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EPIDEMIOLOGY

Survivorship care visits in a high-risk population of breast cancer survivors

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Abstract

Purpose Breast cancer survivors face numerous challenges after diagnosis and treatment. Several models have been developed to attempt to improve quality of care. Here, we describe characteristics and outcomes of patients who participated in survivorship visits (SV) at Johns Hopkins (JH).

Methods We retrospectively reviewed charts of breast cancer patients who participated in an optional SV 1–3 months after completing locoregional therapy and initial systemic therapy. We report patient demographics, comorbidities, tumor characteristics, treatments, and responses to symptom questionnaires. We compared the characteristics of SV participants to stage I–III analytical cases in the 2010–2015 JH Cancer Registry (JHCR).

Results We identified 87 women with stage I–III breast cancer who participated in SVs from 2010 to 2016. Compared to patients in the JHCR ($n=2942$), SV participants were younger, more likely to be African American and more likely to have a higher TNM stage, hormone receptor-negative disease, and HER2-positive disease. They were more likely to have received chemotherapy and radiation therapy. They also have similar recurrence rates despite the SV cohort's shorter median follow-up time. Among SV participants, the prevalence of comorbidities including peripheral neuropathy, anemia, lymphedema, anxiety, deep vein thrombosis, and depression increased significantly from time of diagnosis to most recent follow-up.

Conclusions Compared to the JHCR cohort, SV participants had higher risk cancers and a high frequency of comorbidities potentially associated with breast cancer and therapy. These high-risk patients may benefit most from specific interventions targeting survivorship care, and their experiences may help improve care delivery models.

Keywords Breast cancer · High-risk · Survivorship · Survivorship visits

Introduction

Breast cancer survivors are the largest subgroup among the growing number of cancer survivors worldwide [1]. Many face ongoing challenges after diagnosis and treatment, including management of treatment-related toxicities, fear of recurrence, and difficulties with resumption of personal and professional obligations. A 2006 Institute of Medicine (IOM) report recognized the difficulties experienced by cancer survivors and proposed standardizing practices for survivorship care to improve patient education and to facilitate communication between cancer and non-cancer care providers in order to encourage health promotion and care coordination [2].

The cornerstone of the 2006 IOM report was the recommendation that all cancer survivors receive a survivorship care plan (SCP), which includes a treatment summary and a

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plan for follow-up care to be provided to both the patient and her primary care provider. SCPs quickly became a standard requirement for cancer program accreditation by the American College of Surgeon's Commission on Cancer [3]. However, attempts to broadly implement SCPs have faced resistance. Initial target goals for SCP delivery were set at 10% of eligible patients by January 2015, 50% by January 2017 and 75% by January 2018 [3], but surveys described that no more than 20–30% of programs were confident or able to achieve those targets, and the targets have since been revised. Barriers to provision of SCPs include time, lack of role clarity with providers, inadequate reimbursement, and limited evidence on their effectiveness [4]. A systematic review of prospective studies and randomized trials evaluating SCPs demonstrated high levels of patient satisfaction and self-reported understanding, but no significant effect on distress, care satisfaction, care coordination, or cancer outcomes [5]. As such, survivorship groups have worked to develop unique programs tailored to their population's needs such as a one-time visit to discuss survivorship concerns. While various models of care delivery continue to be tested, data on the impact of survivorship care on patient-reported outcomes, including physical, emotional, and social measures, are still limited [6–8].

In 2008, we established a breast cancer survivorship program at Johns Hopkins (JH) and in 2010, we began offering a one-time survivorship visit (SV) with a breast cancer nurse practitioner to patients completing local therapy and initial systemic therapy for early stage breast cancer (usually within 6–12 months of diagnosis) [9]. At these visits, patients completed questionnaires to assess ongoing symptoms and to screen for depression and anxiety. They also received a SCP to be shared with their other healthcare providers. SCPs included a treatment summary containing (1) information regarding completed and ongoing therapy and on toxicities and comorbidities that might impact long-term care, and (2) recommendations for cancer surveillance, new cancer screening, and general health maintenance measures [9, 10].

In our study, we evaluated a retrospective cohort of JH breast cancer patients, primarily those who received adjuvant chemotherapy and were subsequently referred by their medical oncology providers for a single SV. We describe patients' demographic data, tumor characteristics, treatment modalities, and survival data. Finally, we summarize patients' persistent symptoms identified at the SV as well as comorbidities at the time of breast cancer diagnosis and at most recent follow up.

Methods

We retrospectively reviewed the charts of a cohort of patients who participated in a 60- to 90-min SV at JH medical oncology clinics at the JH Hospital or at JH Green Spring Station from January 2012 through December 2016. SVs were conducted by one of two nurse practitioners after referral by patients' medical oncology providers and occurred about 1–3 months after completion of locoregional therapy and initial systemic therapy. To obtain data, each patient chart was accessed once between December 2016 through February 1, 2017. Data from three time points were collected: (1) at the time of diagnosis, (2) at the SV, and (3) at the most recent follow-up. Characteristics of SV participants were compared to stage I-III analytical cases in the 2010–2015 JH Cancer Registry (JHCR).

Participant characteristics collected include (time point being at most recent follow-up unless otherwise noted): age (at time of diagnosis), race and ethnicity, insurance, marital status, employment status, menopausal status (at time of diagnosis), parity, body mass index (at the time of diagnosis, SV and most recent follow-up), family history, comorbidities (at the time of diagnosis and most recent follow-up), and genetic counseling and testing. We retrospectively calculated patients' Charlson Comorbidity Index (CCI) [11] at time of diagnosis and at most recent follow-up. Cancer characteristics collected included stage at diagnosis and tumor phenotype. Treatment data collected included participation in surgery, radiation, and systemic therapy. Survival data collected at most recent follow-up included vital status, cancer status, time from diagnosis to survivorship visit, time from diagnosis to most recent recorded follow-up, and use of a palliative care consult. For patients alive at the end of the follow-up period, survival data were administratively censored on February 1, 2017.

Questionnaires administered at the SV included a locally developed patient symptom questionnaire, the generalized anxiety disorder 7-item scale (GAD-7) [12], and the patient health questionnaire (PHQ-9) [13]. The results of these questionnaires were available for 66 of 87 patients. Of those 66 patients, 7 left some questions blank on the patient health questionnaire. For the 21 patients for whom questionnaires were not available, it is likely they completed the questionnaire but it was not uploaded to chart and/or paper copies were not saved. For the symptom questionnaire, patients used a 4-item Likert scale ranging from none to severe to rate their concerns in the following areas: musculoskeletal pain, mobility, neuropathy, fatigue, sleep difficulty, memory decline, hot flashes, menstrual cycle pattern, sexuality, vaginal dryness, fertility, weight changes, inability/difficulty working, and difficulty with family/relationships.

We used descriptive statistics to describe our data. Rank sum testing was used to compare the median age of the patients in the two cohorts and chi-squared testing was utilized to compare categorical variables (e.g., race, stage, node positive disease, etc.) between the two cohorts. p-values were considered significant if less than 0.050. This study was approved by the Johns Hopkins Institutional Review

Board (IRB Number: NA_00079523) with informed consent obtained from each participant or each participant's guardian.

Results

Patient demographics

We collected data from 87 women with early-stage breast cancer (stages I-III) who participated in a SV between January 2012 and December 2016 (Table 1). Median age was 53 (IQR 43, 65). Most were Caucasian (62%) or African American (33%), married (64%), employed (66%), had children (84%), and had private insurance (74%). By comparison, patients in the JHCR ($n = 2942$) had a median age of 55 (IQR 46, 65). Most were Caucasian (71%) or African American (22%), were married (56%), and had private insurance (53%), with no data regarding employment or parity. The populations did not differ substantially in any demographic characteristics, except for race and that the SV cohort was more likely to be married and have known private insurance (Table 1).

Patient family history

Family history and germline mutation results were available for the SV cohort. Thirty percent of patients had a first-degree family member age 50 or younger with a history of breast cancer, 7% had a first-degree family member with a history of ovarian cancer, and 9% were Ashkenazi Jewish. Fifty-seven patients (66%) were referred for genetic counseling. Among 42 patients who had germline testing, five had a *BRCA1* mutation, one had a *BRCA2* mutation, and one had a *PALB2* mutation.

Cancer characteristics, therapy received, and outcomes

When compared to the JHCR cohort (Table 2), SV participants had a higher TNM stage and were more likely to have node-positive, triple negative, or HER2 -positive disease. SV participants were also more likely to have hormone receptor-negative disease. Half of the SV participants were post-menopausal at diagnosis (unknown in JHCR cohort). All SV participants had breast surgery and more patients in the SV cohort had chemotherapy and radiation therapy. Overall, 95% of the SV cohort and 89% of the JHCR cohort were alive at a median follow-up of 29 and 42 months, respectively ($p < .001$), and a similar number had a recurrence (13% vs. 8%) (Table 2).

Comorbidities and symptoms in the SV cohort

Comorbidity data were available for 86 of 87 SV cohort patients. Median BMI remained stable from diagnosis (28.9 kg/m^2) to SV (28.5 kg/m^2); however, 41.5% of all patients in the SV cohort and 48% of African American patients in the SV cohort had a BMI of 30 kg/m^2 or higher at diagnosis (Table 1). Median Charlson Comorbidity Index (CCI) at diagnosis was 0 (IQR 0, 1). Among the 77 who remained disease-free, the median CCI at most recent follow-up was 2 (IQR 2, 3), which was not significantly different. There was a significant increase in the prevalence of peripheral neuropathy, anemia, lymphedema, anxiety, depression, and deep vein thrombosis from diagnosis to most recent follow-up (Table 3). While the CCI represents diagnoses of specific problems, the patient questionnaires allow symptom description of specific problems. Among 65 patients who completed the GAD7 and PHQ9 at their SV, the median GAD-7 score for anxiety was 4 ("none") with an IQR of 1 ("none") to 7 ("mild"), and the median PHQ-9 score for depression was 3 ("minimal") with an IQR of 1 ("minimal") to 6 ("mild"). Commonly reported symptoms at the time of the SV included fatigue (78%), sleep difficulty (70%), numbness or tingling (62%), weight changes (62%), muscle aches (59%), and pain (50%) (Table 4).

Discussion

In our study, we characterized a cohort of patients referred by their medical oncology providers for a SV after completion of locoregional and initial systemic therapy. Our SV cohort was younger and more likely to self-identify as African American than the non-SV cohort. The SV participants had few medical comorbidities at diagnosis (median Charlson Comorbidity Index of 0), but were more overweight than cancer survivors at large. SV participants also reported a high prevalence of comorbidities and complications from cancer and its treatment, including a high prevalence of peripheral neuropathy, anemia, hypertension, gastrointestinal disorders, anxiety, and depression and commonly report persistent symptoms like fatigue, sleep difficulty, numbness or tingling, weight changes, muscle aches, and pain. In particular, the rates of anxiety (33%) and depression (24%) in our SV cohort are higher than the estimated prevalence of anxiety (17.9%) and depression (11.6%) in the general cancer survivor population, not limited to breast cancer survivors [14]. Altogether, our data suggest that our SV cohort is a population of breast cancer survivors with high-risk tumors treated with combined modality therapy. Post treatment, they have a high frequency of specific comorbidities and persistent symptoms. Overall, this supports the IOM

Table 1 Participant demographics in the SV cohort ($n=87$) as compared to the breast cancer registry

	Survivorship cohort ($n=87$), N (%)		Breast cancer registry ($n=2942$), N (%)	p-value
Age at diagnosis				0.1395
Median (IQR)	53 (43, 65)		55 (46, 65)	
20–39	12 (13.8)		299 (10.16)	
40–49	25 (28.7)		690 (23.45)	
50–59	22 (25.3)		794 (26.99)	
60–69	16 (18.4)		704 (23.93)	
70+	12 (13.8)		455 (15.47)	
Race				0.041
Caucasian	54 (62.07)		2074 (70.50)	
African-American	29 (33.33)		653 (22.20)	
Other	4 (4.6)		215 (7.31)	
Hispanic/Spanish origin				0.550
Yes	3 (3.45)		57 (1.94)	
No	84 (96.55)		2878 (97.82)	
Unknown			7 (0.24)	
Insurance status				<0.001
Private	64 (73.56)		1565 (53.20)	
Public	22 (25.29)		741 (25.19)	
Insured but not specified	0 (0)		465 (15.81)	
Uninsured	1 (1.15)		37 (1.26)	
Unknown	0 (0)		134 (4.55)	
Marital status				<0.001
Married	56 (64.37)		1658 (56.36)	
Living with partner	1 (1.15)		0 (0)	
Separated/divorced	8 (9.20)		288 (9.79)	
Widowed	10 (11.49)		232 (7.89)	
Single	11 (12.64)		380 (12.92)	
Unknown	1 (1.15)		384 (13.05)	
Employment status*				
Employed	57 (65.62)			
Retired	21 (24.14)			
Other	6 (6.9)			
Children*				
Yes	73 (83.91)			
No	12 (13.79)			
Unknown	2 (2.30)			
Body mass index*	At diagnosis	At SV ($n=84$), N		
Underweight (<18.5)	3 (3.7)	1 (1.2)		
Normal (18.5–24.9)	21 (25.6)	27 (32.1)		
Overweight (25–29.9)	24 (29.3)	23 (27.4)		
Obese, class 1 (30–34.9)	22 (26.8)	21 (25.0)		
Obese, class 2 (35–39.9	6 (7.3)	7 (8.3)		
Obese, class 3 (>39.9)	6 (7.3)	5 (6.0)		

Statistics for age determined by two-sample Wilcoxon rank-sum (Mann–Whitney) test. For all others, Pearson χ^2 test

*Employment status, children, and BMI data were not available from the Breast Cancer Registry

Table 2 Cancer characteristics and treatments in the SV cohort compared to the breast cancer registry

	Survivorship cohort ($n=87$), *N* (%)	Breast cancer registry ($n=2942$), *N* (%)	*p*-value
Menopausal status at diagnosis			
Yes	44 (50.57)		
No	40 (45.98)		
Unknown	3 (3.45)		
Stage			< 0.001
I	23 (26.44)	1433 (48.71)	
II	42 (48.28)	1075 (36.54)	
III	22 (25.29)	434 (14.75)	
Node status			< 0.001
Positive	52 (59.77)	983 (33.41)*	
Negative	35 (40.23)	1848 (62.81)	
Unknown	0 (0)	111 (3.7)	
Hormone receptor status			< 0.001
Positive	49 (56.32)	2146 (72.94)	
Negative	38 (43.68)	539 (18.32)	
Unknown	0 (0)	257 (8.74)	
Her2 receptor status			< 0.001
Positive	33 (37.93)	406 (13.80)	
Negative	54 (62.07)	2113 (71.82)	
Unknown	0 (0)	423 (14.38)	
Initial treatment			0.009
Surgery	52 (59.77)	1766 (60.03)	
Chemotherapy	35 (40.23)	928 (31.54)	
Started at same time	0 (0)	248 (8.43)	
Total who underwent surgery	87 (100)	2511 (86.23)	< 0.001
Type of Surgery			0.481
Mastectomy	48 (55.17)	1283 (51.10)	
Breast-conserving	39 (44.83)	1228 (48.90)	
Surgery of unknown type	0 (0)	26 (0.89)	
Chemotherapy	82 (94.25)	1255 (42.66)	< 0.001
Radiation	68 (78.16)	1580 (53.70)	< 0.001
Hormone therapy			
Of total cohort	52 (59.77)	1749 (59.45)	0.952
Of hormone receptor positive patients	47 (95.92)	1689 (78.70)	0.488
Vital status			0.062
Alive	83 (95.40)	2622 (89.12)	
Dead	4 (4.60)	320 (10.88)	
Current cancer status			
Disease free	76 (87.4)	2499 (84.9)	0.534
Recurrence	11 (12.6)	235 (8.2)	0.141
Unknown	0 (0)	208 (6.9)	
Months from DX to most recent follow-up		$n=2935$	
Median (IQR)	29 (21, 43)	42 (24, 61)	< 0.001
Months from DX to visit			
Median (IQR)	11 (9, 14)	N/A	

Statistics for age determined by Pearson χ^2 test

DX diagnosis, *N/A* not applicable/available

*Positive nodes include pN: p1 = 687 (23.3%), p2 = 202 (6.9%), p3 = 94 (3.2%)

Table 3 Comorbidities at diagnosis and at most recent follow-up among SV patients who never developed metastases ($n=76$*)

	At diagnosis, *N* (%)	At most recent follow-up, *N* (%)	*p*-value
Peripheral neuropathy	6 (8)	54 (71)	< 0.001
Anemia	12 (16)	37 (48)	< 0.001
Hypertension	29 (38)	32 (42)	0.250
Gastrointestinal disorders	22 (29)	27 (36)	0.063
Anxiety	11 (14)	25 (33)	< 0.001
Elevated cholesterol	18 (24)	22 (29)	0.125
Lymphedema	0 (0)	20 (26)	< 0.001
Thyroid problems	14 (18)	19 (25)	0.063
Arthritis	14 (18)	18 (24)	0.125
Depression	9 (12)	18 (24)	0.004
Deep venous thrombosis	6 (8)	12 (16)	0.031
Asthma	7 (9)	7 (9)	1.000
Diabetes without complications	6 (8)	8 (10)	0.500
Chronic pulmonary disease	5 (7)	7 (9)	0.500
Gastrointestinal bleed	2 (3)	7 (9)	0.063
Congestive heart failure	0 (0)	5 (7)	0.063
Secondary cancers	1 (1)	1 (1)	1.000

Statistics for percentage with a particular comorbidity at diagnosis and at most recent follow-up compared using the sign binomial test

*For 1 patient no comorbidity data were available

Table 4 Patient symptom questionnaire ($n=66$*) responses by SV cohort with symptoms categorized as none, mild, moderate, or severe

Symptom	None, *N* (%)	Mild, *N* (%)	Moderate, *N* (%)	Severe, *N* (%)
Fatigue	14 (22)	36 (56)	11 (17)	3 (5)
Sleep difficulty	20 (30)	24 (36)	15 (23)	7 (11)
Weight changes	25 (38)	21 (32)	16 (25)	3 (5)
Numbness or tingling	25 (38)	20 (31)	15 (23)	5 (8)
Muscle aches	27 (41)	21 (32)	16 (24)	2 (3)
Pain	32 (50)	20 (31)	7 (11)	5 (8)
Weakness or decreased mobility	34 (53)	19 (30)	9 (14)	2 (3)
Hot flashes	37 (58)	13 (20)	10 (16)	4 (6)
Only patients pre-menopausal at DX	26 (79)	4 (12)	3 (9)	0 (0)
Memory decline	38 (58)	20 (30)	5 (8)	3 (5)
Menstrual changes	39 (80)	2 (4)	4 (8)	4 (8)
Only patients pre-menopausal at DX	24 (100)	0 (0)	0 (0)	0 (0)
Vaginal dryness	40 (63)	12 (19)	8 (13)	3 (5)
Sexuality changes	41 (69)	7 (12)	8 (14)	3 (5)
Difficulty working	43 (72)	10 (17)	4 (7)	3 (5)
Difficulty with family relations	53 (82)	7 (11)	4 (6)	1 (2)
Fertility concerns	54 (95)	2 (4)	1 (2)	0 (0)

*For 21 patients no questionnaire data were available

conclusions that survivors face a large number of issues after completing initial treatments.

Our data come at an important moment in the history of survivorship care as the selection of optimal models of care delivery is in flux. Care models that rely on one or more encounters with a dedicated provider are costly, difficult to sustain, and may not fully meet the diverse needs of survivors. Thus, it is necessary to develop solutions that can be integrated in electronic health record systems to help identify patients for such interventions. While cancer survivors undergoing SCPs may not as a whole derive improved outcomes, such as significantly improved mortality,

management of treatment complications, and improved care coordination and compliance [5, 6, 15], individual groups, like those with poorer mental health and physical functioning and lower-than-average quality of life, may benefit from targeted interventions [7, 16, 17]. Minority groups are more likely to experience greater morbidity and worse outcomes including those regarding physical and quality of life [1, 18–21]. In fact, there are data showing improved outcomes of focused interventions in specific at-risk populations. For example, in low-income, predominantly Latina survivors with stage 0 to III breast cancer a randomized controlled trial showed that a SCP with or without a nurse counseling session that focused on discussing three individualized survivorship goals and role play of how to discuss this with their primary physician, led to greater patient-reported physician implementation of and patient adherence to recommended cancer survivorship care (such as management of treatment complications). Of note, this was positively associated with improved satisfaction with care and information [22]. As our cohort also appears to have a high prevalence of poor physical and psychosocial outcomes, we may have identified a population who might benefit more from such individualized, in-depth interventions.

Going forward, this knowledge may allow better allocation of resources for the care of cancer survivors. Future studies should focus on standardizing the process of SVs in addition to defining more objective criteria to identify patients at risk who might benefit from such specific interventions. We will assess the effect of SVs on improving care coordination, compliance with health care maintenance (including monitoring for recurrence), and management of treatment complications. Additionally, we hope to improve SV outcomes by identifying patients experiencing psychological distress or comorbidities that could be targeted with specific interventions, recognizing that these goals may require follow-up survivorship visits dedicated to these outcomes. Improving metrics for evaluating the short and long-term impact of such outcomes will also help to streamline the system. However, the optimal timing for such interventions still needs to be determined.

Our study has limitations. First, our study was not designed to assess the effectiveness of survivorship visits. The retrospective nature of our study may also have resulted in an incomplete assessment and underestimation of comorbidities. Despite SVs being a unique experience tailored to the needs and experience of each patient, all SVs were conducted by the same two mid-level providers to reduce variability. Additionally, there is referral bias given oncology providers selected who to refer based on gestalt.

In summary, our study offers one of the first descriptive analyses of survivorship visits, including detailed information on demographics and persistent cancer-related symptoms. Altogether, our data suggest that our SV cohort is a population of breast cancer survivors with high-risk tumors, who receive more therapy and have a high risk of comorbidities and complications. Thus, we expect that a more systematic screening of higher risk patients would enrich for patients more likely to benefit from individualized interventions, particularly those that impact patient satisfaction, knowledge, and management of complications and recurrence. Our long-term goal is to inform the design and delivery of breast cancer survivorship care models, with a potential focus on one-on-one interventions limited to patients who may face a higher risk of short and long-term complications from their disease and have greater barriers toward resumption of personal, family, and professional activities. We hope such models will allow for more streamlined and effective use of health care resources.

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Compliance with ethical standards

Conflict of interest SS, JS, NZ, CR, JR, KCS, and AC declare no conflicts of interest. CS receives funding from Genentec. KLS receives funding from the National Comprehensive Cancer Network and Pfizer. VS receives funding from Pfizer, Novartis, Medimmune, Puma, and AbbVie.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Human and animal rights This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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