cause and breast cancer-specific (BC-specific). We hypothesized that higher GOB scores would be associated with lower all-cause and BC-specific mortality. Moreover, we hypothesized that GOB would independently predict mortality, and included potential confounding clinical and HRQoL variables in our analysis to test this hypothesis. Fig. 1 summarizes these hypothesized relationships: HRQoL measures have

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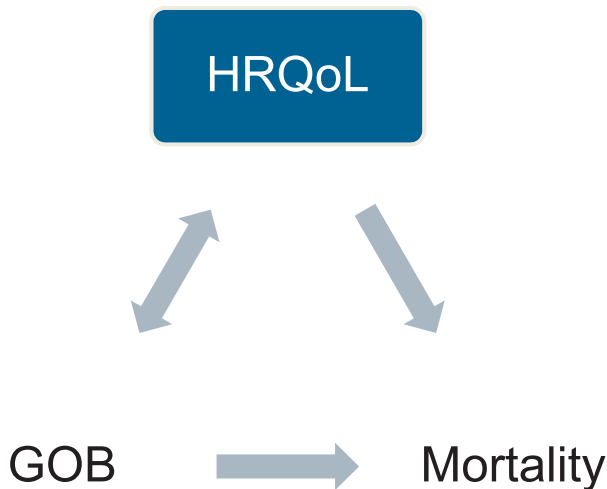


Fig. 1. Hypothesized relationships among Getting Out of Bed (GOB), health-related quality of life (HRQoL) variables, and mortality.* *GOB affects mortality and is associated with HRQoL, which also affects mortality. Therefore, any observed effect GOB may have on mortality might in fact be due to its association with HRQoL [12]. This confounding situation can be solved by adjusting for HRQoL, such that GOB is an independent predictor for mortality.

a direct effect on mortality and are associated with GOB. Knowledge of HRQoL will therefore allow an investigation into whether GOB has an independent effect on mortality [12].

2. Materials and Methods

2.1. Study Population

The longitudinal study design and subject recruitment procedures have been reported previously [13]. In brief, 660 women ≥ 65 -years old with stage I tumor diameter ≥ 1 cm or stage II–IIIA disease and permission from attending physicians to be contacted in four geographic regions (Los Angeles, California; Minnesota; North Carolina; Rhode Island) were identified through regular pathology report review at hospitals or collaborating tumor registries. Women could not have a prior primary breast cancer or simultaneously diagnosed or treated second primary tumor. Data were collected by medical record review (definitive surgery date, surgery type, tumor characteristics) and telephone interviews (socio-demographic, HRQoL variables, breast cancer therapy) beginning at least three-months after surgery and continuing annually for 10 years. Causes of death – characterized as breast cancer-specific, all-cause, all-cancer-related – were collected through 10 years of follow-up.

2.2. Mortality, All-cause and Breast Cancer-specific

Decedents were identified by first and last name, middle initial, Social Security number, date of birth (DOB), sex, race, marital status, and state of residence matched against National Death Index (NDI) and Social Security Death Index (SSDI) records [14]. Survival status at the end of 2007 was complete for all women.

2.3. Socio-demographic Characteristics

We classified patient age as 65–69, 70–79, ≥ 80 -years; race as white, other; education as < 12 -years, 12-years, > 12 -years; and marital status as married (yes/no).

2.4. Breast Cancer Characteristics

We categorized stage as I–III using the TNM classification [15]. Definitive primary therapy was mastectomy plus axillary lymph node dissection (ALND) or breast-conserving surgery (BCS) plus ALND.

2.5. Getting Out of Bed (GOB)

GOB (Table 1) consists of four items scored on an ordinal scale of 1 to 5. The language used in these items was intended to be straightforward using concepts and terms universally understood at a layperson's level of understanding. GOB total score is calculated as an equally weighted sum of items (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent) giving a total score range from 4 to 20. The final score is transformed to 0–100, with a higher score indicating greater motivation [8].

2.6. Health-related Quality of Life Characteristics

To further evaluate an independent association between GOB and mortality, we studied other HRQoL measures as potentially confounding variables in adjusted analyses, including physical function, general mental health, emotional health, psychosocial function, and social support. Physical function has been linked to mortality in older patients with cancer [7,16]. Moreover, physical function has been shown to be associated with other measures similar to motivation [8,17–19]. We calculated physical function using the 10-item Physical Function Index (PFI-10) from the Medical Outcomes Study Short Form-36 (MOS SF-36) [20]. PFI-10 specifically has previously been linked to mortality in men and women [21,22]. Mental health has also been linked to survival in both older and younger patients with cancer [23,24]. Furthermore, mental health has been shown to be associated with GOB and other measures similar to motivation [8,25–27]. General mental health was assessed by the Mental Health Index (MHI-5), a five-item measure of mental health from the MOS-SF-36 [20]. MHI-5 specifically has been linked to mortality in patients with cancer and in other populations [14,28,29].

Emotional health, psychosocial function, and social support have all been associated with measures similar to motivation [8,30,31]. Breast cancer-specific emotional health (BCSEH) was assessed using a four-item measure reflecting how well the respondent was dealing with breast cancer-specific worries [32]. We used the Psychosocial Summary Scale of the 17-item Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) to capture cancer-specific psychosocial function [33]. The CARES-SF item scores range from 1 to 4 (a higher score indicating more problems). Social support is related to survival in patients with breast and other cancers [34,35]. Social support was measured using a reduced set of eight items derived from the 19-item MOS Social Support Scale (mMOS-SS) [36].

All of the above HRQoL measures were transformed to a 0–100 score, with higher scores indicating better physical function, mental health, emotional health, social support, and psychosocial function, respectively.

2.7. Statistical Methods

The study population was described by counts, percentage (%), mean, standard deviation (SD), median, and interquartile range (IQR). We used Spearman's rank correlation coefficient as an estimate of correlation. Mortality rates were calculated by the number of events divided by the total person-years under observation. We used Multiple Imputation (MI) to address missing baseline data, using a fully conditional specification approach [37]. We assumed missing data to be missing at random (MAR) [38]. In addition to variables used in the main analysis model, including GOB, age, stage of breast cancer, PFI-10, MHI-5, BCSEH, CARES-SF, and mMOS-SS, we used enrollment site, education, number of comorbidities, body mass index, type of therapy, tamoxifen prescribed, recurrence of breast cancer, and received chemotherapy in

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