Comparison of younger and older breast cancer survivors and age-matched controls on specific and overall QoL domains

Victoria L. Champion, PhD[1], **Lynne I. Wagner, PhD**[4], **Patrick O. Monahan, PhD**[1], **Joanne Daggy, PhD**[1], **Lisa Smith, MS**[1], **Andrea Cohee, BSN, RN**[1], **Kim W. Ziner, PhD**[1], **Joan E. Haase, PhD**[1], **Kathy Miller, MD**[1], **Kamnesh Pradhan, MD**[1], **Frederick W. Unverzagt, PhD**[1], **David Cella, PhD**[4], **Bilal Ansari, MD**[5], and **George W. Sledge Jr, MD**[2]

[1]Indiana University, Indianapolis, Indiana

[2]Stanford University, Stanford, California (current location), Indiana University, Indianapolis, Indiana (former location)

[3]Memorial Hospital of South Bend, South Bend, Indiana

[4]Northwestern University, Chicago, Illinois

[5]Northern Indiana Cancer Research Consortium, South Bend, Indiana

Abstract

Background—Younger survivors (YS) of breast cancer often report more survivorship symptoms *such as fatigue, depression, sexual difficulty, and cognitive problems than older survivors (OS). We* sought to determine the effect of breast cancer and age at diagnosis on Quality of Life (QoL) by comparing 3 groups: 1) YS diagnosed at age 45 or before, 2) OS diagnosed between 55 and 70, and, 3) for the YS, age-matched controls (AC) of women not diagnosed with breast cancer.

Methods—Using a large Eastern Cooperative Oncology Group (ECOG) data base, we recruited 505 YS who were ages 45 or younger when diagnosed and 622 OS diagnosed at 55 to 70. YS, OS, and AC were compared on physical, psychological, social, spiritual, and overall QoL variables.

Results—Compared to both AC and to OS, YS reported more depressive symptoms (p=.005) and fatigue (p<.001), poorer self-reported attention function (p<.001), and poorer sexual function (p<.001) than either comparison group. However, YS also reported a greater sense of personal growth (p<.001) and perceived less social constraint (p<.001) from their partner than AC.

Conclusions—YS reported worse functioning than AC relative to depression, fatigue, attention, sexual function, and spirituality. Perhaps even more important, YS fared worse than both AC and OS on body image, anxiety, sleep, marital satisfaction, and fear of recurrence, indicating that YS are at greater risk for long term QoL problems than survivors diagnosed at a later age.

Corresponding author: Victoria Champion, PhD, Indiana University School of Nursing, 1111 Middle Drive, NU 318, Indianapolis, IN 46202, Telephone: 317-274-4187, Fax: 317-278-2021, vchampio@iupui.edu.

Keywords

Young survivors; Quality of Life; Breast Cancer; Comparison of Younger; Comparison of Older Survivors

Introduction

With earlier diagnosis and better treatment options, the population of breast cancer survivors in the United States is now estimated to be over 2.7 million, and most can expect to live a full life.[1] The average age of diagnosis is 61; however, a significant number of women are diagnosed at a younger age.[2] Survivorship research has described the physiological, psychological, and social distress caused by a breast cancer diagnosis, but most studies have focused on survivors who have recently completed treatment.[3,4] Quality of life (QoL) problems persist long after treatment and diagnosis, and research is needed to better understand problems faced by long-term survivors. Additionally, emerging research indicates these persistent problems may be different or more severe in YS than OS.[5] Current research on YS is limited by small sample sizes,[5,6] making interpretation of results difficult. Finally, current research is limited by the lack of comparison groups of young age-matched women without breast cancer.

Symptoms such as psychological distress, pain, fatigue, depression, sleep difficulties, and anxiety have been well-documented among breast cancer survivors. However, YS seem to experience more declines in health-related quality of life (HRQOL) than OS.[6–8] Compared to AC, YS report more cognitive problems as well as sexual difficulty, depression, and fatigue.[3,4,6,9] As a group, increased symptomatology by YS may be related to experiencing an abrupt menopause.[10] Menopause may also result in infertility at a time when survivors still desire children.[4] Over 50% of survivors who experience early menopause suffer from one or more symptoms that can affect sexual functioning, including hot flashes, vaginal dryness, loss of libido, and night sweats resulting from lack of estrogen.[11,12]

Studies have compared YS to AC or YS to OS, but have not simultaneously compared YS to AC and OS within one study using a common methodology and measurement. Comparison of YS to AC can inform us of problems that are related to breast cancer diagnosis and treatment, whereas comparison to YS to OS can identify symptoms that may differentially impact YS. Identifying unique problems associated with diagnosis of breast cancer at a younger age will allow researchers and clinicians to identify potential problems when breast cancer is diagnosed, thereby intervening to decrease or eliminate long-lasting morbidities.

The purpose of this study was to improve our understanding of unique survivorship issues facing YS by comparing them with both AC and OS. We recruited large samples from each of these three cohorts and applied the same assessment methods for all groups. Collaborating with the Eastern Cooperative Oncology Group (ECOG), we accrued a sample of 505 YS, 622 OS, and 404 AC who were age-matched to the YS cohort. We selected both YS and OS who were 3 to 8 years from diagnosis and without recurrence of breast cancer to investigate QoL problems that may linger over time. Constructs identified for this study included five QoL domains based on the theoretical work of Ferrell and colleagues: 1)

physical, 2) psychological, 3) social, 4) spiritual, and 5) overall QoL.[13] We sought to identify the degree to which a diagnosis of breast cancer at a young age (< 45 years) accounted for particular physical, psychosocial, social, spiritual, and overall QoL factors. We addressed this question by comparing YS to AC and OS. All analyses controlled for significant demographic and treatment variables.

Method

Sample

Eligible breast cancer survivors treated on previous ECOG clinical trials at one of 97 ECOG sites were identified using the ECOG statistical center database. Eligibility criteria included being age 45 or younger or 55–70 at initial diagnosis, being 3 to 8 years from diagnosis without a recurrence, and being treated with a similar chemotherapy regimen that included Adriamycin, Pacitaxel, and Cyclophosphamide. The 10-year gap between age groups ensured distinct, nonoverlapping groups. We sought to identify YS who were premenopausal, thus using the age criterion of 45 or younger. Eligible women in the AC group were age-matched to the YS and had not been diagnosed with breast cancer.

Procedures

The ECOG Statistical Center generated a list of eligible patients by selecting YS who had been treated on 1 of 5 clinical trials (C9741, E1199, E2197, E2198, N9831) or at ECOG sites and who were 3–8 years post-diagnosis. Once sites provided ECOG with confirmation of local IRB approval, sites were given lists of eligible women treated at their center. The treating oncologists or their designee asked the breast cancer survivor for permission to have Indiana University researchers contact them. If survivors gave permission for contact, the identifying information for each survivor was sent to researchers. A brochure explaining the study was mailed to the survivor prior to contact. Research assistants called survivors 1 week following this initial mailing to answer any questions and determine interest in participation. For survivors who agreed to be enrolled, an information packet, informed consent form, and HIPAA form were mailed with postage-paid return envelopes. If consents were not returned within 2 weeks, participants were called and, if necessary, mailed a second consent. When not initially reached by phone, 10 attempts were made at varying times of day. If a participant could not be reached by phone and did not return the consent, she was deleted from the data base. A total of 744 eligible YS were contacted, 86% consented, and 67% (n=505) completed data collection. A total of 937 OS were contacted, 68% consented, and 66% (n=491) completed data collection.

YS were asked to supply the names and contact information of 3 women who were within 5 years of their own age and without a diagnosis of breast cancer to be used as age-matched controls. The process for consenting AC was identical to the process for survivors. The AC were age-matched, within 5-year age intervals, to YS. Out of 1013 AC, 466 (46%) agreed to participate and 404 (40%) completed the questionnaires.

Both women who were currently in a partnered relationship and those who were not were included in the study. Four scales required a partnered relationship, including marital

satisfaction, sexual functioning, social support, and social constraint. Nonpartnered women were instructed to leave these scales blank. Thus, analyses that included partnered variables had a smaller sample size.

Measures

Socio-demographic variables (age, race, education, marital status, occupational status, and insurance status), as well as medical history (cancer history and treatment, cancer stage, gynecological history, and presence of other diagnosed health conditions) and current use of estrogen blockers, were collected through self-report and medical records. Comorbidity was measured as the sum of reported comorbid conditions such as arthritis, heart disease, hypertension, and others. Patient-reported outcomes were used to assess physical, psychological, social, and spiritual functioning as well as overall quality of life.

Physical Health—Physical health functioning was measured by the *Short-Form Health Survey (SF-36)*.[14] Fatigue was measured by the *Functional Assessment of Cancer Therapy Fatigue Subscale (FACT–F)*, a 13-item instrument.[15] Sleep was measured by the *Pittsburgh Sleep Quality Index (PSQI)*, a 19-item self-report questionnaire commonly used to measure sleep quality and disturbance.[16] *The Attention Function Index* was used to measure participants' perceived cognitive functioning.[17] Internal consistency coefficients were reported for this instrument of 0.84 in a sample of women with breast cancer and 0.89 in a sample of healthy controls.

Psychological Indices—Depression was measured by the *CES-D*, an instrument with 20 items that measure the presence and severity of depressive symptomatology.[18] Anxiety was measured by the *State-Trait Anxiety Inventory (STAI)*. This scale has 40 items with higher scores indicating more anxiety.[19] Body image was assessed by 8 investigator-developed items to measure the degree to which a participant is satisfied with her body. In this study the instrument had a Cronbach alpha of .89. Two other measures within the psychological domain were the Post-Traumatic Growth Inventory(PTGI),[20] whose internal consistency was .94, and the Impact of Event Scale-Revised (IES-R),[21] whose internal consistency was .91. Fear of Recurrence was measured by the Concerns about Recurrence Scale (CARS), developed specifically for breast cancer survivors and having a Cronbach alpha of .97 in this sample.[22]

The IES measures symptoms resulting from exposure to a stressful event such as hyperarousal, intrusion, and avoidance. The PTGI was developed to measure positive coping outcomes reported by persons who experience a traumatic event. AC were instructed to complete the IES and PTGI by recalling a traumatic event that had occurred in the past 5 years such as the loss of loved one, major relationship change, serious personal illness, or loss of job. A higher score on both scales is reflective of greater positive growth.[20]

Social Indices: Measures of social variables included scales for social support, social constraint, marital satisfaction, and sexual functioning. The *Northouse Social Support Scale* was used to assess perceived support from a partner.[23] The *Lepore Social Constraint Scale* was used to measure social constraint.[24] Marital satisfaction was measured by the *Marital*

Satisfaction Scale (ENRICH MSS), a 15-item scale with extensive reported validity and reliability.[25] Sexual function data were measured by a scale that consists of two components:1) sexual enjoyment and 2) sexual functioning.[26]

Spiritual Indices

The Reed Spiritual Perspective Scale (SPS) measured spirituality and consisted of 12 items related to subjects' spiritual views and their participation in spiritually related activities.[27]

Overall QoL

Overall QoL was measured using the Index of Well-Being (IWB),[28] which measures life satisfaction and subjective well-being.[18] The Cronbach alpha was .91 in this sample.

Statistical Analysis

Statistical analysis was performed using SAS V9.3.[29] Using ANCOVA, we compared YS to AC, as well as YS to OS, on all domains theoretically identified, adjusting for demographic variables as potential confounders. Both unadjusted and adjusted p-values (using the false discovery rate method) were computed.[30] Demographic covariates used with ANCOVA models are listed in a footnote of Table 2.

Results

A sample of 505 YS were compared to both AC (n=404) and OS (N=622). YS were between 23 and 45 at initial diagnosis, and current age was between 28 and 54. As can be seen on Table 1, both YS and OS were predominately White and had mean educational levels of 14.8 and 14.1 years, respectively.. More YS were in a committed relationship (83.6%) than OS (75.3%) or AC (77.7%). Both YS and OS had a higher percentage of Catholic Christians than AC. Differences in menstrual status, hot flashes, and co-morbidities are also reported in Table 1. A total of 76% of YS reported having the same partner as when they were diagnosed. Most survivors indicated that their relationship had gotten better (49%) or stayed the same (42%), with only a few reporting it was worse (9%). A total of 47% of survivors had had a lumpectomy and 53% a mastectomy. Almost 75% of women indicated their periods had stopped and only 15% reported regular cycles. Of those whose periods had stopped, 43% indicated it was due to breast cancer treatment and 29% due to hysterectomy. Many YS (63%) reported having hot flashes and 96% of these survivors reported that the hot flashes bothered them. A total of 14% reported that breast cancer had prevented them from having desired children. An estrogen blocking medication such as Tamoxifen was used by 40% of YS and 52% of OS. Three women in the AC group reported use of an estrogen-blocking medication, probably as a preventive measure because they were at high risk.

Adjusted QoL differences among YS, AC, and OS

Comparisons among groups are reported in Table 2. For analyses requiring a partnered relationship, the sample size was 1039 (YS n = 399; AC n = 291; OS n = 349). Analyses not including partner-related variables yielded a larger sample size (n= 1322). YS experienced greater fatigue (p<.0001), poorer attention function (p<.001), and worse sexual function (p<.001).

Younger survivors reported more depression than AC (p<.001). A total of 27% of younger survivors were over the cutoff score for likely clinical depression, whereas only 18% of OS and 17% of AC reported scores of 16 or above. Younger survivors also reported less spirituality than AC (p<.04). YS reported more social support from their partner (p<.05) and less social constraint (p<.001) than AC, as well as scoring significantly better on the post-traumatic growth inventory (p<.001), which reflects perceived benefits from the cancer experience, and on the Impact of Events Scale (p<.001).

YS reported greater fatigue (p<.001), poorer sleep (p<.001), less perceived attention function (p<.001), and poorer overall sexual functioning (p<.001). Nearly one-half of YS (48%) reported decreased sexual interest, decreased arousal (44%), decreased lubrication (52%), decreased orgasm (38%), decreased frequency (41%), decreased ability to relax (41%), and decreased fantasies (41%). A total of 41% of YS indicated their sexual relationship had changed for the worse and 40% that their sexual enjoyment had decreased.

Younger survivors experienced significantly more anxiety than OS as measured by both State and Trait anxiety (p<.001). YS had poorer body image, (p<.001), more depressive symptoms (p<.001), greater fear of recurrence (p<.001), and lower levels of spirituality (p<.001) than OS.

For measures requiring partners, YS reported less social support (p<.001), more social constraint (p<.01), and less marital satisfaction (p<.001). Additionally, perceived benefit from the cancer experience was less in YS than OS. For the Impact of Events scale, higher scores are reflective of greater overall difficulty. Scores on the Impact of Events scale were significantly higher for YS than OS (p<.001) on every dimension, indicating that YS perceived greater difficulty. For overall QoL as measured by the Index of Well-Being, YS scored relatively lower. (p<.001).

Discussion

Comparison of YS to AC

Overall, 27% of YS scored at or above the clinical cutoff for likely depression compared to 17% for their age-matched group, a difference reported in past research.[4,31,32] Many studies have found that breast cancer survivors at diagnosis and treatment have high rates of depression and that as many as 25% of survivors suffer depression five years from treatment, a finding consistent with our results.

YS reported more menopausal symptoms than AC including more hot flashes. Many survivors reported use of Tamoxifen or Aromatase inhibitors, which block estrogen and thus increase the likelihood of problems with vaginal lubrication or even sexual desire.[33] We compared YS currently taking an anti-estrogen with those not on this medication but did not find significant differences. An obvious problem of premature menopause for YS is infertility, a concern often mentioned.[4] A total of 16% of our YS reported that breast cancer prevented them from having additional desired children. Although we controlled for menopausal status, these differences remained, requiring additional analyses that might suggest possible causes of sexual dysfunction. Because menopausal status can influence

many QoL variables, we compared women who had had periods within the last 12 months with women who had not. All tests were completed using multiple comparisons and p <.01 was the criterion for significance. Several significant differences were found. Fear of recurrence was less in women who were post-menopausal. Post-menopausal women had worse reported physical function, worse sleep, worse sexual functioning, better scores on finding meaning within life, more social support, and less social constraint, and they perceived a greater impact of events.

Compared to AC, YS reported less sexual interest, decreased arousal, decreased lubrication, lower frequency of orgasm, and less ability to relax, findings reported by other researchers.[34] These areas of sexual dysfunction were also reported in a sample of 186 breast cancer patients whose mean age was 38 years.[5] YS but not OS reported that their sexual relationship had gotten worse since the breast cancer diagnosis.

Fatigue, often considered one of the most problematic symptoms after breast cancer treatment, was significantly higher for YS than AC, a finding reported in other research.[35] One study reported chronic fatigue had an overall prevalence of 48%.[36] Chronic fatigue is often strongly associated with depression, and our findings indicate that both depression and fatigue were more problematic for YS than AC.[37] YS were also found to have worse self-reported cognitive function, which most researchers believe is related to chemotherapy.[38]

Not all differences between YS and AC would be considered negative. YS reported more support and less social constraint compared to AC, although this result should be interpreted with the caveat that AC rated social constraint in relation to a self-identified stressor that was different from the anchor of cancer diagnosis. These self-selected stressors for AC varied widely, ranging from a child leaving for college to death of a loved one, perhaps rendering comparisons difficult. A diagnosis of breast cancer may have required more interaction as a couple—in fact, it is often referred to as a "we" illness -- leading to the perception of greater social support and less constraint.[39]

Young survivors compared to their controls reported more personal growth, including relating to others, personal strength, spiritual change, and new possibilities, findings supported by other studies.[40] Breast cancer may have created a greater opportunity for positive life changes than did the stressors reported by AC.

Differences between YS and OS

Our results also indicated that YS experienced greater anxiety and fear of recurrence than OS, a conclusion reached by other researchers[4,41] and one that has also been linked with sexual dysfunction,[33] Consistent with the comparisons of YS to AC, YS compared to OS reported more depressive symptoms and fatigue, worse attention function and sexual functioning, as well as lower scores on spirituality, a finding reflected in other research.[42] YS have often been reported to have worse sexual functioning compared to peers, but our findings also indicate that a breast cancer diagnosis and treatment probably impact sexual function to an even greater extent than in OS.[34] Menopausal status has been reported as a causative factor for sexual dysfunction in YS. The fact that YS were more likely to have experienced an abrupt menopause could have made symptoms such as hot flashes and

vaginal dryness a greater problem, thus partially accounting for the greater number of problems experienced by YS. Body image, which was worse in YS than OS, has been found to be a significant problem in YS.[43–45]

Eligibility for this study required that both YS and OS had received similar chemotherapy regimens to control for potential drug-induced differences in cognitive function. Because cognitive function decreases with age, we anticipated that YS would be more likely to report better cognitive function; yet despite age-related cognitive declines, YS reported more problems with attention function. Prior research has reported worse attention function in survivors than controls, but little is known about whether treatment-induced cognitive dysfunction is different as a result of age at diagnosis.[45,46] One possible explanation involves age-related demands for cognitive function. YS are more likely to be employed full-time and engaged in activities requiring greater cognitive ability, thus creating a greater difference between perceived need and ability. Cognitive limitations have also been associated with the use of estrogen inhibitors.[33] In our study 40% of YS used these medications compared to 52% of OS, and therefore the medication was probably not related to the differences found in our sample.

YS reported significantly more anxiety and sleep difficulty than OS. Prior research has reported anxiety at or within a year of diagnosis but frequently reported a decrease in anxiety over time.[47] Our sample included YS who were 3 to 8 years from diagnosis but still reporting more anxiety than OS. Anxiety may be related to fear of recurrence, which was also significantly greater in YS than OS. YS reported a mean fear of recurrence score of 39.2, almost three-fourths of a standard deviation from the mean of 22.76 for OS.

Although YS fared better than AC on dimensions such as social support, social constraint, impact of events, post-traumatic growth, and overall QoL, they were significantly worse than OS on these constructs. Similar results were reported by Stava, who found that, although a cancer diagnosis in general resulted in more social support, YS perceived less intimate or partner support than a cohort of OS.[48] Finally, younger survivors reported less religiosity and greater social constraint than OS. In conclusion, we found that YS fared worse than AC on depression, fatigue, attention function, sexual function, and spirituality. More importantly, YS reported more difficulty than OS on the variables of body image, anxiety, sleep, marital satisfaction, and fear of recurrence. Symptoms persisted even though our sample was 3 to 8 years from diagnosis.

Post-menopausal women experienced less fear of recurrence, but significantly lower scores on physical functioning, sleep, and sexual functioning. We can only speculate on why fear of recurrence was lower in women without periods. Perhaps having periods were reminders of being a woman, which triggered fear of breast cancer. Worse scores on physical function including sleep and sexual functioning are commonly reported for both women who have experienced breast cancer and those who haven't. Women who had gone through menopause reported more social support and less social constraint, but also reported less ability to find meaning in life.

Our findings suggest a major differential impact of breast cancer for survivors diagnosed at age 45 or younger compared to survivors diagnosed from 55 to 70. Although the clinical relevance of any single construct may differ, it is apparent when considering mean differences and standard errors (Table 2) that differences between groups were not marginal. Research is needed to understand the mechanisms underlying the differential impact of breast cancer diagnosis and treatment for YS and OS. It is also important to note that, overall, YS fared worse on many outcomes. These findings show that a diagnosis of breast cancer results in lifelong symptoms for many survivors, as well as that YS may be especially vulnerable to effects of diagnosis and treatment. Proactive symptom assessment and treatment for YS at the time of treatment must be a priority. The breast cancer survivor population will continue to increase as early diagnosis and better treatment make long-term survivorship a reality. This, along with the increase in life span, will impose significant burdens on both the survivors and our health care system. Additionally, it must be recognized that problems associated with breast cancer diagnosis and treatment may be compounded by the aging process, an important issue for our aging population.

Limitations

Although these data provided a unique opportunity to explore QoL in breast cancer survivors several years after diagnosis and treatment, the study has several limitations. First, the data are cross-sectional, limiting the ability to determine how one set of factors may have led to others. Secondly, on some measures such as the Post Traumatic Growth Inventory or the Impact of Events Scale, AC were asked to identify a stressor in order to complete the measure. We cannot know if the stressor of breast cancer was equivalent to those selected by AC. A prospective analysis might have provided more insight into the relationships among variables. Furthermore, the sample included women who had previously been involved in ECOG trials and therefore might not have been representative of the general population of survivors diagnosed at 45 or younger. However, data generated from this and other studies support the need to develop interventions that will help alleviate long-term problems resulting from the cancer diagnosis and its treatment.

Acknowledgments

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Table 1

Comparison of demographic characteristics across the three cohorts (N=1,531).

Variable	Young survivor (n=505)	Acquaintance control (n=348)	Older survivor (n=507)	p-value
Race, No. (%)				
Caucasian	459 (90.9)	369 (91.3)	582 (93.6)	.2037
Other	46 (9.1)	35 (8.7)	40 (6.4)	
Education (yrs), mean (SD)	14.8 (2.6)	15.1 (2.5)	14.1 (2.7)	<.0001
Income, No. (%)				
<=$50,000	109 (22.0)	106 (26.8)	294 (49.5)	<.0001
>$50,000 and <=$100,000	227 (45.9)	175 (44.3)	215 (36.2)	
>$100,000	159 (32.1)	114 (28.9)	85 (14.3)	
Relationship (time of diagnosis), No. (%)				
Married (or long term commitment)	417 (83.6)	313 (77.7)	467 (75.3)	<.0001
Divorced	29 (5.8)	38 (9.4)	54 (8.7)	
Widowed	4 (0.8)	5 (1.2)	66 (10.7)	
Single	49 (9.8)	47 (11.7)	33 (5.3)	
Married (or long term commitment)	417 (83.6)	313 (77.7)	467 (75.3)	.0032
Other	82 (16.4)	90 (22.3)	153 (24.7)	
Relationship (current), No. (%)				
Married (or long term commitment)	417 (83.1)	324 (80.6)	419 (69.0)	<.0001
Divorced	37 (7.4)	33 (8.2)	43 (7.1)	
Widowed	4 (0.8)	4 (1.0)	100 (16.5)	
Single	44 (8.8)	41 (10.2)	45 (7.4)	
Married (or long term commitment)	417 (83.1)	324 (80.6)	419 (69.0)	<.0001
Other	85 (16.9)	78 (19.4)	188 (31.0)	
Religious affiliation, No. (%)				
Christian, Catholic	164 (32.8)	82 (20.5)	171 (27.6)	<.0001
Christian, non-Catholic	266 (53.2)	274 (68.5)	395 (63.8)	
Other	70 (14.0)	44 (11.0)	53 (8.6)	
Number of comorbidities, mean (SD)	1.3 (1.5)	1.4 (1.6)	2.8 (1.8)	<.0001
Number of comorbidities>=3, No. (%)				
Yes	92 (18.2)	82 (21.3)	329 (52.9)	<.0001
No	413 (81.8)	318 (78.)	293 (47.1)	
Alcohol use, No. (%)				
Any use	362 (71.8)	268 (66.7)	373 (60.4)	.0003
No use (non-drinker)	142 (28.2)	134 (33.3)	245 (39.6)	
Number of alcohol drinks (week), mean (SD)	2.5 (4.8)	2.5 (5.3)	2.5 (4.7)	.9920
Hot flashes past 4 wks, No. (%)				
Yes	314 (62.8)	147 (36.5)	267 (43.3)	<.0001
No	186 (37.2)	256 (63.5)	350 (56.7)	
Had hysterectomy, No. (%)				

Variable	Young survivor (n=505)	Acquaintance control (n=348)	Older survivor (n=507)	p-value
Yes	153 (30.5)	55 (13.7)	258 (41.8)	<.0001
No	349 (69.5)	348 (86.4)	359 (58.2)	
No menstrual period past 12 mo, No. (%)				
Yes	333 (66.6)	146 (36.5)	582 (99.5)	<.0001
No	167 (33.4)	254 (63.5)	3 (0.5)	
Total Menstrual and Gyn Symptom Score, mean (SD)	4.9 (1.4)	4.8 (1.5)	4.5 (1.3)	.0056
Current use of estrogen blocking therapies, N (%)	198 (40.0)	3 (0.8)	315 (52.0)	<.0001
BMI (self-reported weight), mean (SD)	27.9 (6.2)	27.8 (7.1)	28.5 (5.9)	.1486

Notes: Comparisons on categorical variables were performed using a chi-square test; comparisons on continuous variables were performed using the t test from a general linear model.

Table 2

Adjusted means (with standard errors in parentheses) and p-values for outcomes of older survivor vs. young survivor and acquaintance vs. young survivor comparisons (N=1,322).

Variable*	Adjusted means*			p-values from model		
	Young survivor (YS; n=467)	Acquaintance control (AC; n=348)	Older survivor (OBREAST CANCER SURVIVORS; n=507)	Overall F test; p-value**	AC vs. YS*** p-value	OBREAST CANCER SURVIVORS vs. YS*** p-value
Psychological domain scales						
CES-D total score	11.64 (0.39)	9.43 (0.51)	6.87 (0.43)	31.21; <.0001 (<.0001)	.0011 (.0021)	<.0001 (<.0001)
Body image total score	23.39 (0.30)	24.03 (0.38)	27.96 (0.31)	52.88; <.0001 (<.0001)	.3019 (.3842)	<.0001 (<.0001)
State-Anxiety scale (STAI)	34.50 (0.48)	34.14 (0.62)	29.11 (0.52)	27.86; <.0001 (<.0001)	.8660 (.8873)	<.0001 (<.0001)
State-Trait scale (TRAI)	37.03 (0.45)	36.46 (0.58)	30.65 (0.49)	44.16; <.0001 (<.0001)	.6605 (.7113)	<.0001 (<.0001)
Concerns about Recurrence (CARS) – Total worries	39.21 (1.18)	Na	22.76 (1.12)	82.56; <.0001 (<.0001)	na na	<.0001 (<.0001)
Physical domain scales						
SF-36 Physical Function score	81.94 (0.81)	83.34 (1.05)	80.84 (0.88)	1.34; .2633 (.2633)	.4823 (.5402)	.6046 (.6262)
Pittsburgh Sleep Quality index (PSQI)	6.90 (0.16)	6.56 (0.21)	5.34 (0.18)	18.44; <.0001 (<.0001)	.3584 (.4363)	<.0001 (<.0001)
FACT-F (Fatigue)	37.79 (0.44)	39.57 (0.56)	43.24 (0.47)	32.30; <.0001 (<.0001)	.0224 (.0348)	<.0001 (<.0001)
Attention Function index	6.41 (0.08)	6.88 (0.10)	7.49 (0.08)	40.91; <.0001 (<.0001)	.0003 (.0006)	<.0001 (<.0001)
Sexual Functioning total score	19.59 (0.28)	22.11 (0.37)	21.37 (0.35)	18.13; <.0001 (<.0001)	<.0001 (<.0001)	.0003 (.0006)
Sexual Functioning Enjoyment	11.59 (0.16)	12.67 (0.21)	12.63 (0.20)	13.10; <.0001 (<.0001)	<.0001 (<.0001)	.0001 (.0002)
Sexual Functioning Difficulty	10.00 (0.16)	8.56 (0.21)	9.30 (0.20)	16.23; <.0001 (<.0001)	<.0001 (<.0001)	.0157 (.0207)
Spiritual domain scales						
Reed Spiritual Perspective scale (SPS)	4.50 (0.06)	4.76 (0.08)	4.76 (0.06)	6.20; .0021 (.0023)	.0119 (.0196)	.0076 (.0110)
Reed Spiritual Beliefs	4.62 (0.06)	4.85 (0.08)	4.92 (0.07)	6.64; .0014 (.0016)	.0290 (.0427)	.0020 (.0031)
Reed Spiritual Behaviors	4.33 (0.06)	4.62 (0.08)	4.53 (0.07)	5.15; .0059 (.0061)	.0078 (.0137)	.0579 (.0700)
Post-Traumatic Growth Inventory (PTGI)	65.29 (1.11)	51.60 (1.44)	63.76 (1.21)	29.92; <.0001 (<.0001)	<.0001 (<.0001)	.6007 (.6262)
PTGI factor 1: relating to others	22.43 (0.40)	17.65 (0.52)	23.25 (0.43)	33.83; <.0001 (<.0001)	<.0001 (<.0001)	.3310 (.3840)
PTGI factor 2: new possibilities	12.18 (0.31)	9.71 (0.41)	10.94 (0.34)	12.63; <.0001 (<.0001)	<.0001 (<.0001)	.0217 (.0274)
PTGI factor 3: personal strength	13.29 (0.24)	10.55 (0.31)	12.96 (0.26)	26.62; <.0001 (<.0001)	<.0001 (<.0001)	.5906 (.6262)
PTGI factor 4: spiritual change	5.99 (0.16)	5.03 (0.21)	6.13 (0.18)	7.90; .0004 (.0005)	.0006 (.0012)	.8146 (.8146)
PTGI factor 5: appreciation for life	11.40 (0.18)	8.66 (0.23)	10.49 (0.19)	46.65; <.0001 (<.0001)	<.0001 (<.0001)	.0018 (.0031)

Variable*	Adjusted means*			p-values from model		
	Young survivor (YS; n=467)	Acquaintance control (AC; n=348)	Older survivor (OBREAST CANCER SURVIVORS; n=507)	Overall F test; p-value**	AC vs. YS p-value***	OBREAST CANCER SURVIVORS vs. YS p-value***
Social domain scales						
Northhouse Spouse/Partner total score	26.47 (0.30)	25.27 (0.40)	28.36 (0.37)	13.23; <.0001 (<.0001)	.0321 (.0449)	.0003 (.0006)
Social Constraint Partner total score	21.83 (0.44)	26.30 (0.58)	19.76 (0.54)	29.40; <.0001 (<.0001)	<.0001 (<.0001)	.0086 (.0119)
ENRICH marital satisfaction scale	51.21 (0.69)	51.70 (0.91)	55.49 (0.85)	7.18; .0008 (.0009)	.8873 (.8873)	.0004 (.0007)
Overall QoL scales						
Index of well-being	11.35 (0.10)	11.15 (0.13)	12.35 (0.11)	23.78; <.0001 (<.0001)	.4103 (.4787)	<.0001 (<.0001)
Impact of events scale (IES-Rev) total	14.41 (0.53)	19.22 (0.69)	8.32 (0.57)	60.34; <.0001 (<.0001)	<.0001 (<.0001)	<.0001 (<.0001)
IES avoidance	4.95 (0.22)	6.85 (0.29)	3.81 (0.24)	26.84; <.0001 (<.0001)	<.0001 (<.0001)	.0019 (.0031)
IES Hyper	3.49 (0.16)	3.91 (0.20)	1.47 (0.17)	42.99; <.0001 (<.0001)	.1771 (.2361)	<.0001 (<.0001)
IES Intrusion	5.98 (0.25)	8.46 (0.32)	3.04 (0.27)	68.36; <.0001 (<.0001)	<.0001 (<.0001)	<.0001 (<.0001)

*
Comparisons on outcomes were performed using a general linear model adjusted for years of education, income, current marital status, number of comorbidities, had hysterectomy, had hot flashes in past 4 wks, had menstrual period in last 12mo, body mass index, total menstruation/gynecology total scale score and current use of hormone therapies. Sexual functioning and social domain scales (Northhouse, social constraint and ENRICH marital satisfaction) contained missing values due to not currently being married or having long-term partner (75–79 missing for YS; 203–215 missing for OBREAST CANCER SURVIVORS; 72–74 missing for AC).

**
from Type III sum of squares for 3-group comparison. Adjusted p-values from false discovery rate method shown in parentheses.

***
obtained from Dunnett's multiple comparison test. Adjusted p-values from false discovery rate method shown in parentheses.

Table 3

Differential finding for YS comparing AC and OS

Group	YS worse than AC	YS worse than OS
Depression	YS worse than AC	YS worse than OS
Body Image		YS worse than OS
State and Trait Anxiety		YS worse than OS
Sleep		YS worse than OS
Fatigue	YS worse than AC	YS worse than OS
Attention Functioning	YS worse than AC	YS worse than OS
Sexual Functioning	YS worse than AC	YS worse than OS
Reed Spiritual	YS worse than AC	YS worse than OS
Social Support	YS better than AC	YS worse than OS
Social Constraint	YS better than AC	YS worse than OS
Marital Satisfaction		YS worse than OS
Fear of Recurrence		YS worse than OS
Positive growth index	YS better than AC	
Impact of Events	YS better than AC	YS worse than OS
Index of Well being		YS worse than OS

Table 4

Effect of menopausal status on QoL variables

Comparing women with and without having menstrual cycle in past 12 months, N=1531

Variable	Menstrual cycle			No menstrual cycle			p-value
	N	Mean (SD)		N	Mean (SD)		
Psychological domain scales							
CES-D total score	423	8.49 (8.62)		1058	9.68 (9.05)		.0202
Concerns about Recurrence (CARS) – Total worries	170	37.12 (24.41)		914	29.30 (23.42)		<.0001
Physical domain scales							
SF-36 Physical Function score	424	89.55 (16.27)		1061	77.89 (21.70)		<.0001
Pittsburgh Sleep Quality index (PSQI)	414	5.40 (3.35)		1014	6.55 (3.75)		<.0001
FACT-F (Fatigue)	424	41.15 (9.68)		1059	40.00 (10.12)		.0449
Sexual Functioning total score	367	23.63 (5.23)		772	19.58 (5.62)		<.0001
Sexual Functioning Enjoyment	368	13.15 (3.09)		775	11.77 (3.10)		<.0001
Sexual Functioning Difficulty	366	7.54 (2.91)		768	10.21 (3.20)		<.0001
Spiritual domain scales							
Post-Traumatic Growth Inventory (PTGI)	422	56.20 (25.09)		1059	63.22 (22.87)		<.0001
PTGI factor 1: relating to others	422	19.49 (9.02)		1060	22.34 (8.24)		<.0001
PTGI factor 2: new possibilities	422	10.46 (6.79)		1059	11.36 (6.44)		.0173
PTGI factor 3: personal strength	422	11.60 (5.26)		1059	12.82 (4.81)		<.0001
PTGI factor 4: spiritual change	422	5.18 (3.41)		1055	6.07 (3.37)		<.0001
PTGI factor 5: appreciation for life	422	9.47 (4.08)		1059	10.64 (3.63)		<.0001
Social domain scales							
Northhouse Spouse/Partner total score	365	25.93 (5.80)		781	27.07 (5.92)		.0023
Social Constraint Partner total score	365	23.89 (8.89)		776	21.71 (8.58)		<.0001

*
mean comparisons based upon t-test, N=1531

*
mean comparisons based upon t-test.

**
adjusted using false discovery rate method for multipl