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Health care utilization, lifestyle, and emotional factors and mammography practices in the Childhood Cancer Survivor Study

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Abstract

Background—Women with a history of chest radiotherapy (RT) have an increased risk of breast cancer however many do not undergo annual recommended screening mammography. We sought to characterize the relationship between mammography and potentially modifiable factors, with the goal of identifying targets for intervention to improve utilization.

Methods—Of 625 female participants sampled from the Childhood Cancer Survivor Study who were treated with chest RT, 551 responded to a survey about breast cancer screening practices. We used multivariate Poisson regression to assess several lifestyle and emotional factors, health care practices, and perceived breast cancer risk, in relation to reporting a screening mammogram within the last two years.

Results—Women who had a Papanicolaou test (Prevalence Ratio [PR]: 1.77, 95% confidence interval [CI]; 1.26–2.49), and who perceived their breast cancer risk as higher than the average woman were more likely to have had a mammogram (PR: 1.26, 95% CI: 1.09–1.46). We detected an attenuated effect of echocardiogram screening (PR: 0.70 (0.52–0.95) on having a mammogram

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among older women compared to younger women. Smoking, obesity, physical activity, coping, and symptoms of anxiety, depression and somatization were not associated with mammographic screening.

Conclusion—Our findings suggest that compliance with routine and risk-based screening can be an important indicator of mammography in childhood cancer survivors. Additionally, there is a need to ensure women understand their increased breast cancer risk, as a means to encouraging them to follow breast surveillance guidelines.

Impact—Screening encounters could be used to promote mammography compliance in this population.

Introduction

It is well established that younger women treated with radiation to the chest area have a substantially increased risk of breast cancer, often at a young age (1–6). Given this markedly greater risk, the Children's Oncology Group (COG) and the International Guideline Harmonization Group for Late Effects of Childhood Cancer, recommend that women treated with 20 Gy or more of radiation potentially exposing the breast (hereafter referred to as chest RT) receive breast cancer surveillance beginning either 8 years post-radiation or at age 25 years (whichever occurs last) (5, 7, 8). Studies suggest, however, that many of these high-risk women do not undergo mammography or breast MRI as recommended. In a study of 90 Hodgkin lymphoma (HL) survivors who were at least 8 years past treatment, Diller et al. reported that fewer than half of women surveyed had received a mammogram within the past two years (9). More recently, (in a prior analysis of the study population reported on here), among 551 women in the U.S. and Canada who had previously been treated for a childhood cancer with chest RT, we found that only 36.5% of those between the ages of 25 and 39 had undergone mammographic screening within the previous two years; less than 3% reported ever having a breast MRI (10).

Several studies have identified a relation between potentially modifiable factors, including health behaviors, health care practices, and emotions, and mammogram utilization in the general population. Women who do not regularly see a primary care provider are also less likely to undergo mammography (11). Higher body mass index (BMI) has generally been found to be inversely related to mammography utilization, with obese women less likely to adhere to general population screening guidelines (12). Studies have also reported that female smokers are less likely to follow screening guidelines (11, 13–16). Additionally, there is some evidence that women who exhibit symptoms of depression have lower rates of screening (17, 18). The relationship between perceived breast cancer risk and mammography is less clear, with some studies reporting an association between lower perceived breast cancer risk and mammography utilization while other studies have found a higher perceived risk to be associated with mammography use (19, 20).It is unknown, however, whether any of these findings are generalizable to childhood cancer survivors.

Using data collected as part of a large, multi-institutional cancer survivor cohort, we sought to evaluate the association between modifiable lifestyle factors, health care practices, perceived risk, and emotional factors and having had a recent mammogram in women at

high-risk for breast cancer due to a history of chest RT. Identifying whether there is a relationship between mammography utilization and other health behaviors can ultimately lead to broader, more comprehensive interventions for this high-risk population. Furthermore, a better understanding of how emotional factors, such as depressive symptoms and coping style, relate to mammography utilization can help identify additional targets for intervention.

Materials and Methods

The Childhood Cancer Survivor Study (CCSS)

The CCSS is a retrospectively ascertained and prospectively followed cohort established in 1994 to study long-term outcomes following treatment of childhood cancer. Characteristics of the cohort, as well as details about study accrual and follow-up, have been described extensively (21–23). Briefly, the CCSS cohort includes individuals who were younger than 21 years of age when diagnosed with one of the most common cancer types between 1970 and 1986 at one of 26 institutions in the United States and Canada (21). Cohort members must have survived at least 5 years (from time of diagnosis) to have been eligible to enroll in the study, with baseline information, including treatment and disease history, available for over 14,000 survivors (21). All study protocols were approved by the Institutional Review Boards at each CCSS participating institution. Follow-up surveys have been administered periodically to the cohort.

To characterize the breast cancer surveillance practices among female cancer survivors who were treated with chest radiation, we conducted a survey through the CCSS between June 2005 and August 2006 (10). The Mammogram Practices Survey (MPS) consisted of 114 items. In addition to querying women about the history, frequency, and indications for mammographic screening and other breast cancer surveillance practices, the survey included items pertaining to other health care behaviors, including frequency of Papanicolaou (Pap) testing and primary care utilization. Also included were items measuring a range of health and personal beliefs. Of 625 eligible female survivors (Figure 1) who had been treated with at least 20 Gy of chest RT, 551 (88.2%) responded (10).

We conducted a cross-sectional analysis using data from the MPS together with data about specific health behaviors and psychological factors captured in the CCSS Follow-Up 2 Survey administered in 2003–2004. We restricted the analysis to women who responded to the MPS and were treated with at least 20 Gy of chest RT. Questionnaires are available at http:ccss.sjude.org/documents/original-cohort-questionnaires. Of note, at the time of the survey, the United States Preventive Services Task Force recommended that women in the general population initiate breast cancer screening at age 40 (24).

Outcome assessment

The primary outcome of interest was having self-reported a screening mammogram within the previous two years (vs. > 2 years/never). While surveillance guidelines are for annual mammograms (7, 8), we used a two-year window to allow for women who might have

received a mammogram 13 or 14 months apart to be considered adherent for the purposes of this analysis.

Exposure assessment

We assessed a range of modifiable lifestyle factors, health care practices, and emotional characteristics, which were evaluated from items included on the MPS (Pap test, BMI, coping, perceived breast cancer risk) or the CCSS Follow-Up 2 Survey (tobacco use, physical activity, cardiac screening, long-term follow-up clinic or oncology center visits, symptoms of depression, anxiety, and somatization).

Modifiable lifestyle factors

Tobacco use was dichotomized as current/former vs. never smoker. Physical activity was evaluated as inactivity vs. reporting participation in any physical activity (e.g., running, calisthenics, golf, gardening, bicycling, swimming, wheelchair basketball, or walking for exercise), within the last month. Self-reported height and weight were used to calculate BMI. Women with a BMI less than or equal to 18.5 were categorized as "underweight", women with a BMI greater than 18.5 but less than 25 were categorized as "normal weight", women with a BMI greater than or equal to 25 but less than 30 were categorized as "overweight", and those with a BMI greater than or equal to 30 were categorized as "obese."

Health care practices

Health care practices were dichotomized as follows: Pap test within the last two years (yes vs. no), visit to a clinic for Long-Term Follow-Up (LTFU) for cancer survivors or an oncology center or clinic within the last two years within the last two years (yes vs. no), and screening echocardiogram (recommended by COG guidelines for childhood cancer survivors who had RT) (7) within the last two years (yes vs. no/don't know).

Perceived breast cancer risk

Perceived breast cancer risk was evaluated with a single question asking women to estimate their likelihood of developing breast cancer in the future relative to the average women (25). Women who responded "much more than the average woman" or "more than the average woman" were categorized as "high perceived risk" whereas women who responded the "same as the average woman," "less than the average woman," or "much less than the average woman" were categorized as "low perceived risk."

Emotional distress

The Brief Symptom Inventory-18 (BSI-18) was used to assess symptoms representing three separate psychological domains: anxiety, depression, and somatization. Each domain is made up of a six-item subscale, and respondents are asked to rate on a 5-point scale (ranging from "not at all" to "extremely") how much a particular problem has been bothersome to them over the past week. Each subscale was scored individually and was normalized against a T-distribution. A T-score of 63 on any subscale was used as a cutoff, with scores falling at or above the cutoff classified as "symptomatic" while scores falling below the cutoff

classified as "asymptomatic" (26, 27). The BSI-18 is widely used as a screening tool and has been validated among adult survivors of childhood cancer (28, 29).

Coping

Coping was measured using the following six subscales from the COPE Inventory: active coping, planning, acceptance, denial, mental disengagement, and behavioral disengagement (30). Completed with reference to how participants generally cope with stressful experiences, the rating for each item ranges from 1 (I usually don't do this at all) – 4 (I usually do this a lot), and a mean score (range: 1–4) is calculated for each subscale. Because the active coping and planning subscales were highly correlated (r=0.76), they were averaged into an "active-planning" subscale (31).

Statistical analysis

Frequencies and means were calculated for categorical and continuous variables, respectively. To identify whether any of the health care practices, modifiable lifestyle, and emotional factors were associated with screening mammography within the last 2 years, we calculated prevalence ratios (PR) and 95% confidence intervals (CI) using Poisson regression models with robust variance estimates (32). All models were adjusted for age, which was identified as a strong determinant of mammogram utilization in a prior analysis (10). All independent variables that were significant at the p 0.15 level in the age-adjusted models were included in the multivariable model. Because having had a physician (or other health care provider) recommend a mammogram within the past year was also identified as a predictor of screening in a prior analysis (10), we adjusted for this factor, as well as for insurance status in the multivariable analysis. To assess whether there was a differential effect of factors by age, we tested for interaction between age and covariates included in the multivariable analysis. Missing covariate data was imputed using fully conditional specification (FCS), a semi-parametric method of multiple imputation for both continuous and categorical data (33). All multiple imputation models included age (40 vs. <40) and screening mammogram within the last two years as covariates; additional covariates were selected for each imputation model, *a priori* (e.g., model for Pap test included visit to a LTFU or oncology center/clinic and insurance status, model for smoking status included BMI and physical inactivity). Analyses based on imputed data yielded very similar results to those from a complete case analysis of the data and those with imputed data are presented. All analyses were conducted in SAS version 9.3/9.4 (SAS Institute, Cary, N.C.).

Results

Study population characteristics

Table 1 includes socio-demographic characteristics and cancer diagnosis information. The median age at the time of MPS completion was 39.2 years (range, 25.7 to 50.7). The majority of women were insured and over 90% of the sample identified as white non-Hispanic (WNH). Hodgkin lymphoma was the most common cancer diagnosis (58%) and approximately two-thirds of women were between the ages of 10 and 20 when their cancer was diagnosed.

Health care practices, modifiable lifestyle, and emotional factors

Frequencies of health care practices, modifiable lifestyle, and emotional factors are listed in Table 2. Fifty-five percent of women reported having a screening mammogram within the past two years. As reported previously (data not shown), among women younger than 40, only 36.5% of women younger than age 40 had a recent mammogram (10) while among the women aged 40 and older, the rate of mammography screening was more than double that in younger women, with 76.5% of women reporting a mammogram within the prior two years.

Cardiac screening was infrequent, with only 30% of women reporting an echocardiogram within the prior two years. Similarly, fewer than 20% of women reported receiving care at a LTFU clinic or at an oncology center/clinic in the past two years. In contrast, 88% of women reported having a Pap test within the last two years. Thirty-one percent of women were former or current smokers; 69% were never smokers. While the majority of women (80%) reported participation in some type of physical activity in the last month, over 40% of women were either obese (18%) or overweight (24%), while only 6% of women were classified as underweight.

Sixty percent of the women correctly perceived their breast cancer risk as higher compared to that of an average woman. Symptoms of anxiety and depression were relatively uncommon, with approximately 6% and 9% of women categorized as either anxious or depressed, respectively. Most women demonstrated a high level of active coping: on a scale ranging from 1–4, the mean scores for the active-planning subscale was 3.16.

Factors associated with recent mammogram utilization

Table 3 includes results from the age-adjusted and multivariable analyses. In the multivariable analysis, women who reported having had a Pap test within the last two years (PR: 1.77, 95% CI 1.26–2.49) and women who perceived themselves as high-risk (PR: 1.26, 95% CI 1.09–1.46) were more likely to report a recent mammogram.. When we tested for potential effect modification by age (age 40 vs. age <40), we detected an attenuated effect of both echocardiogram screening (PR: 0.70, 95% CI 0.52–0.95) and perceived risk on having a recent mammogram (PR: 0.73, 95% CI: 0.52–1.03) among older women compared to younger women, though the association between perceived risk and mammography did not reach statistical significance (p=0.07). When we included age as a continuous variable in the model, results did not change substantially. There were no significant associations between having a recent mammogram and visiting a LTFU or oncology center/clinic, BMI, smoking status, physical activity level, coping, or symptoms of anxiety, depression or somatization. Additionally, we explored associations separately by age group and mostly found similar relationships between the factors and mammography with the strength of the relationships somewhat attenuated in women 40 years of age (Supplementary Table 1a and 1b).

Discussion

In this, one of the largest studies of women treated for a childhood or adolescent cancer with chest radiation, we found no clear relationship between breast cancer screening practices and

their lifestyle behaviors and most emotional factors. However, we identified health care utilization practices that were related to having had a recent mammogram. In addition to an elevated breast cancer risk, women who are treated with chest RT are also at risk for cardiac sequelae and therefore periodic echocardiographic screening is indicated in this population (7).

The relationship between mammography use and having had a Pap test reinforces the importance of educating primary care physicians and gynecologists about screening guidelines for high-risk women, particularly those under 40. Recommendation from a health care provider has been cited as one of the strongest predictors of compliance with breast screening guidelines in cancer survivors, as well as in the general population (34–36), and both routine and risk-based screening can be useful opportunities to engage high-risk women and educate them about the importance of breast cancer screening. This is especially critical, given that a substantial proportion of women in our study – 40% - did not perceive themselves as high-risk.

Misperception of susceptibility to a breast cancer diagnosis as a consequence of treatment many years earlier is likely one of the driving factors behind the low rates of mammography among younger women. Importantly, we detected an attenuated effect of both echocardiogram screening and perceived risk on mammography among older women, indicating that women age 40 and older are likely to undergo mammography because of general population guidelines, while those younger than 40 are getting screened because they or their doctor are aware of their increased risk. While interventions designed to enhance risk communication have been moderately successfully in changing underlying perceptions (37), it is uncertain whether this ultimately translates into changing screening behavior, particularly in high-risk populations.

In contrast to our findings, other studies have found physical activity and obesity/overweight to be associated with lower mammography utilization in the general population, as well as women who are at higher risk due to a family history of breast cancer. In a cross-sectional study of Canadian women aged 50 to 69, women who were less physically active were more likely to never have had a screening mammogram (16). Similarly, in a study of screening behaviors in women with a family history of breast or ovarian cancer, Wu et al. reported that women who met or went beyond physical activity guidelines were less likely to under-utilize screening mammography (38). We detected an inverse, though non-significant, relationship between underweight and mammography, which is consistent with some studies that have also found lower breast screening rates among underweight women (39–42). Interestingly, some of these health behaviors have been found to be associated with other screening behaviors among (survivors of other childhood cancers) CCSS participants. For instance, Cox et al. also reported survivors who were inactive were more likely to have had a recent echocardiogram (survivors with cardiac problems might have more physical limitations and might be more likely to see a physician and be screened because of cardiac symptoms) and that lower BMI was associated with having had a recent bone density scan if indicated (43).

Several studies have reported on the relationship between psychological factors, and breast cancer screening behaviors. Depressive symptoms have generally been found to be

associated with lower rates of mammographic screening in the general population (17, 18). Among women with a family history of breast cancer, there have been mixed results regarding the association between generalized symptoms of anxiety and mammogram utilization. Some studies have reported no association, others have found anxiety to be related to compliance with screening guidelines or even over-screening (e.g., small or moderate amounts of anxiety can serve as a motivator to engage in health screening practices) while there is also evidence women who exhibit anxious symptoms are less likely to undergo breast cancer surveillance, which is explained in part by avoidance behavior (25, 44, 45). While we did not find a relationship between these factors and mammography, these symptoms, particularly depression and anxiety, were fairly uncommon, which might have precluded us from detecting an association.

There is some evidence that coping is associated with health behaviors, including mammography (46, 47). In a study of factors associated with compliance to breast cancer screening guidelines, Bowen et al. reported coping was related to mammographic intention but not actual mammography use (48). Most women in our study demonstrated a high level of active coping, and we did not discern any meaningful differences in mammography utilization among these women and the small proportion of women who did not cope actively in stressful situations. However, it should be noted that in an earlier analysis of our study population, Smith et al. reported relationships of high use of active coping and low use of acceptance coping with higher mammogram utilization among a distinct sub-group: those women who were younger than 40, had a doctor who recommended mammographic screening, and who perceived mammography positively (31).

Our findings suggest targets for intervention at both the patient and provider level. Most women (88%) reported having a Pap test within the past 2 years and they are likely visiting a primary care provider (PCP) for this screening. However, PCPs are often unfamiliar with treatment sequelae, as well as risk-based screening guidelines for cancer survivors (49, 50). Findings from a recent study indicate that most primary care physicians are not aware of the current surveillance guidelines for these survivors. In this study, fewer than 10% of general internists who were surveyed correctly recommended annual breast MRI and mammography for a 29-year-old female who had been treated with chest RT for HL as a teenager (51). Increasing PCP awareness of the late effects of cancer treatment represents an area that could be targeted. Recent attempts at facilitating the shift from oncologic to primary care in the adult population have included the implementation of survivorship care plans, which can help inform both patient and provider of appropriate follow-up guidelines, including risk-based screening (52). However, there has been only limited widespread use of these plans. Several models of care, designed to account for the unique issues childhood cancer survivors face as they move from pediatric oncologic care to adult medical care, have been proposed; however it is unclear whether these will sufficiently help most survivors navigate this transition (49, 53, 54).

Our findings should be considered within the context of the following limitations. As most women in our study were white, non-Hispanic and reported having health insurance, our findings may not be generalizable to other racial/ethnic or socioeconomic groups. Additionally, frequency of screening and participation in other health care practices and

behaviors are based on self-report and were not validated (i.e., medical records were not reviewed to verify mammography or echocardiogram screening). The data used in this analysis were collected between 2005 and 2006 and it is possible that our findings might not apply to the current mammogram practices of survivors given the ongoing dissemination of information about breast cancer risk among childhood cancer survivors who had chest RT. Further, study participants receive annual newsletters that frequently highlight issues related to the late effects of cancer treatment, including second cancer risks and are likely more educated about these risks than other pediatric cancer survivors. While awareness might be increased, this does not diminish the need to identify effective strategies to further improve adherence rates, as well as correct risk misperceptions, particularly among women under 40.

This study demonstrates how both routine screening and risk-based screening can be important indicators of mammographic screening in a high-risk population of childhood cancer survivors. Further, there is a need to ensure women are informed about and understand their increased risk of breast cancer, as a means to encouraging them to follow screening guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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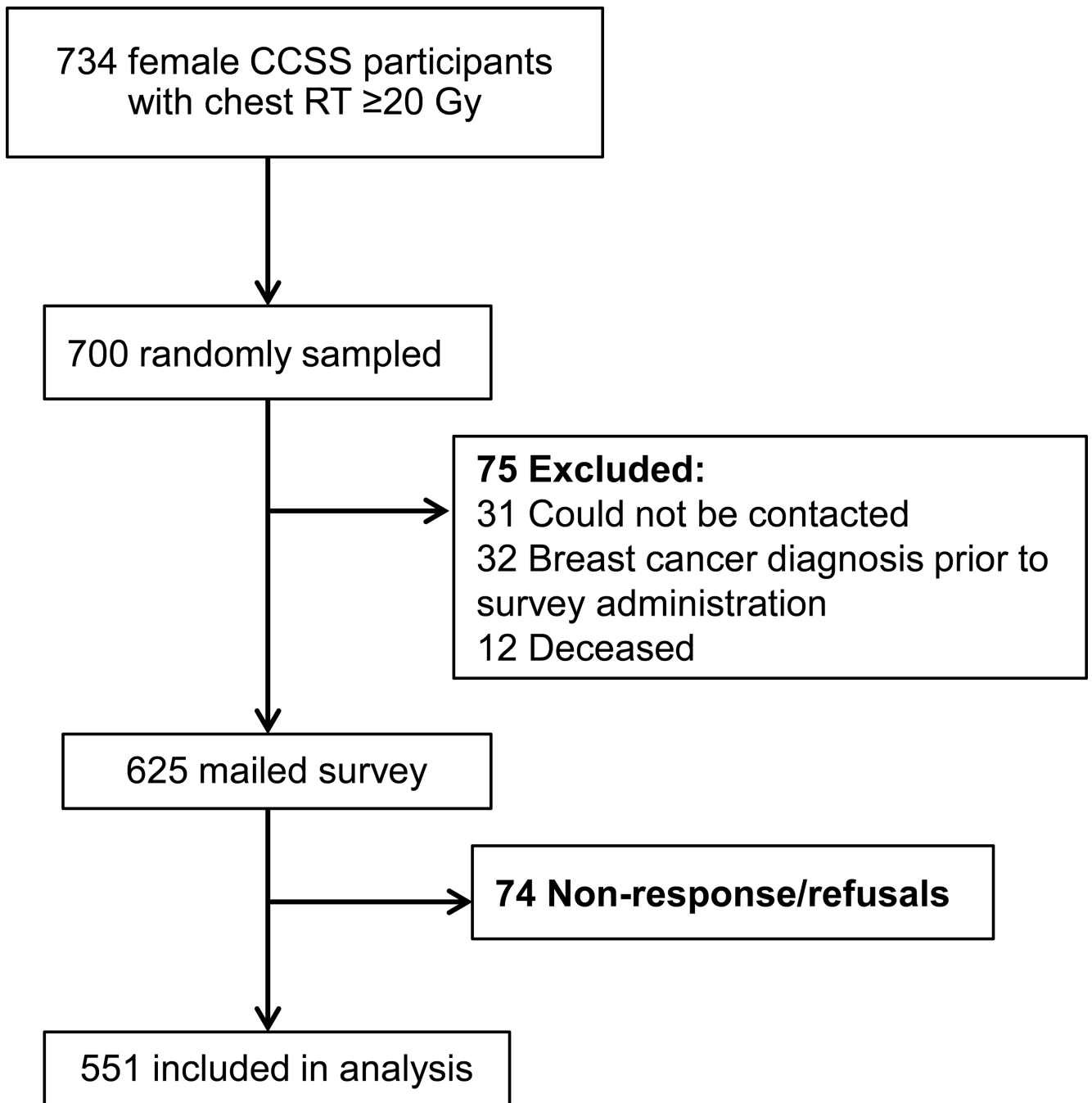
Figure 1.
Study flow chart
Abbreviations: CCSS, Childhood Cancer Survivor Study; RT, radiotherapy

Table 1

Study population characteristics (N=551)

	N	%
Age at time of study, years		
25–29	63	11
30–34	100	18
35–39	133	24
40–44	157	28
45	98	12
Race/ethnicity		
White non-Hispanic (WNH)	508	92
Minority	42	8
Missing	1	
Living area		
Rural	168	32
Urban	132	25
Suburban	231	4
Missing	20	
Household income		
<$40,000	127	27
$40,000–$79,999	182	38
$80,000	171	36
Missing	71	
Health insurance		
Yes	444	87
No	31	6
Canadian	34	7
Missing	42	
Cancer diagnosis		
Hodgkin lymphoma	318	58
Wilms tumor	75	14
Non-Hodgkin lymphoma	47	9
Neuroblastoma	33	6
Bone cancer	31	6
Soft-tissue sarcoma	26	5
Leukemia	15	3
Central nervous system tumor	6	1
Age at diagnosis, years		
0–9	183	33
10–20	368	67

Table 2

Distribution of healthcare practices, lifestyle behaviors, and emotional factors (N=551)

	N	%
Mammogram history		
Within last two years	303	55
> 2 years or never	248	45
Echocardiogram history		
Within last 2 years	155	30
>2 years or never/Don't know	357	70
Missing	*39*	
Visit to LTFU program or oncology center/clinic		
Within last 2 years	102	20
>2 years or never	398	80
Missing	*51*	
Pap test		
Within last 2 years	485	88
>2 years or never	65	12
Missing	*1*	
Smoking status		
Never	356	69
Former or current	157	31
Missing	*38*	
Physical activity		
Inactive lifestyle	104	20
Active lifestyle	407	80
Missing	*40*	
BMI		
Overweight	130	24
Obese	100	18
Underweight	34	6
Normal weight	287	52
Perceived breast cancer risk[a]		
High	325	60
Low	218	40
Missing	*8*	
BSI-18 (score 63)		
Global	47	10
Anxiety	29	6
Depression	41	9

	N	%
Somatization	87	18
Missing	*75*	
COPE	*Mean*	*SD*
Active/Planning[b]	3.16	0.62
Denial[b]	1.26	0.45
Accept[c]	2.89	0.66
Behavioral disengagement[d]	1.43	0.54
Mental disengagement[d]	2.10	0.59

LTFU: long term follow-up

[a]High= much more/more than average woman; Low= same/less/much less than average woman

[b]N=541

[c]N=538

[d]N=542

Table 3

Multivariable logistic regressions of factors associated with having a screening mammogram within the prior two years (N=551)

	Age-Adjusted[a]		Multivariable[b]		Multivariable+interaction[c]	
	PR (95% CI)	p-value	PR (95% CI)	p-value	PR (95% CI)	p-value
Former or current smoker	0.91 (0.77–1.07)	0.24	---		---	
Inactive lifestyle	0.92 (0.75–1.12)	0.38	---		---	
BMI (reference=normal weight)						
Underweight	0.63 (0.38–1.05)	0.08	0.72 (0.46–1.12)	0.15	0.72 (0.46–1.14)	0.17
Overweight	0.96 (0.82–1.14)	0.66	1.01 (0.87–1.17)	0.89	1.01 (0.87–1.17)	0.89
Obese	0.96 (0.79–1.16)	0.67	0.95 (0.79–1.13)	0.54	0.96 (0.81–1.15)	0.68
Echocardiogram[d]	1.34 (1.17–1.54)	<0.0001	1.13 (0.99–1.29)	0.07	2.05 (1.18–3.56)	0.01
Echo × age	---		----		0.70 (0.52–0.95)	0.02
Pap test[d]	2.31 (1.59–3.36)	<0.0001	1.77 (1.26–2.49)	0.001	1.78 (1.26–2.51)	0.001
Visit to LTFU or oncology center/clinic[d]	1.36 (1.17–1.57)	<0.0001	1.08 (0.95–1.25)	0.25	1.06 (0.93–1.22)	0.38
BSI-18 (ref=score <63)						
Global	1.16 (0.93–1.46)	0.19	----			
Anxiety symptoms	1.27 (1.02–1.59)	0.04	1.09 (0.86–1.39)	0.48	1.12 (0.88–1.41)	0.36
Depressive symptoms	0.96 (0.73–1.27)	0.78	----			
Somatization symptoms	1.06 (0.88–1.26)	0.55	----			
High perceived breast cancer risk	1.44 (1.22–1.69)	<0.0001	1.26 (1.09–1.46)	0.002	2.13 (1.12–4.03)	0.02
Perceived risk × Age	---		----		0.73 (0.52–1.03)	0.07
COPE scale						
Active/Planning	1.08 (0.95–1.22)	0.26	----			
Denial	0.95 (0.78–1.14)	0.55	----			
Acceptance	0.93 (0.84–1.04)	0.22	----			
Mental disengagement	0.94 (0.83–1.06)	0.30	----			
Behavioral disengagement	0.89 (0.77–1.02)	0.10	0.95 (0.84–1.08)	0.41	0.93 (0.82–1.06)	0.29

PR: Prevalence Ratio; CI: Confidence Intervals; LTFU: long term follow-up clinic visit

[a] Adjusted for age   40 vs. <40

[b] Adjusted for age, physician recommendation, insurance status, and variables where p ≤ 0.15 in age-adjusted model

[c] Adjusted for age, physician recommendation, insurance status, and variables where p ≤ 0.15 in age-adjusted model; includes interaction of 1) echocardiogram and age ≥ 40 vs. <40; 2) perceived breast cancer risk and age ≥ 40 vs. <40

[d] Within the last two years