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BREAST CANCER SCREENING IN PATIENTS WITH CANCERS OTHER THAN BREAST

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Abstract

Background—Screening mammography can detect early breast cancers and reduce subsequent cancer mortality. However, there is a lack of consensus as to when to discontinue screening. The absence of clear-cut guidelines on when not to screen means that many patients with advanced malignancies continue screening despite unclear benefit.

Methods—We performed a retrospective cohort study of female patients diagnosed with a non-breast malignancy to explore the incidence and effects of screening mammography. Female patients diagnosed with a non-breast malignancy stage II or higher between 2007 and 2012 were identified through the Vermont Cancer Registry and cross-referenced with mammography screening logs from January 1, 2007 to September 30, 2014. Additional data were collected through chart review, in May 2016.

Results—Twenty-six percent of women (398/1501) with a stage II or greater cancer (other than breast) diagnosed between 2007 and 2012 had a screening mammogram within the first 5 years of their diagnosis. Of these 398 women, 193 (48.5%) were alive without cancer, 132 (33.2%) had died, and 73 (18.3%) were alive with cancer at the time of chart review. Of those who died, 84 (63.6%) had a stage III or IV cancer. Eighteen (4.5%) had a breast biopsy following a screening mammogram suspicious for cancer, resulting in 13 (3.3%) benign diagnoses and 5 (1.3%) breast cancer diagnoses. No patient died of breast cancer.

Conclusions—Except for highly curable cancers, female patients diagnosed with an advanced non-breast malignancy experienced mortality that outweighs a breast cancer mortality benefit from screening mammography as estimated from prior studies.

BACKGROUND

Screening for breast cancer with mammography detects early cancers and reduces breast cancer mortality¹. Many agencies have published guidelines that are summarized on the CDC website at <https://www.cdc.gov/cancer/breast/pdf/BreastCancerScreeningGuidelines.pdf>. In 2015 the United States Preventative Services Task

Force (USPSTF) released updated guidelines for breast cancer screening¹. These guidelines also include specific recommendations on when to increase screening for selected populations, such as those with a family history of breast or ovarian cancer. There is a recommendation to discontinue screening in patients with moderate to severe comorbid conditions that negatively affect their life expectancy^{1,2}. Advanced cancer is not mentioned in the USPSTF guidelines, although affected patients have a decreased life expectancy.

Screening is a doubled edge sword, where over-diagnosis could lead to more harm than good. For example, the identification of a cancer that is irrelevant to the patient's overall morbidity or mortality prognosis might lead to non-beneficial medical interventions. This has been well established for prostate and thyroid cancers^{3,4}. A meta-analysis of screening trials demonstrates that between 472 and 2463 women (depending on age group) need to undergo screening mammography to prevent 1 breast cancer death over a 15-year period⁵. The true estimate of over-diagnosis is unknown, but could be as high as 24%⁶. The cost of false-positive screening mammography and breast cancer over-diagnosis in women aged 40–59 years old is estimated at \$4 billion a year⁷. Thus, over-diagnosis of breast cancer is prevalent and expensive.

Currently, there are only two guidelines which identify populations that may no longer benefit from breast cancer screening⁸. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older¹. The American Cancer Society recommends that screening continue if a woman is in good health and is expected to live 10 more years or longer². Despite these published guidelines, data is limited as to what diseases should preclude a woman from undergoing screening mammography, and at what age. For women diagnosed with a high-risk malignancy other than breast cancer, there are currently no established recommendations for screening mammography. About 9% of women with a terminal cancer (<6-month survival) continue to receive mammograms⁹.

We hypothesized that breast cancer screening in patients with advanced cancers other than breast is not likely to add clinical benefit. To investigate the incidence of screening mammography in women of all ages who carry a recent diagnosis of high-risk cancer other than breast, we used data from the Vermont Breast Cancer Surveillance System (VBCSS), a statewide registry of all mammography performed in Vermont. We then evaluated the outcomes of those who underwent breast cancer screening in this subgroup.

METHODS

This is a retrospective cohort study of female patients diagnosed with a malignancy other than breast cancer who underwent subsequent mammography screening. The study protocol was approved, with a waiver of informed consent, by the local Institutional Review Board. The objectives of the study were to determine the incidence of screening mammography in women with non-breast malignancies, stage II to IV, and whether a survival advantage existed in the patients who were diagnosed with breast cancer.

Study Population

All Vermont-residing female patients diagnosed and treated at the University of Vermont Cancer Center with a non-breast malignancy stage II or higher between the years 2007 and 2012 were identified through the Vermont Cancer Registry (VCR). This population was then cross referenced with the state-wide VBCSS's records for patients who were screened with mammography between January 1, 2007 and September 30, 2014. Patient information was obtained predominantly from VCR and the VBCSS. Missing data points were then collected via an in-depth chart review on all patients who had both a diagnosis of cancer (non-breast malignancy, stage II or greater) and received mammography screening in that time-frame. Parameters that were collected included start date of non-breast cancer treatment, types of treatment, disease outcome after primary treatment, and family history of breast or ovarian cancer. Chart review was conducted during May of 2016; giving between 4.5 and 9.5 years of follow-up after diagnosis of their primary stage II or greater non-breast cancer.

Statistical Analyses

Descriptive statistics were used to analyze the data. Median and range were used for patient characteristics and percentages were used for incidences.

RESULTS

From 2007 to 2012, 1,501 women were diagnosed with a cancer other than breast, stage 2 or greater. 147,382 women underwent screening mammography in Vermont between January 1, 2007 and September 30, 2014. A screening mammogram was performed in 398 (26.5%) of women with an advanced non-breast cancer diagnosis and these patients were enrolled in the study (Fig. 1). Characteristics of subjects with a stage 2 or greater cancer that underwent subsequent screening mammography are shown in Table 1.

At the time of chart review, 193 of these 398 women (48.5%) were alive without cancer after treatment, 132 (33.2%) had died of their original cancer, and 73 (18.3%) were alive with it. Of the 193 alive without cancer, the median number of mammograms is three (range, 1–8). Of the 73 patients, alive with cancer, the median number of mammograms is two (range, 1–7). Of the 132 patients who died of cancer, the median number of mammograms is one (range, 1–6). Sixty-eight women died after receiving only one mammogram and 34 died after the second mammogram. Thus, 77.2% of deaths (102/132) happened after one or two mammograms. The greatest proportion of subjects who died after receiving a screening mammogram had been diagnosed with a stage 3 cancer (40.9% of total deaths). Stage 4 was next most common (22.7%), followed by stage 2 (21.2%), and lastly unstageable malignancies (14.4%).

Eighteen (4.5%) women had biopsy recommended after positive findings on screening mammography TABLE 2. All patients underwent breast biopsies. Thirteen (3.3%) subjects had a negative biopsy for breast neoplasms, and 5 had positive breast biopsies for cancer. Of these positive biopsies, one (0.3%) patient had ductal carcinoma in-situ (DCIS), three (0.8%) were diagnosed with breast cancer stage 1A and one (0.3%) stage 2A. Of the five subjects who were diagnosed with new breast cancers following screening mammography, four had

stage 3 non-breast cancer, including melanoma, ovary, ileum, or lung; and one had a spinal cord astrocytoma. All women who were diagnosed with a new breast malignancy underwent surgery. Two women underwent lumpectomy with subsequent radiation, two underwent lumpectomy without radiation (one with re-excision), and one underwent complete unilateral mastectomy with lymph node dissection. After surgery, two women had hormone modulating therapy and the one patient with stage 2A breast cancer underwent chemotherapy. One of these women was treated for breast cancer while her non-breast cancer was not in clinical remission.

Additionally, two (0.5%) women in our cohort were diagnosed with breast cancer after presenting with clinical symptoms, and then underwent diagnostic mammography and biopsy. One (0.3%) woman was diagnosed with stage Ib and the second (0.3%) was diagnosed with stage Ic disease. One subject was treated with mastectomy and hormone modulation therapy. The other subject was treated with partial mastectomy, radiation therapy and hormone modulation therapy. One of these women, was treated for breast cancer immediately after completing adjuvant chemotherapy for advanced colon cancer, and is currently in hospice care because of the recurrent colon cancer.

Reported adverse events were not always documented in the patient's charts; however, most commonly reported adverse events were lymphedema, alopecia, mastitis, repeat surgery, and skin desquamation at the radiation site. No women died of breast cancer.

DISCUSSION

None of the women diagnosed with a stage II or greater malignancy, who were subsequently diagnosed with breast cancer after screening mammography died of the breast cancer. At the time of diagnosis, their first cancer conferred a less than 50% chance of cure. The diagnosis of an early breast cancer did not impact this prognosis. Additionally, 72% patients with a positive mammogram underwent a biopsy demonstrating benign disease, which did not contribute to improving their outcome. Overall, 1.3% of women who underwent screening mammography were diagnosed with breast cancer and were treated for it, which was accompanied by substantial treatment burden. Treatment of an asymptomatic breast cancer had an unclear impact on their overall survival, in light of the prognosis conferred by an advanced cancer. However, our numbers are very small and need to be interpreted cautiously.

A meta-analysis shows that to prevent one breast cancer death over a 15-year period in women aged 60–69, 472 women need to be regularly screened⁵. In our study, 126 subjects with stage II or higher non-breast cancer were between 60 and 69 years of age; of these, 46 (36.5%) died during the observation period, which was 5 years less than the observation period of the meta-analysis⁵. Thus, patients in our cohort were approximately 172 times more likely to die from their initial cancer diagnosis (36.5%) than they would be expected to benefit from undergoing screening mammography ($1/472=0.2\%$). We propose that the mortality rate of women with non-breast cancer stage II and higher meets the criteria set forth by the American Cancer Society to discontinue mammographic screening².

In the data examined, 193 (48.5%) subjects were alive without any evidence of cancer. Not all advanced stage cancers have an equally poor prognosis. For example, stage II papillary thyroid cancer has a 10-year survival of nearly 100%. Conversely, a patient with stage IV pancreatic adenocarcinoma has a very poor prognosis, with only 2.6% of those afflicted surviving 5 years¹⁰. Women diagnosed with good prognosis cancers, such as stage II thyroid cancer, have the potential to receive a survival benefit from screening mammography until it is no longer recommended due to age or other comorbidities. The same is true for Hodgkin's disease, which confers an increased risk of breast cancer if mediastinal radiation was used.

The implementation of this study's findings may not be easy. First, a practitioner recommending the cessation of breast cancer screening may elicit a feeling of hopelessness in the patient, and the patient may lose hope because of the poor prognosis of their current malignancy. Difficult conversations are commonly avoided. However, effective methods can be taught to engage specifically in difficult communication with patients¹¹. Second, mammographic screening is usually by self-referral¹². Many facilities allow for self-referral for mammography, giving the patient the ability to avoid the discussion with their oncologist or primary care physician as to whether mammography is appropriate in their current circumstances. Third, mammography services send automated mailings to women, independently of their medical history, re-inviting women for annual screening.

Our data have implications for care. Oncologists or primary care providers need to continue educating patients about cancer prevention and consider a discussion of the appropriateness of prevention tests when moderately and severely life threatening diagnoses occur. Electronic health maintenance schedules need to be updated with the medical history of each patient.

We do not propose to abstain from treating a breast cancer found clinically or incidentally after the cessation of mammography. The few studies comparing the natural history of untreated breast cancers report worse survival than that of many other malignancies that are appropriately treated^{13–15}.

Limitations of our study include (1) a low power because of a small sample size, (2) the use of registries for patient identification, (3) various malignancies at different stages, with different prognoses, and (4) absence of other comorbidity notation. Thus, we cannot rule out a selection bias related to the limiting factors of working with a pre-generated dataset. The robustness of the observed outcomes could overcome the limitations of the study, and sets the stage for additional research on screening.

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References

1. Siu AL. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med.* 2016; 164:279–96. [PubMed: 26757170]
2. Smith RA, Andrews K, Brooks D, et al. Cancer screening in the United States, 2016: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA: a cancer journal for clinicians.* 2016; 66:95–114.
3. Moyer VA. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2012; 157:120–34. [PubMed: 22801674]
4. US Preventive Services Task Force. Guide to Clinical Preventive Services: Report of the US Preventive Services Task Force. 2. Baltimore (MD): Williams & Wilkins; Screening for Thyroid Cancer; 1996. p. 18 Available from: <http://www.ncbi.nlm.nih.gov/books/NBK15464/>
5. Myers ER, Moorman P, Gierisch JM, et al. Benefits and Harms of Breast Cancer Screening: A Systematic Review. *Jama.* 2015; 314:1615–34. [PubMed: 26501537]
6. Welch HG, Black WC. Overdiagnosis in cancer. *Journal of the National Cancer Institute.* 2010; 102:605–13. [PubMed: 20413742]
7. Ong MS, Mandl KD. National expenditure for false-positive mammograms and breast cancer overdiagnoses estimated at \$4 billion a year. *Health affairs (Project Hope).* 2015; 34:576–83. [PubMed: 25847639]
8. Lansdorp-Vogelaar I, Gulati R, Mariotto AB, et al. Personalizing age of cancer screening cessation based on comorbid conditions: model estimates of harms and benefits. *Ann Intern Med.* 2014; 161:104–12. [PubMed: 25023249]
9. Sima CS, Panageas KS, Schrag D. Cancer screening among patients with advanced cancer. *Jama.* 2010; 304:1584–91. [PubMed: 20940384]
10. SEER Cancer Statistics Review, 1975–2013. National Cancer Institute; Jul. 2016 at http://seer.cancer.gov/csr/1975_2013/.
11. Epner DE, Baile WF. Difficult conversations: teaching medical oncology trainees communication skills one hour at a time. *Academic medicine : journal of the Association of American Medical Colleges.* 2014; 89:578–84. [PubMed: 24556763]
12. Monsees B, Destouet JM, Evens RG. The self-referred mammography patient: a new responsibility for radiologists. *Radiology.* 1988; 166:69–70. [PubMed: 3336703]
13. Joseph K, Vrouwe S, Kamruzzaman A, et al. Outcome analysis of breast cancer patients who declined evidence-based treatment. *World journal of surgical oncology.* 2012; 10:118. [PubMed: 22734852]
14. Bloom HJ, Richardson WW, Harries EJ. Natural history of untreated breast cancer (1805–1933). Comparison of untreated and treated cases according to histological grade of malignancy. *British medical journal.* 1962; 2:213–21. [PubMed: 13870135]
15. Verkooijen HM, Fioretti GM, Rapiti E, et al. Patients' refusal of surgery strongly impairs breast cancer survival. *Annals of surgery.* 2005; 242:276–80. [PubMed: 16041219]

FIGURE 1.
Consort Diagram

Table 1

Characteristics of the 398 patients

Average age		60 (range 22–81)
Diagnoses	Lung cancers	60
	Colon/Rectum/Appendix cancers	47
	Endometrial/Uterine	44
	Ovarian/Fallopian tube/Peritoneal	44
	Lymphomas	34
	Thyroid	20
	Head & neck cancers	18
	Melanoma	14
	Anal cancers	12
	Chronic leukemias	11
	Other Bone Marrow Disorders/Unspecified leukemias	11
	Hodgkin disease	10
	Bladder/Ureter	9
	Central nervous system	9
	Liver/Pancreas cancers	8
	Soft tissue sarcoma	8
	Myelomas	7
	Acute leukemias	7
	Renal	7
	Esophageal/Gastric/Small intestine cancers	6
	Cervical	6
	Vulvar	3
	Other epithelial malignancy	3
Stage at diagnosis	2	111
	3	162
	4	71
	Other (Primary CNS, leukemia, other non-staged malignances)	54
Vital status	Alive without evidence of cancer	193
	Alive with evidence of cancer	73
	Dead	132

Table 2

Breast cancer diagnoses in patients with advanced non-breast cancers

Number of patients = 398 (denominator)		
		N (%)
Biopsy recommended after positive screening mammogram		
	Negative breast biopsy	13 (3.26)
	Positive breast biopsy	5 (1.25)
Symptomatic presentation (Positive diagnostic mammograms)		
		2 (0.5)
Characteristics of patients with additional breast cancer (N=7)		
First cancers	Melanoma, ovary, colon, thyroid, ileum, lung, & spinal cord astrocytoma	All stage III cancers except the astrocytoma (Primary CNS)
Stage	In-situ	1
	1	5
	2	1
Treatment	Lumpectomy	5
	Mastectomy	2
	Lymph node dissection	1
	Radiation	3
	Hormonal treatment	4
	Chemotherapy	1
Outcome	Alive without cancer	5
	Alive with non-breast cancer	2