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The Impact of Mammographic Screening on the Surgical Management of Breast Cancer

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Abstract

Background & Objectives—Mammographic screening has been shown to result in downward stage migration, reflected by smaller tumor sizes and less extensive nodal involvement. New national guidelines restrict screening recommendations in women age 40-49. The purpose of this study is to evaluate the specific impact of mammographic screening patterns on the surgical management of breast cancer in women aged 40-49.

Methods—The study is a population-based retrospective review of the Vermont Breast Cancer Surveillance System of women aged 40 to 49 with a diagnosis of breast cancer. Tumor stage and related characteristics at the time of diagnosis, as well as the type of surgical intervention performed were recorded for women presenting with screen-detected versus non-screen-detected breast cancer.

Results—Screen-detected breast cancers in women aged 40-49 were associated with a greater incidence of DCIS, smaller invasive tumor size, fewer cases of positive nodes, and higher rates of breast conservation compared to non-screened women presenting with symptomatic disease.

Conclusions—Mammographic screening is associated with less aggressive surgical treatment of breast cancer including higher rates of breast conservation. The observed changes in surgical management should factor into individual decision-making regarding screening mammography.

Keywords

mammogram; screening; quality; breast cancer; breast conserving surgery

Introduction

Screening mammography has demonstrated significant mortality reduction in both randomized controlled trials and evaluations of large, population-based organized screening programs. [1-8] Concerns have been raised, however, over potential risks and harms of mammographic screening including the risk of over-diagnosis. [9,10] In 2009, the US Preventive Services Task Force issued new guidelines for screening mammography, notably

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restricting recommendations in women aged 40-49 to shared decision-making, while recommending biennial screening for women ages 50-74.[11] These guidelines are a departure from the prior USPSTF recommendations of routine screening every 1 to 2 years for all women starting at age 40,[12] and have generated considerable controversy. Other organizations such as the American Cancer Society (ACS) have also amended prior guidelines. The ACS now endorses a process of informed decision making where women aged 40-44 are given the option to consider screening based on individual priorities, whereas routine annual screening is only recommended for women beginning at age 45.[13,14] The central argument has focused on the number of lives saved compared to the risks of screening, which include over-diagnosis and false-positive findings.[15] Despite the differing views on the benefits/harms of mammography, there has been increasing consensus for a more personalized approach based on patient preferences and individual risk assessment.[16,17]

The fundamental goal of mammographic screening is to reduce the incidence rate of advanced disease. It is important to note that screening mammography leads to significant downward stage migration, reflected by smaller tumor size and fewer cases of positive nodes at the time of treatment, which may impact options and outcomes for breast cancer surgery.[18-24] Woman presenting with smaller, node-negative tumors are more likely to be candidates for breast conservation and minimal (if any) axillary node staging. These benefits in surgical management associated with screening may greatly affect patient morbidity, satisfaction, and cost of care.

We have previously shown a decline in state-wide screening rates among low-risk women aged 40-49 following the introduction of the USPSTF guidelines in 2009.[25] It remains unknown how variations in screening patterns in this age group have influenced their surgical management. The purpose of this study is to evaluate the influence of state-wide mammography screening patterns on surgical management at the time of breast cancer diagnosis in women aged 40-49. We hypothesize that tumor size and axillary node status are affected by screening patterns, and that this in turn influences the surgical treatment performed.

Methods

Overview

We conducted a retrospective review of data from the Vermont Breast Cancer Surveillance System (VBCSS), to identify patients diagnosed with breast cancer between January 1, 1996 and December 31, 2012. The VBCSS includes a statewide registry of all breast imaging with linked patient, radiology, and pathology data.[26] It is part of the National Cancer Institute's Breast Cancer Surveillance Consortium (BCSC)[27] and the National Cancer Institute's recently formed Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) program.[28] This study was compliant with the Health Insurance Portability and Accountability Act and was approved by the University of Vermont Institutional Review Board with a waiver of informed consent. Approximately 5% of the women in the VBCSS indicated that they did not wish their data to be used in research via an opt-out mechanism and were thus excluded from the study.

At each mammography visit to any breast imaging facility in Vermont, each patient completes a standardized questionnaire including health history and demographic information, which is provided to the VBCSS. Radiologists and mammography technologists provide information on the clinical mammography findings and the reason for the visit. Pathology reports are provided to the VBCSS for all breast specimens. Linkage with the Vermont Cancer Registry provides detailed data on all malignant breast diagnoses. Information on biopsies and treatments received were obtained from pathology reports (via specimen type) and from information within the Vermont Cancer Registry.

Study population

We identified 1,449 women (aged 40 to 49) with a diagnosis of breast cancer from the VBCSS records. Eligibility was restricted to first primary breast cancer cases diagnosed between 1996 and 2012 with a known method of detection. Patients with an unknown stage at diagnosis were removed from analyses (n=100).

Screening classification

Cases were characterized into “screened” vs. “non-screened” categories based on the following definitions. “Screened” cases were those diagnosed with breast cancer within 12 months following a screening or short interval follow-up mammogram. Non-screened, symptom-detected cases were defined at those diagnosed among women without a screening mammogram in the past year who presented at mammography a diagnostic evaluation of symptoms (such as a palpable lump, pain, nodal enlargement, or swelling).

Tumor classification and Surgical Management

Breast cancers were classified based on data provided by the mandatory statewide Vermont Cancer Registry, including SEER summary stage (in situ, localized, regional, or distant), tumor size, tumor grade, estrogen receptor status, lymph node removal, and nodal status (positive vs. negative). For certain analyses, late stage disease was defined as SEER summary stage regional or distant and large tumors were defined as those greater than 20 mm in diameter. First course of treatment for each case was also obtained from the Vermont Cancer Registry, including surgery type (breast conserving surgery vs. total mastectomy).

Statistical analyses

Descriptive statistics were used to characterize patient characteristics, cancer characteristics, and surgical management according to screening classification (screened vs. non-screened symptomatic). Pearson chi-square tests were used to assess differences in these factors between screened and non-screened cases. All reported P values are two-sided, with $p < 0.05$ indicative of significance. Multivariable logistic regression was used to compare the frequency of adverse tumor characteristics by screening classification, with adjustment for age and year of diagnosis. All statistical analysis was performed using SAS software.

Results

Between 1996 and 2012, there were 1,449 women between ages 40 to 49 diagnosed with breast cancer with known stage and mode of detection. The demographic data for patient

characteristics at the time of diagnosis for the study cohort of women ages 40-49 are presented in Table 1. Sixty-eight percent of the breast cancer diagnoses in patients 40-49 were associated with a screening mammogram. The vast majority of women with screen-detected and non-screen detected breast cancer had no family history of breast cancer, 72.1% and 71.5%, respectively.

The percent of patients with non-invasive disease (DCIS) was significantly higher in the screened population (29.4%) than in the non-screened symptomatic group (7.0%) ($p<0.0001$). Screened women with invasive disease were more likely to have a lower stage at diagnosis ($p<0.0001$), smaller tumor size ($p<0.0001$) and lower tumor grade ($p=0.04$) than women in the non-screened, symptomatic group. (Table 2).

The surgical management and treatment data for women with primary breast cancer is shown in Table 3. Women aged 40-49 who received a screening mammogram were less likely to require removal of lymph nodes than non-screened symptomatic patients (30.8% vs. 20.4%, $p<0.0001$). In addition, women in the screened group were more likely to receive a sentinel node biopsy rather than a regional node dissection compared to the non-screened symptomatic patients (21.3% vs. 13.4%, $p<0.0001$). The frequency of positive nodes encountered was lower in patients receiving screening mammograms when compared to the non-screened group (22.4% vs. 43.4%, $p<0.0001$). Patients in the non-screen-detected group were more likely to undergo total mastectomy when compared to the screen detected group (31.1% vs. 25.3%, $p<0.0001$). Similarly, the rate of breast conservation surgery was higher in the screened detected group compared to the non-screened group (69.6% vs. 58.7%, $p<0.0001$). The remaining patients either had no surgery or the specific surgical intervention was unknown.

Results from the multivariable-adjusted regression models are presented in Table 4. After adjusting for age and year of diagnosis, cancers diagnosed among non-screened symptomatic women were more likely to have adverse tumor characteristics and undergo more aggressive treatments compared to cancers diagnosed among screened women. Specifically, breast cancers among non-screened symptomatic women were more frequently invasive, larger in size, later in stage, higher grade, more frequently node positive (all $p<0.0001$), and were more likely to be treated with total mastectomy ($p=0.05$).

Discussion

Although much of the discussion about breast cancer screening traditionally centers on survival, our data suggests that other clinically relevant outcomes are affected by screening recommendations and should be considered when weighing the potential benefits and harms in individualized screening recommendations. Specifically, our study demonstrated an increase in the stage of disease at presentation in non-screened women aged 40-49, compared to screened women in the same age group. The Breast Health Global Initiative (BHGI)[29] uses median invasive tumor size as an indicator of the quality of breast cancer detection and the ability of a screening system to optimize early identification of disease. In our study, the comparison of screen-detected versus non screen-detected breast cancer for women in their 40s not only demonstrated smaller tumor size, but also less invasive surgical

procedures associated with screened versus non-screened patient populations. Women aged 40-49 who did not receive screening mammograms were less likely to be treated with breast conservation and more frequently required axillary node dissections. Similar findings have been reported by Malmgren *et al.*,[18] who showed that screening mammograms resulted in lower rates of mastectomy in women aged 40-49 at a single institution prior to the USPSTF recommendations. Our study confirms this finding on a larger state-wide scale, adding evidence to the impact of breast cancer screening on surgical management.

Although not directly measured in our data, undergoing more invasive surgical procedures for breast cancer has been associated with poorer function and lower quality of life scores in breast cancer survivors.[30-35] Disruption in body image, sexual health and lifestyle is observed in women requiring more aggressive procedures such as total mastectomy and axillary node dissection; especially in the younger patient population. [36,37]

It is important to note that we intended to compare women participating in a screening program to women who were not participating in a screening program. The cases among woman participating in a screening program will inevitably include interval cases. Interval cases will have a different set of characteristics from true screen-detected cases (which is an interesting question in its own right), but the focus of this study was to determine overall how cases among women involved in screening program (screen-detected and interval) compare to women not involved in a screening program. Similarly, our population of screened women includes a mix of women being screened for the first time, screened for the Nth consecutive annual exam, screened after a lag of 5 years, and so on. Future analyses could examine treatments received in relation to these details among the regularlyscreened cases (ideally in a national dataset).

One noted limitation is that some screening classifications could not be determined either due to 1) not having mammography records for that individual within the time period of the cancer diagnosis, or 2) not having the indication for exam known (i.e. screening vs. diagnostic). The first scenario occurred most frequently when records from the Vermont Cancer Registry were from an individual living in Vermont who may have received breast imaging out of state. Of note, the second scenario occurred with relative rarity. We postulate that the missing data reflect limitations in the completeness of the database (e.g., not capturing out of state imaging) but does not reflect limitations in accuracy. For this study caution was taken to ensure that the screening classification was performed accurately, such that the results reflect the true differences between screen-detected cancers and those presenting with symptomatic disease. We have no reason to believe that the results would be different for the cases with imaging performed out of state and the exclusion of these cases is very unlikely to bias the results. Another recognized limitation is the lack of data on adherence to regular screening. As mentioned previously, since the classification of patients into screened (including intervals) and non-screened cohorts was made primarily to distinguish cancer detection between groups of women in a screening program compared to those with “symptomatic” cancer detection, determining adherence rates, or proportion of interval detections would not alter the main findings of the study.

Our study is also subject to limitations inherent to retrospective observational studies. Women undergoing screening often differ in many ways from women not undergoing screening.[38,39] Differences in breast cancer risk according to screening utilization could influence our results. To minimize bias, we used multivariable-adjusted regression analyses that controlled for family history of breast cancer and mammographic breast density, which are the strongest breast cancer risk factors in the general population (i.e., aside from rare high penetrance mutations such as BRCA1/2).

Other limitations included our inability to assess more detailed aspects of surgical management as we did not have access to timing or dosing of neoadjuvant, adjuvant and radiation treatments. Finally, our study population reflects a relatively homogenous Caucasian patient population which may limit the applicability of our findings to more ethnically diverse regions. Nevertheless, a key strength of our data is the statewide coverage of the VBCSS and the inclusion of breast cancer cases from all health care systems in the state.

Conclusions

Mammographic screening leads to downward stage migration of breast cancer and less aggressive surgical treatment. Screened women aged 40-49 diagnosed with breast cancer have smaller tumor size, higher rates of DCIS, fewer cases of positive nodes, and undergo less aggressive surgical procedures for the management of breast cancer compared to non-screened women presenting with symptomatic/palpable disease. The extent of surgical intervention has implications for patient satisfaction, treatment-related morbidity, cost and quality of life. We believe that women, health care providers and policy makers should consider these findings as they consider individual breast cancer screening decisions and policy guidelines.

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Synopsis

A statewide clinical database demonstrated that mammographic screening was associated with smaller tumor size and fewer positive nodes at the time of diagnosis. This in turn resulted in higher rates of breast conservation and fewer axillary lymph node dissections performed in the treatment of breast cancer. These findings have implications for the quality of clinical outcomes as well as cost of cancer care.

Table 1

Description of patient characteristics in the Vermont Breast Cancer Surveillance System (VBCSS) (1996-2012) AGES 40-49

Variable	Screened (%) (n=979)	Non-screened (%) (n=470)	P-value
Body Mass Index			0.08
<18.5 kg/m^2	12 (1.2)	13 (2.8)	
18.5-24.9 kg/m^2	490 (50.1)	225 (47.9)	
25.0-29.9 kg/m^2	248 (25.3)	98 (20.9)	
30.0+ kg/m^2	188 (19.2)	93 (19.8)	
Unknown	41 (4.2)	41 (8.7)	
First-Degree Family History			0.02
No	706 (72.1)	336 (71.5)	
Yes	200 (20.4)	66 (14.0)	
Unknown	73 (7.5)	68 (14.5)	
Education			<0.0001
Less than high school diploma	21 (2.2)	31 (6.6)	
High school diploma	216 (22.1)	120 (25.5)	
Some college	197 (20.1)	111 (23.6)	
College degree	541 (55.3)	197 (41.9)	
Unknown	4 (0.4)	11 (2.3)	
Breast Density			0.30
Almost entirely fat	18 (1.8)	8 (1.7)	
Scattered fibroglandular elements	234 (23.9)	99 (21.1)	
Heterogeneously dense	418 (42.7)	198 (42.1)	
Extremely dense	113 (11.5)	69 (14.7)	
Unknown	196 (20.0)	96 (20.4)	

Table 2

Description of primary breast cancer characteristics in the Vermont Breast Cancer Surveillance System (VBCSS) (1996-2012) AGES 40-49

Variable	Screened (%) (n=979)	Non-screened (%) (n=470)	P-value
Diagnosis Type			<0.0001
In situ	288 (29.4)	33 (7.0)	
Invasive	691 (70.6)	437 (93.0)	
Stage at Diagnosis			<0.0001
In situ	288 (29.4)	33 (7.0)	
Localized	447 (45.7)	206 (43.8)	
Regional	221 (22.6)	201 (42.8)	
Distant	12 (1.2)	24 (5.1)	
Unknown	11 (1.1)	6 (1.3)	
Tumor Size			<0.0001
In situ	288 (29.4)	33 (7.0)	
≤ 2.0 cm	491 (50.2)	208 (44.3)	
2.1-5.0 cm	147 (15.0)	162 (34.5)	
≥ 5.0 cm	26 (2.7)	47 (10.0)	
Unknown	27 (2.8)	20 (4.4)	
Tumor Grade			0.04
Low	181 (18.5)	70 (14.9)	
Intermediate	386 (39.4)	187 (39.8)	
High	271 (27.7)	162 (34.5)	
Unknown	141 (14.4)	51 (10.9)	

Table 3

Surgical management and treatment data for women with primary breast cancer (1996-2012) AGES 40-49

Variable	Screened (%) (n=979)	Non-screened (%) (n=470)	P-value
Lymph Node Surgery			<0.0001
No nodes removed	301 (30.8)	96 (20.4)	
Sentinel Lymph Node Biopsy	208 (21.3)	63 (13.4)	
Regional nodes removed	457 (46.7)	308 (65.5)	
Unknown	13 (1.3)	3 (0.6)	
Nodal Disease			<0.0001
All nodes negative	478 (48.8)	197 (41.9)	
Positive nodes found	219 (22.4)	204 (43.4)	
No nodes examined	274 (28.0)	61 (13.0)	
Unknown	8 (0.8)	8 (1.7)	
Surgical Management of Tumor			<0.0001
None	39 (4.0)	44 (9.4)	
Breast Conservation Surgery	681 (69.6)	276 (58.7)	
Total mastectomy	248 (25.3)	146 (31.1)	
Unknown	11 (1.1)	4 (0.9)	

Table 4

Age- and year-adjusted odds ratios for adverse tumor characteristics according to screening participation (1996-2012). AGES 40-49

	Odds Ratios* (95% Confidence Interval)		
	Screened	**Non-Screened**	**P-value**
Invasive (vs. in situ)	1.00 (Ref)	4.85 (3.40, 6.91)	<0.0001
Late stage	1.00 (Ref)	2.77 (2.20, 3.48)	<0.0001
Large size	1.00 (Ref)	3.70 (2.90, 4.73)	<0.0001
High grade (vs. low/intermediate)	1.00 (Ref)	1.33 (1.04-1.69)	0.02
ER negative	1.00 (Ref)	1.50 (1.11, 2.03)	0.01
Any nodes removed	1.00 (Ref)	1.89 (1.44, 2.48)	<0.0001
Regional nodes removed	1.00 (Ref)	1.94 (1.54-2.44)	<0.0001
Nodes positive	1.00 (Ref)	2.48 (1.97, 3.13)	<0.0001
Mastectomy	1.00 (Ref)	1.28 (1.00, 1.62)	0.05

*All analysis adjusted for year and age