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REVIEW

Survivorship issues in older breast cancer survivors

Steven S. Coughlin[1,2] · Raheem J. Paxton[3] · Nicole Moore[4] · Jessica Lynn Stewart[4] · Judith Anglin[4]

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Abstract

Purpose Almost half of breast cancer survivors are aged ≥ 65 years and the proportion is likely to increase due to the aging of the population. The objectives of this article were to review studies of health outcomes among older breast cancer survivors ≥ 65 years to identify gaps in the published literature and offer suggestions for future research.

Methods The present review is based upon bibliographic searches in PubMed and CINAHL and relevant search terms. Articles published in English from January 1, 1970 through October 1, 2018 were identified using the following MeSH search terms and Boolean algebra commands.

Results This review has revealed that older breast cancer survivors cope with health issues related to cancer treatment and the aging process, including comorbidities, osteoporosis, symptoms, physical functioning, cognitive functioning, nutrition, and physical activity.

Conclusions Additional research is needed to examine therapeutic interventions to address the health conditions older breast cancer survivors are coping with. Particular focus of further research should be on the nutritional status and physical activity levels of older breast cancer survivors. Individualized nutrition plans and tailored physical activity programs for older survivors are needed that meet people where they are and that form habits.

Keywords Breast cancer survivors · Cognition · Comorbidity · Diet · Nutrition · Osteoporosis · Physical activity · Quality of life

Introduction

There are currently about 2.5 million breast cancer survivors in the U.S. and many of them are elderly [1]. The median age of breast cancer diagnosis in women is 62 years [2]. Women ≥ 65 years of age comprise 55% of breast cancer survivors in the U.S. [3]. Almost 19,000 breast cancer deaths occur annually in women 70 years and older, accounting for approximately 47% of all breast cancer deaths in the U.S. [4], but over half of older breast cancer patients die of other causes [5, 6].

Breast cancer patients cope with many side of effects and symptoms, not only during cancer treatment but after remission that impacts quality of life [7, 8]. Common side effects of breast cancer treatment include lymphedema, loss of strength, and sexual dysfunction [9]. However, symptoms such as sleep disturbances, cognitive impairment, depression, fatigue, and pain may persist for years after survivors are in remission [10–12]. Breast cancer survivors also experience comorbidities in addition to secondary malignancies that include cardiovascular disease, obesity, osteoporosis, injuries through falls, and bone fractures. Lastly, when compared to age-matched controls, survivors also experience declines in physical function, and other conditions that affect physical and emotional well-being [13, 14].

In this article, we review studies of health outcomes among older breast cancer survivors aged 65 years or older.

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✉ Steven S. Coughlin
scoughlin@augusta.edu

[1] Department of Population Health Sciences, Medical College of Georgia, Augusta University, 1120 15th Street, Augusta, GA 30912, USA

[2] Research Service, Charlie Norwood Veterans Administration Medical Center, Augusta, GA, USA

[3] Department of Community Medicine and Population Health, University of Alabama, Tuscaloosa, AL, USA

[4] Department of Interdisciplinary Health Studies, College of Allied Health Sciences, Augusta University, Augusta, GA, USA

We identify gaps in the published literature and offer suggestions for future research about the health of older breast cancer survivors.

Methods

The present review is based upon bibliographic searches in PubMed and CINAHL and relevant search terms. Articles published in English from January 1, 1970 through October 1, 2018 were identified using the following MeSH search terms and Boolean algebra commands: breast cancer survivors AND (elderly OR older). The searches were not limited to words appearing in the title of an article nor to studies in a particular country or geographic region of the world. The references of review articles were also reviewed. Information obtained from bibliographic searches (title and topic of article, information in abstract, study design, and key words) was used to determine whether to retain each article identified in this way. Only studies written in English that examined the impact of breast cancer survivorship care plans on health outcomes were eligible for inclusion. A total of 4359 article citations were identified in PubMed and non-duplicates in CINAHL. After screening the abstracts or full texts of these articles and reviewing the references of previous review articles, a total of 50 studies met the eligibility criteria (Fig. 1).

Comorbidities

The majority of older breast cancer patients have at least one comorbidity [15]. Common comorbidities include cardiovascular disease and obesity. Multiple comorbidities can result in poorer functional status and health outcomes [16–18]. Bellury et al. [19] in a study of breast cancer survivors aged 70 years and older found that comorbidities were strongly associated with lower physical function. In a study of older breast cancer survivors, Winters-Stone et al. [20] found that comorbidities, symptom severity, and fatigue explained 17.3–33.1% of the variance across physical function measures. However, there is still some uncertainty as to whether cancer survivors experience more comorbidities than controls. For example, in a sample of older early-stage breast cancer survivors and age-matched controls, Jordan et al. [21] found that breast cancer survivors were not more likely to acquire comorbidities (HR 1.0, 95% CI 0.93–1.1) than controls. In subsequent analyses of these data, incident comorbidities were associated with a higher mortality rate (HR 4.8, 95% CI 4.1–5.6). In a cohort study of older breast cancer survivors, survivors experienced a 40% higher all-cause mortality hazard for each unit increase in the Charlson Comorbidity Index [22] after controlling for prevalent comorbidities at baseline [23].

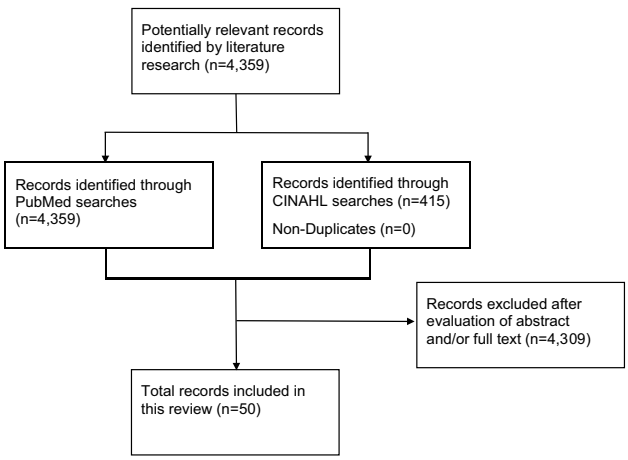

Fig. 1 Flowchart of record selection process

Bone mineral density, osteoporosis, and fractures

Adjuvant hormonal therapy and chemotherapy-induced amenorrhea can cause a rapid loss in bone mineral density, leading to osteoporosis and fractures [24]. Women receiving treatment for breast cancer can lose 2–8% of their bone mineral density each year [25–27]. In a study of older breast cancer survivors and controls, Peppone et al. [24] found that breast cancer survivors had a higher prevalence of osteoporosis (adjusted OR 1.32, 95% CI 1.08–1.61) compared to controls. Up to 80% of breast cancer patients experience cancer treatment-induced bone loss [13, 28]. Preventive measures such as vitamin D and exercise can delay bone loss if instituted early on [24].

Breast cancer patients have a higher rate of falls compared to women who are cancer-free [29, 30]. Due to bone loss and falls, breast cancer patients have a fivefold increase in fracture risk compared to women without cancer [31, 32]. In cancer patients undergoing chemotherapy, muscle weakness is an independent predictor of falls [33]. Huang et al. [34] found that the adjusted prevalence of balance/walking problems is higher after cancer treatment than it is prior to diagnosis. Haung et al. [25] also found that self-reported falls within the past year was about 26%. A history of falls (odds ratio [OR] 4.95, 95% CI 2.44–10.04) and sensory impairment in feet (OR 3.33, 95% CI 1.51–7.32) were significant predictors of falls. However, it should be noted that not all studies have found significant differences between breast cancer survivors and controls. Pawloski et al. [35] found no difference in fracture rates between groups (HR 1.1, 95% CI 0.9–1.3).

Adjuvant hormonal therapy

In a study of older breast cancer survivors with ≤ stage 2 disease, Bluethmann et al. [36] found that 43% discontinued adjuvant hormonal therapy before 5 years. Those who reported lower cognitive function in the period prior to discontinuation had greater hazards of discontinuing therapy. In a separate study of the same cohort, Sheppard et al. [37] found that frail women were more likely (OR 1.63, 95% CI 1.11–2.40) to not initiate adjuvant hormonal therapy than robust (non-frail) women. The risk of discontinuation of hormonal therapy was higher with increasing age and lower for stage ≥ IIB than for stage I. Arthralgias are common side effects experienced by women treated with adjuvant endocrine therapy [38].

Symptoms and symptom clusters

Older breast cancer survivors experience multiple symptoms that appear to cluster [39]. These symptoms may be late effects of cancer, cancer treatment, or just a part of the normal aging process and chronic illness [40]. Roiland and Heidrich [39] in a sample of older breast cancer survivors identified seven clinically distinct symptom clusters involving 36 different symptoms. The symptom clusters were significantly related to quality of life. In a study of overweight breast, colorectal, and prostate cancer survivors, Kenzik et al. [41] found that symptom severity, weight loss, and physical activity were significantly associated with lower overall physical functioning scores ($\beta = -0.63$, $p < 0.001$). Similarly, Bellury et al. [19] found that high levels of symptom bother (the extent to which symptoms cause worry, annoyance, or discomfort for a patient) were strongly associated with lower physical function.

Physical functioning and frailty

Physical functioning in older breast cancer survivors has been found to decline following treatment [16, 33, 42]. Decline in physical functioning after breast cancer diagnosis has been associated with decreased 10-year survival in older women [43]. Derks et al. [16] examined physical functioning in older breast cancer patients using prospective data from the TEAM Trial. Among patients treated with breast surgery and adjuvant hormonal therapy, age 70 years and older was independently associated with functional decline 1–2 years after diagnosis ($p = 0.028$). Leach et al. [42] studied breast, prostate, lung, and colorectal cancer survivors who were Medicare beneficiaries and matched controls. All cancer groups demonstrated significant ($p < 0.05$) declines in physical functioning, and all exceeded the minimally important difference in mean physical function over time in comparison with the controls. In a study of breast cancer survivors aged 65 years or older, Clough-Gorr et al. [44] found that women with persistent lymphedema consistently reported poorer physical function.

In a case–control study of estrogen receptor-positive breast cancer survivors on adjuvant aromatase inhibitors 1–2 years post surgery and age-matched controls, Extermann [33] found that grip strength, physical performance, and long-distance walking speed were similar between the two groups. However, self-reported physical function was marginally lower in cases than controls. Declines in physical functioning are of concern because of the consistent association with inability to perform activities of daily living, which is a potential threat to independent living among older breast cancer patients. Physical activity's positive effect on muscular strength and balance may prevent functional decline [41].

Frailty and pre-frailty are not uncommon in older breast cancer survivors and may occur at an earlier age than in women without a history of cancer [45]. Frailty is a common clinical syndrome in older adults that carries an increased risk for poor health outcomes including falls, incident disability, hospitalization, and mortality. Frailty is a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems. Frailty has been operationally defined by Fried et al. [46] as meeting three out of five phenotypic criteria indicating compromised energetics: low grip strength, low energy, slowed waking speed, low physical activity, and/or unintentional weight loss. A pre-frail stage, in which one or two criteria are present, identifies a subset at high risk of progressing to frailty.

In a study of breast cancer survivors aged 53–87 years, Bennett et al. [45] found that 18% of breast cancer survivors aged 70–79 years were frail, compared to 11% of women in the Cardiovascular Health Study and Women's Health and Aging Study. Higher body mass index increased the odds of frailty (OR 1.12, $p = 0.003$).

Cognitive function

Accelerated cognitive decline and memory problems have been associated with exposure to chemotherapy. In a study of older breast cancer survivors, Dura-Ferrandis [47] found accelerated decline in cognitive function in 7.6% of the women. Levkovich et al. [48] found that older breast cancer survivors aged 60–82 years reported lower levels of cognitive difficulties than younger breast cancer survivors aged 24–59 years. In a cohort study of older (> 70 years) and younger patients (50–69 years) with breast or colorectal cancer stage I–III, Deckx et al. [49] found that over the course of 1 year following a diagnosis of cancer, the older cancer patients faced increasing difficulties in cognitive functioning ($p < 0.01$).

Health-related quality of life

Health-related quality of life (HRQOL) encompasses multiple domains of well-being including physical function and mental health. Higher social support has been associated with better psychological adjustment to cancer and higher quality of life [47]. In a cohort study of women aged 65 years or older with early-stage breast cancer, DuMontier et al. [50] found that HRQOL predicts 10-year morality independently of prognostic variables. Dura-Ferrandis [47] examined quality-of-life trajectories in a sample of older breast cancer survivors. Three trajectories were identified for each quality-of-life domain. Accelerated decline in emotional and physical function was observed in 6.9% and 31.8% of the women, respectively. Jones et al. [51] examined depression and quality of life before and after breast cancer diagnosis in older women from the Women's Health Initiative. Compared with pre-cancer levels, depressive symptoms increased, while physical function and mental health decreased in the first year after diagnosis ($p < 0.01$). Depressive symptoms returned to pre-cancer levels after 10 years but quality of life remained significantly lower.

Therapy for older women with breast cancer has been found to influence HRQOL in some studies [52], but not others [53]. In a study of women aged 67–87 years, Swanick et al. [52] found that less irradiation and less surgery were associated with better long-term quality-of-life outcomes. In contrast, in a study of breast cancer survivors aged 65 years or older, Neuner et al. [53] found that HRQOL was similar to that seen in non-cancer populations. Breast cancer treatments (i.e., surgery and radiation, adjuvant hormonal therapy, and cytotoxic chemotherapy) were not associated with worsened HRQOL. However, the development of lymphedema was associated with substantial reductions in HRQOL [53].

Surveillance mammography

There is limited evidence about the benefits of annual mammography surveillance in older breast cancer survivors with limited life expectancy, and there are important risks [54]. Surveillance mammography is conducted to detect possible breast cancer recurrence. In a non-randomized cohort study of breast cancer survivors aged 65 years or older, Buist et al. [55] found a modest reduction in breast cancer-specific mortality with receipt of surveillance mammography in the preceding year (incident rate ratio 0.82, 95% CI 0.56–1.19, $p = 0.29$). Lash et al. [56] studied stage I and II breast cancer patients aged 65 years or older at six health care delivery systems. One hundred seventy-eight women died of breast cancer during 5 years of follow-up. Each additional surveillance mammogram was associated with a 0.69-fold decrease in the odds of breast cancer mortality (95% CI 0.52–0.92).

Once a breast cancer is diagnosed, current guidelines encourage annual surveillance mammography for all patients with residual breast tissue and do not specifically tailor follow-up strategies [57, 58]. Freedman et al. [54] offered guidance on how clinicians should approach surveillance mammography in older breast cancer survivors while taking into account life expectancy and patient preferences.

Freedman et al. [5] found that 56.7% and 65.9% of those with estimated life expectancy of ≤ 5 and ≤ 10 years, respectively, reported mammography in the past year. Conversely, about 14.1% of those with life expectancy > 10 years did not report mammography in the past year. Massimino et al. [59] studied ductal carcinoma in situ or invasive breast cancer survivors aged 80 years and older who underwent surgery for at a single institution. Patients had a median of four follow-up mammograms. The 1466 mammograms detected 17 biopsy-proven cancers and generated 18 benign biopsies. In the 305 women who had had breast-conserving surgery, 18 (5.9%) experienced local recurrence, 9 detected by mammography alone, and 9 palpable. Overall, 13 non-palpable breast cancers were detected.

Nutrition and physical activity

Physical inactivity and excessive weight gain following treatment increases risk of breast cancer recurrence, other chronic diseases, and all-cause and breast cancer-related mortality [60, 61]. However, in the Women's Healthy Eating and Living (WHEL) trial, over the mean 7.3-year follow-up period, a diet very high in vegetables, fruit, and fiber and low in fat was not associated with decreased risk of an invasive breast cancer event (adjusted hazard ratio 0.96, 95% CI 0.80–1.14, $p = 0.63$) [62]. Eating a healthy diet that includes adequate fruits and vegetables, whole grains, and little or no red meat protects against several chronic diseases. Consuming an unhealthy diet and physical inactivity increase risk of obesity and non-breast cancer mortality [9]. Poor diet also increases risk of fatigue.

There is little published research on the diet and nutrition of older breast cancer survivors. The majority of observational studies and randomized controlled trials on diet and nutrition have focused on breast cancer survivors < 65 years of age or have not explored age-differences. A majority of older breast cancer survivors take supplements such as multivitamins [63]. Malnutrition is a prevalent complication of cancer and a risk factor for adverse outcomes such as poor treatment response, reduced survival, and impaired quality of life [64]. Malnutrition in the elderly is associated with other geriatric syndromes including functional dependence, decreased cognitive function, and depression [65]. Malnutrition is more common after 70 years of age, when intakes of protein and nutrients are frequently inadequate [66]. Several age-related conditions increase the risk of malnutrition

including oral and dental disorders and eating dependency [64, 67].

Exercise can lower circulating levels of estrogen and potentially reduce tumor proliferation. Physical activity has been associated with improved quality of life in older breast cancer survivors [68–70]. Only about one-third of breast cancer survivors engage in the recommended level of physical activity and less than 18–37% consume the recommended amounts of fruits and vegetables [61]. Demark-Wahnefried et al. [71] in Leading the way in Exercise and Diet found that a physical activity and dietary intervention could improve lifestyle behaviors and prevent functional decline in older cancer survivors. In a cohort study of 533 women aged 65 years or older with breast cancer, Reeves et al. [72] found that the risk of mortality was 1.4 times higher for a body mass index of 27.3 kg/m^2 (95% CI 1.03–2.01) and 2.4 times higher for a body mass index of 34.0 kg/m^2 (95% CI 1.07–5.45) compared with women with a BMI of 22.6 kg/m^2. Maliniak et al. [73] studied 4226 women aged 65 years or older with local or regional breast cancer. Pre- and post-diagnosis body mass index was associated with a higher risk of breast cancer-specific mortality (pre-diagnosis, hazard ratio [HR] 1.27, 95% confidence interval [CI] 1.14–1.41; post-diagnosis, HR 1.19, 95% CI 1.04–1.36). Neither pre- nor post-diagnosis physical activity was associated with breast cancer-specific mortality. Body mass index and physical activity were both significantly associated with all-cause mortality.

Conclusions

The older breast cancer survivor has ongoing health issues that seem to be a combination of side effects of treatment and the aging process. This population has unique needs that are worthy of further research to aid these people in coping with these health conditions. The research on health outcomes in this population is limited, but shows increased prevalence of some conditions. Several conditions that are higher in this population can result in poorer functional status and higher mortality risk. Additional concerns for the older population are ability to perform activities of daily living and quality of life, which can also be impacted by health issues of the breast cancer survivor. Several comorbidities and symptoms experienced by older breast cancer survivors can be treated and prevented with lifestyle, diet, and exercise interventions.

Addressing nutrition and physical activity may impact the health conditions experienced by older breast cancer survivors and promote better health outcomes in this population [74]. Development of the best nutrition and physical activity tailored to the older breast cancer survivor is warranted to improve health outcomes. Additional research is needed to examine the nutritional status and physical activity levels of older breast cancer survivors, according to age and stage at cancer diagnosis. Tailored physical activity programs for older survivors are needed that meet people where they are and that form habits. Rather than advocating for exercise at recommended levels, increasing light intensity physical activity and reducing sedentary time could provide initial efficacy beliefs to get cancer survivors moving.

Older breast cancer survivors have health impacts from the cancer treatment and the aging process. To improve these health conditions, functional status, and quality of life, consideration should be given to diet and exercise therapies as a component of survivorship care. Further research is needed to determine the extent of lifestyle therapy for older breast cancer survivors. Diet and exercise should be tailored to the individual to aid in improving functional status and quality of life.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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