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Original article

Quality of life among a population-based cohort of older patients with breast cancer

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ABSTRACT

Background: Growing numbers of older women receive adjuvant breast cancer therapies, but little is known about the long-term effects of current therapies upon health-related quality of life outside of clinical trials.
Methods: A population-based cohort of postmenopausal women with incident breast cancer aged sixty-five and older was identified from Medicare claims from four states and followed over five years. General health-related quality of life (HRQOL) was assessed using the Medical Outcomes Study SF-12 Health Survey, and breast cancer-related HRQOL was assessed using the breast cancer subscale of the functional assessment of cancer therapy (FACT-B BCS). The association of HRQOL with sociodemographic variables, comorbidity, and breast cancer variables (stage, treatments, and treatment sequelae) was examined in longitudinal models.
Results: Among the 3083 older breast cancer survivors, general HRQOL as measured by SF-12 mental and physical component scores was similar to norms for non-cancer populations, and remained stable throughout follow-up. Breast cancer treatments, including surgery and radiation, adjuvant hormonal therapy, and cytotoxic chemotherapy were not associated with worsened general health scores. A similar pattern was seen for breast cancer-related HRQOL scores, except that chemotherapy was associated with slightly worse scores. Lymphedema occurred in 17% of the cohort, and was strongly associated with all measures of HRQOL. Reductions in general HRQOL with lymphedema development were larger than those with an age increase of 10 years.
Conclusions: There is little association of breast cancer treatment with HRQOL in older breast cancer patients followed for up to five years, but the development of lymphedema is associated with substantial reductions in HRQOL.

Introduction

Breast cancer treatment advances have contributed to increases in survival – from 76% five-year survival in 1976 to 90% in the 2000s [1] – but many of these treatments have potential long-term adverse effects. Randomized trials suggest that treatment-related reductions in long-term health-related quality of life (HRQOL) are rare, but these studies have important limitations [2]. Only 5% of women enroll in breast cancer trials, and those women are substantially younger, have less comorbidity and higher functional status than those treated outside of trials [3]. Many trials cannot follow patients long enough to assess outcomes like congestive heart failure that can substantially impact quality of life [4,5]. Finally, for ethical reasons, many trials compare newer with older treatment regimens, and are therefore unable to directly assess reductions in HRQOL with newer therapies [6,7].

Trial reports regarding breast cancer therapies and HRQOL also appear to conflict with longer-term population-based studies from the 1990s [8]. In particular, two large, population-based cohort studies from that era reported early HRQOL reductions with chemotherapy or tamoxifen [9,10] and one of them subsequently

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reported reductions that persisted for 5–10 years [11]. Another more recent body of literature suggests an important role for lymphedema or upper extremity symptoms in reducing HRQOL [12–15] but these studies have limitations. Most were small or single center, unable to examine lymphedema in concert with nonsurgical treatments, or had cross-sectional designs [8]. One large population-based study [12] examined a large number of patients treated in the 1980s and earlier 1990s when extensive axillary radiation and surgery techniques resulted in higher lymphedema risk and potentially worse lymphedema symptoms. Finally, a number of studies have examined depression, anxiety, and measures of emotional distress after cancer [10,11,16–30]. Several studies showed that most patients improved substantially by 2–8 years, resulting in average HRQOL scores among survivors that were no different than general population norms, but most either studied patients treated in the early 1990s or drew from randomized trials or other select populations [10,11,17–21,30].

It is particularly important that HRQOL after newer therapies be examined for older patients. Few women over 65 have been enrolled in clinical trials of chemotherapy, yet its use in this group more than doubled by the end of the 1990s. Several SEER-Medicare analyses demonstrating that chemotherapy improves survival among these older women [31,32] are likely to further support that trend. Aromatase inhibitor use has also increased rapidly among patients substantially older than those in trials [33,34]. Older women on average have more comorbidities and functional limitations, which might either predispose to or magnify the adverse effects of any therapy. However, even if this is true, the degree to which adverse treatment effects differentially impact long-term HRQOL for older patients is not clear. Literature from non-cancer populations shows that older patients may have enhanced emotional regulation and other strategies for coping with losses [35–37]; consistent with that possibility a study of older breast cancer patients treated in the early 1990s showed minimal reductions in several measures of emotional well-being [38].

We sought to determine whether there are reductions in HRQOL among older patients who received newer breast cancer therapies. We examined both general and breast cancer-specific HRQOL among a large population-based cohort of older 2003 breast cancer survivors who received a range of contemporary surgical, radiation, and adjuvant treatments. We hypothesized that tamoxifen, aromatase inhibitors and chemotherapy would be associated with decreased HRQOL, as would lymphedema. We report HRQOL results at three points in time during five years after breast cancer surgery.

Materials and methods

The data source for the study was the National Cancer Institute-funded "Improving the Care and Outcomes of Women Undergoing Breast Surgery" study [39]. The initial cohort for this population-based longitudinal survey consisted of 3083 community-dwelling breast cancer patients sixty-five and older with incident breast cancer in 2003, and was designed to obtain information on health outcomes of breast cancer care. It was conducted in four states – California, Florida, New York, Illinois – selected for their geographic and racial/ethnic diversity. All survey data was supplemented with tumor stage information from state cancer registries as well as follow up Medicare data through 2008.

Details of the study procedures are provided in Nattinger et al. [39]. In brief, all female state residents ≥65 who had surgery for incident breast cancer in 2003 in the four states were identified using a validated algorithm from Medicare claims [40]. Women were ineligible for the study if they had a diagnosis of dementia or in a long-term care facility. All potentially eligible participants were contacted by mail in 2005 and provided written consent, and the first of four annual telephone surveys was conducted between fall 2005 and summer of 2006. The final survey was performed a median of 60 months after subjects' surgical date.

As reported, participation in the initial survey was 70%, and respondent demographics differed slightly though significantly from non-respondents by age and race/ethnicity. By 60 months, 310 women from the initial cohort had become ineligible because of death or nursing home entry, 172 could not be reached, and 129 refused (90% participation rate among eligible patients) [39]. The Medical College of Wisconsin Institutional Review Board and the CMS Privacy Board approved the study protocol.

Variable definitions

Outcomes

The primary outcomes in this study were measures of health-related quality of life as assessed using two widely used, validated instruments. The first instrument, the 12-item Medical Outcomes Study (MOS) Short Form Survey (SF-12), is a validated questionnaire that uses Likert-scaled responses to assess general health-related quality of life [41]. It is highly correlated with the longer MOS SF-36 [41,42], and has been used in both epidemiologic studies and randomized trials. The SF-12 was scored using published algorithms [41] to convert the survey responses to the Physical Component Summary (PCS-12) and the Mental Component Summary (MCS-12). For each 0-100 summary score, a higher score represents better HRQOL. To allow comparisons between the two scores and between our cohort and other populations, they were standardized using norm-based (1998 US population) methods [41].

The second instrument was the breast cancer subscale (BCS) of the functional assessment of cancer therapy-breast quality of life instrument (FACT-B). The FACT-B BCS includes nine items regarding bother or worry about cancer and symptoms over the previous seven days, and has had extensive reliability and validity testing [43]. It uses Likert-scaled responses from 0 ("not at all") to 4 ("very much"). Scores ranged from 0 to 36, with higher scores corresponding with worse HRQOL. Our analysis is based on longitudinal assessment of HRQOL using these two instruments at three points in time: roughly 30 months post-incident breast surgery (first survey), 48 months post-surgery and 60 months post-surgery.

Independent variables

Independent variables were factors that previous research suggested might be associated with breast cancer survivors' HRQOL [44]. These were drawn from three major categories: sociodemographics, comorbid conditions, and breast cancer variables (breast cancer stage, breast cancer treatments, and major breast cancer treatment sequelae).

Most sociodemographic variables (race/ethnicity, education, and household income) were provided by respondents on the initial survey. Marital status was assessed on each survey. Information on age and state of residence at each survey was derived from Medicare enrollment files. The presence and number of comorbid conditions was derived from Medicare inpatient, outpatient and Carrier claims for the period one year before each survey [45].

The Surveillance, Epidemiology and End Results (SEER) stage was obtained from the four North American Association of Central Cancer gold-standard state tumor registries. Breast cancer treatments including type of breast cancer surgery (mastectomy or breast-conserving surgery), extent of axillary surgery (none, sentinel lymph node biopsy [SLNB], or full axillary lymph node dissection with or without SLNB [ALND]), receipt of radiation therapy and receipt of cytotoxic chemotherapy were identified from Medicare claims [46]. Adjuvant hormonal therapy was based

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