Geographic Variation in Postoperative Imaging for Low-Risk Breast Cancer

Benjamin L. Franc, MD, MS, MBA[a]; Timothy P. Copeland, MPP[a]; Robert Thombley, BS[b]; Miran Park, PhD[b]; Ben Marafino, BS[b]; Mitzi L. Dean, MHA, MS[b]; W. John Boscardin, PhD[c]; Hope S. Rugo, MD[d]; David Seidenwurm, MD[e]; Bhupinder Sharma, FRCR[f]; Stephen R. Johnston, MA, FRCP, PhD[f]; and R. Adams Dudley, MD, MBA[b]

Abstract

Background: The objective of this study was to examine the presence and magnitude of US geographic variation in use rates of both recommended and high-cost imaging in young patients with early-stage breast cancer during the 18 month period after surgical treatment of their primary tumor. **Methods:** Using the Truven Health MarketScan Commercial Database, a descriptive analysis was conducted of geographic variation in annual rates of dedicated breast imaging and high-cost body imaging of 36,045 women aged 18 to 64 years treated with surgery for invasive unilateral breast cancer between 2010 and 2012. Multivariate hierarchical analysis examined the relationship between likelihood of imaging and patient characteristics, with metropolitan statistical area (MSA) serving as a random effect. Patient characteristics included age group, *BRCA1/2* carrier status, family history of breast cancer, combination of breast surgery type and radiation therapy, drug therapy, and payer type. All MSAs in the United States were included, with areas outside MSAs within a given state aggregated into a single area for analytic purposes. **Results:** Descriptive analysis of rates of imaging use and intensity within MSA regions revealed wide geographic variation, irrespective of treatment cohort or age group. Increased probability of recommended postoperative dedicated breast imaging was primarily associated with age and treatment including both surgery and radiation therapy, followed by MSA region (odds ratio, 1.42). Increased probability of PET use—a high-cost imaging modality for which postoperative routine use is not recommended in the absence of specific clinical findings—was primarily associated with surgery type followed by MSA region (odds ratio, 1.82). **Conclusions:** In patients with breast cancer treated for low-risk disease, geography has effects on the rates of posttreatment imaging, suggesting that some patients are not receiving beneficial dedicated breast imaging, and high-cost nonbreast imaging may not be targeted to those groups most likely to benefit.

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Over a number of years or decades, the nearly 3 million US patients with breast cancer who have survived their initial treatment phase will be imaged to screen for additional primary breast cancers and to evaluate for evidence of recurrent or metastatic disease.[1] Optimizing imaging in these patients is critical to their health and to the welfare of the health system. The American College of Radiology recommends that women with personal histories of breast cancer and dense breast tissue, or breast cancer diagnosed by age 50 years, receive dedicated breast MRI annually.[2] ASCO and NCCN have issued guidelines stating that, after initial treatment, surveillance for recurrence in pa-

[a]Department of Radiology and Biomedical Imaging, [b]Philip R. Lee Institute for Health Policy Studies, Center for Healthcare Value, [c]Department of Medicine, Epidemiology & Biostatistics, and [d]Department of Medicine, University of California, San Francisco, California; [e]Diagnostic Imaging, Sutter Medical Group, Sacramento, California; and [f]The Royal Marsden NHS Foundation Trust, Chelsea, London, United Kingdom.

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Correspondence: Benjamin L. Franc, MD, MS, MBA, Department of Radiology and Biomedical Imaging, Center for Healthcare Value, University of California, San Francisco, 3333 California Street, Suite 265, San Francisco, CA 94118. Email: Benjamin.Franc@ucsf.edu

tients with stage I–III breast cancer should include periodic physical examination and mammography, but that, in the absence of symptoms, other imaging tests are not beneficial for patients at low risk of recurrence.[3–6] Although imaging beyond dedicated breast MRI or mammography can be used to detect cancer recurrence before it produces symptoms or signs,[7] large randomized controlled trials, the first of which were published in the 1990s,[8–11] and Cochrane database systematic reviews[12,13] have repeatedly found that such nonbreast surveillance offers no benefit in terms of survival or quality of life for patients with stage I–III (nonmetastatic) disease.[3–6]

The goal of this study was to examine US geographic variation in use rates of postoperative, recommended, dedicated breast imaging and high-cost whole-body imaging with CT, MRI, PET, and/or bone scan—modalities capable of identifying recurrent or metastatic disease in patients with breast cancer receiving treatment consistent with low risk of recurrence or metastases. Identifying geographic regions with low rates of recommended postoperative imaging would allow interventions to target patients not receiving beneficial screening. Identifying geographic regions with high rates of whole-body postoperative imaging, regardless of patient risk of recurrent disease, could focus interventions to reduce unnecessary surveillance imaging.

Methods

This analysis, approved by the University of California, San Francisco Institutional Review Board, retrospectively assessed geographic variations in the likelihood of receiving postoperative dedicated breast imaging and whole-body surveillance imaging at the metropolitan statistical area (MSA) level. MSAs are geographic regions defined by the Office of Management and Budget and are commonly used by medical claims payers for statistical purposes. A complementary descriptive analysis of variation across broad geographic regions (Northeast, North Central, South, and West) was also performed.

Data Sources

We used HIPAA-compliant deidentified patient-level inpatient, outpatient, and outpatient pharmacy claims data from the Truven Health MarketScan Commercial Database, representing the claims of employees and dependents on large employer health benefit programs between January 1, 2010, and December 31, 2013. The claims database originated from approximately 100 insurance companies, including both insurance providers and third-party administrators. The plans represented include a variety of fee-for-service, preferred provider organizations, and capitated health plans. Claims from Medicare, Medicaid, and workers compensation were not included. All new breast cancer diagnoses in the 2010 SEER database were used in a sensitivity analysis of stage at time of diagnosis across regions.

Data Extraction and Cleaning, Calculation of Rates, and Geographic Aggregation

A total of 38,424 women were identified with claims indicating a breast biopsy between January 1, 2010, and March 30, 2012, followed by primary surgical treatment and 18 additional months of postdiagnosis claims (see supplemental eAppendix 1 for Current Procedural Terminology [CPT] codes, available with this article at JNCCN.org). To limit the study to patients who had treatment compatible with early-stage disease, 2,379 patients receiving neoadjuvant or nonhormonal adjuvant therapy (any chemotherapy or trastuzumab; supplemental eAppendix 2) between initial biopsy and 18 months postsurgery were excluded from further analysis, resulting in a study cohort of 36,045 women.

To evaluate groups of patients who received comparable treatment regimens, treatment cohorts were classified via CPT codes based on the combination of breast surgery type and whether the patient received radiation therapy (RT) (supplemental eAppendix 1). These patient groups were then classified into subgroups based on whether they received postsurgical hormonal therapy (supplemental eAppendix 2), resulting in 12 treatment cohorts.

Claims for body CT, brain CT, PET, body MRI, breast MRI, brain MRI, mammography, and whole-body bone scans in the 18 months after surgery were identified (see supplemental eAppendix 3 for imaging CPT codes). Aside from modalities for dedicated breast imaging (ie, mammography and breast MRI), postoperative imaging claims were only included in the study when the claim included an indication of breast cancer (ICD-9 codes 174.0–174.9).

Patient characteristics examined included age group, whether RT was received, whether hormonal

therapy was received, payer class, and MSA. Patients residing outside of an MSA were grouped by state into 47 state-based categories and included within the MSA variable, for a total of 428 geographic regions.

Cross Validation of Imaging Rates

We validated rates of mammographic imaging at the state level by grouping mammographic rates by state and comparing the mean rate of receiving mammography against 2013 rates reported by NCI.[14] We also compared the mean rates of mammography from our data set for each year studied to those reported by the CDC for the same year.[15]

Data Analysis

Main Analysis: We conducted a descriptive analysis of imaging use, defined as a patient receiving at least one imaging study, and imaging intensity, defined by mean number of imaging examinations per imaged patient in a 1-year period. Proportions of patients imaged and mean images per imaged patient were compared simultaneously between treatment cohorts and between Northeast, North Central, South, and West US regions. The variations in proportion of patients receiving imaging between regions were assessed with chi-square tests, whereas variations in mean annualized number of imaging examinations per imaged patient by region were assessed using Kruskal-Wallis test.

To study mean imaging use and intensities within MSA regions, proportions of patients receiving at least one dedicated breast image or at least one nonbreast tomographic image (ie, any CT, MRI, PET/CT, or bone scan) within each MSA region were determined by age group and treatment cohort. Mean nonbreast tomographic imaging intensity within MSA regions was also determined by age group and treatment cohort.

To estimate independent predictors of imaging use, we created 2-level hierarchical models with MSA as a random effect to account for clustering of patients by geographic region. Age group, RT, surgical therapy, drug therapy, and payer type were included as fixed effects. Binary outcome variables assessed with this model include use of brain CT, brain MRI, body CT, body MRI, body PET/CT, bone scan, breast MRI, mammography, tomographic nondedicated breast imaging, and tomographic brain imaging (ie, any brain CT or MRI).

The influence of MSA was summarized by the median odds ratio (OR)—the median ratio of the odds of imaging use between equivalent patients with breast cancer of 2 randomly selected MSAs, with the clusters compared in descending order so ORs consistently exceed 1.[16,17] Median OR was computed from the random effects' estimated variance and was directly comparable to fixed-effect variables' ORs. A fixed effect–only model was compared with the multilevel hierarchical model, and C-statistics were calculated for each model. Models were not reported if C-statistics did not yield acceptable discrimination (ie, a C-statistic of at least 0.7).[18]

Analysis was performed using SAS 9.4 (SAS Institute, Inc.) for sample selection and StataMP 13.1 (StataCorp LP) for statistical analysis.

Geographic Distribution of Stage II–III Breast Cancer: To exclude variation in geographic occurrence of locally aggressive operable cancers as an explanation for any observed geographic variation in imaging rates, the significance of differences in distribution of stage II–IIIA breast cancers diagnosed in women aged 18 to 44 years across regions was estimated. Data from regions defined in the SEER database from 2010 was regrouped to reflect the geographic areas studied in the MarketScan-derived cohort. Chi-square tests assessed variation between the rate of stage IIA/B or IIIA cancers diagnosed across regions.

Results

Cross-Validation of Imaging Rates

Cross-validation of state-level mammography rates among patients aged ≥40 years showed that state mammographic rates in our study and 2014 state rates reported by NCI did not differ significantly (*t*-test P=.11; supplemental eTable 1). The analysis of mammographic rate did not include Hawaii, because the number of patients (n=7) enrolled in employer-based plans included in the MarketScan data for Hawaii were insufficient for meaningful analysis. The CDC's 2013 mammography rates were comparable to study rates in women aged 40 to 49 years (59.6% vs 64.7%, respectively) and in women aged 50 to 64 years (71.4% vs 73.9%, respectively).[19] Overall, this validation of our study data seems to

indicate that our findings are likely to approximate national trends.

Main Findings

Of 36,045 women aged 18 to 64 years diagnosed with unilateral invasive primary breast cancer, treated with surgery, and not exposed to neoadjuvant/adjuvant chemotherapy or trastuzumab within 18 months of diagnosis, 24,802 (68.8%) underwent at least one screening or diagnostic mammogram, 4,602 (12.8%) had at least one breast MRI, 11,418 (31.7%) had at least one high-cost imaging procedure, and 4,490 (12.5%) had at least one PET. A total of 25,501 women (70.8%) had at least one dedicated breast image (ie, at least one mammogram or breast MRI). Patient characteristics are described in Table 1.

Table 2 describes the variations in imaging use (ie, use of at least one imaging modality) and intensity (ie, mean annualized number of imaging examinations per imaged patient). Chi-square and Kruskal-Wallis tests revealed significant variation in both use and frequency between regions within each of the treatment cohorts ($P<.05$). Imaging use and intensity were heterogeneous between cohorts within regions and between regions within treatment cohorts. Notably, among the lowest-risk patients (surgery only), approximately 50% indicated that they received mammography in the 18 months after initial treatment. Between 64% and 70% of patients who received a mastectomy and RT, presumably a group with higher risk, were imaged using a dedicated breast modality. Proportions of patients imaged and mean images per imaged patient also showed heterogeneity at the geographic levels of Northeast, North Central, South, and West regions of the United States (supplemental eTable 2; see eAppendix 4 for states).

The multivariate multilevel hierarchical models of imaging use in the 18 months post–breast surgery revealed 4 modality models with acceptable discrimination: mammography with fixed effects for surgery/RT combination only, mammography, PET, and dedicated breast imaging (Table 2). The combination of breast surgery type with/without RT was among the strongest predictors of imaging use in all models, to the extent that a model using only a surgery/RT combination as an independent predictor of mammography had a relatively small difference in model discrimination when compared with the mammography model including all independent variables (C-statistic, 0.85 vs 0.87). PET imaging was much more common among women who were treated with single mastectomy with RT (OR, 6.66) and double mastectomy with RT (OR, 6.87) compared with the reference class of lumpectomy without RT.

Each successive age group was more likely to have dedicated breast imaging and less likely to have PET imaging than the reference class of age 18 to 34 years. Compared with the reference class of women with PPO insurance plans, those with HMO plans were the least likely to have postoperative dedicated breast imaging of all insurance classes (OR, 0.64).

Table 1. Patient Characteristics, Drawn From MarketScan Data 2010–2013

Patient Characteristics	N	%[a]
Sex		
Female	36,045	100
Surgery + RT combinations		
Lumpectomy without RT	6,196	17.2
Lumpectomy + RT	12,460	34.6
Mastectomy without RT	9,221	25.6
Mastectomy + RT	3,455	9.6
Mastectomy + contralateral prophylactic mastectomy without RT	3,558	9.9
Mastectomy + contralateral prophylactic mastectomy + RT	1,155	3.2
Age at surgery, y		
18–34	978	2.7
35–44	6,110	17.0
45–54	14,823	41.1
55–64	14,134	39.2
RT		
Received RT	18,975	52.6
Did not receive RT	17,070	47.4
Pharmaceutical treatment		
Hormonal therapy only	18,654	51.8
No chemotherapy or hormones	17,391	48.3
Payer class		
PPO	22,253	61.7
Comprehensive	877	2.4
EPO	673	1.9
HMO	3,830	10.6
POS	2,418	6.7
POS with capitation	229	0.6
CDHP	2,011	5.6
HDHP	1,283	3.6
Unknown	2,471	6.9
Region[b]		
Northeast	7,519	20.9
North Central	8,072	22.4
South	14,139	39.2
West	6,315	17.5

Abbreviations: CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; RT, radiation therapy.
[a]All percent values are column percentages.
[b]The MarketScan database grouped patients into 4 large regions within the United States (Northeast, North Central, South, and West) based on state of residence (see supplemental eAppendix 4).

Table 2. Characteristics Associated With Postoperative Imaging by Modality

Characteristic	Mammography (Surgery/RT Combination Model) OR (95% CI)	Mammography OR (95% CI)	Any Dedicated Breast Imaging OR (95% CI)	PET/CT Imaging OR (95% CI)
Surgery + RT combinations				
Lumpectomy without RT	Ref	Ref	Ref	Ref
Lumpectomy + RT	2.61 (2.35–2.91)	2.49 (2.23–2.78)	2.59 (2.30–2.91)	1.75 (1.55–1.98)
Mastectomy without RT	0.16 (0.15–0.18)	0.16 (0.15–0.17)	0.16 (0.15–0.18)	1.94 (1.71–2.20)
Mastectomy + RT	0.26 (0.24–0.29)	0.25 (0.23–0.28)	0.25 (0.22–0.28)	6.66 (5.84–7.59)
Mastectomy + contralateral prophylactic mastectomy without RT	0.01 (0.01–0.02)	0.01 (0.01–0.01)	0.02 (0.02–0.02)	1.80 (1.55–2.10)
Mastectomy + contralateral prophylactic mastectomy + RT	0.02 (0.02–0.03)	0.02 (0.02–0.03)	0.03 (0.02–0.03)	6.87 (2.65–3.27)
Age at surgery, y				
18–34	–	Ref	Ref	Ref
35–44	–	1.72 (1.44–2.05)	1.62 (1.37–1.93)	0.92 (0.76–1.12)
45–54	–	2.27 (1.92–2.69)	2.05 (1.74–2.42)	0.86 (0.72–1.03)
55–64	–	2.66 (2.24–3.15)	2.33 (1.97–2.75)	0.85 (0.71–1.11)
Pharmaceutical treatment				
No pharmaceutical treatment	–	Ref	Ref	Ref
Received hormonal therapy	–	1.42 (1.34–1.5)	1.41 (1.33–1.49)	1.03 (0.97–1.11)
Payer class				
PPO	–	Ref	Ref	Ref
Comprehensive	–	0.91 (0.74–1.11)	0.92 (0.75–1.13)	1.11 (0.88–1.38)
EPO	–	1.13 (0.9–1.41)	1.13 (0.9–1.41)	0.91 (0.71–1.16)
HMO	–	0.63 (0.57–0.69)	0.64 (0.58–0.71)	0.91 (0.80–1.02)
POS	–	0.85 (0.75–0.96)	0.86 (0.76–0.98)	1.03 (0.89–1.18)
POS with capitation	–	1.11 (0.76–1.63)	1.13 (0.77–1.66)	1.03 (0.68–1.55)
CDHP	–	0.87 (0.77–0.99)	0.86 (0.76–0.98)	1.19 (1.03–1.37)
HDHP	–	1.04 (0.88–1.22)	1.08 (0.92–1.28)	1.01 (0.84–1.22)
Unknown	–	0.79 (0.69–0.91)	0.82 (0.71–0.94)	1.17 (0.99–1.38)
Region				
Modified MSA (MOR)[a]	–	1.46 (1.38–1.54)	1.42 (1.35–1.51)	1.82 (1.70–1.97)
C-statistic for area under ROC	0.85	0.87	0.87	0.73

Abbreviations: CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; MOR, median odds ratio; MSA, metropolitan statistical area; OR, odds ratio; POS, point of service; PPO, preferred provider organization; ROC, receiver operating characteristic; RT, radiation therapy.

[a]The influence of MSA was summarized by the MOR, which is the median ratio of the odds of contralateral prophylactic mastectomy between equivalent patients of 2 randomly selected MSAs (n=428).

Median ORs for MSA regions ranged from 1.42 for any dedicated breast imaging (ie, the odds of postoperative dedicated breast imaging between 2 patients in different MSAs varied by a factor of 1.42) to 1.82 for PET/CT imaging, with similar findings in patients who had received RT and/or hormonal therapy. Figure 1 details the variation in adjusted rates of dedicated breast imaging by MSA region from the dedicated breast imaging model in Table 2.

In evaluating mean imaging use and intensities within MSA regions, proportions of patients receiving at least one dedicated breast image or at least one nonbreast tomographic image within each MSA region were described with box plots by age group (Figure 2A) and treatment cohort (Figure 2B). Mean nonbreast tomographic imaging intensity within MSA regions was also described with box plots by age group (Figure 3A) and treatment cohort (Figure 3B).

Figure 2A displays wider variation in imaging use in younger age groups, with median proportions of women receiving nonbreast tomographic imaging within MSA regions decreasing slightly with age. Among treatment cohorts (Figure 2B), the variation between MSA regions displayed wide variation across regions for each patient treatment cohort.

The median MSA's mean annualized number of nonbreast tomographic imaging examinations per imaged patient remained approximately 1 in all age groups (Figure 3B), with smaller interquartile ranges in older cohorts. Irrespective of treatment cohort (Figure 3B), the median MSA's mean annualized number of nonbreast tomographic imaging examinations per imaged patient ranged from approximately 0.5 to 1.5. Mean imaging intensity varied widely, with numerous outliers above the 75th percentile in each treatment cohort.

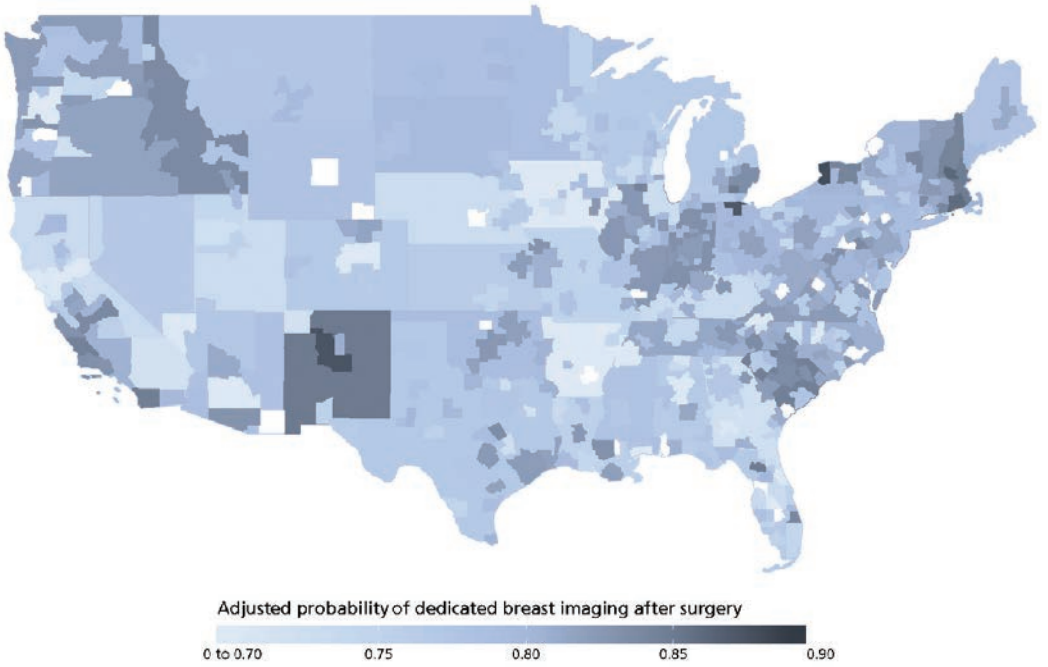

Figure 1. Adjusted probability of dedicated breast imaging in the 18 months after surgery by metropolitan statistical area.

Underlying Differences in Geographic Distribution of Stage II–III Breast Cancer

When 2010 SEER data for patients with breast cancer aged 18 to 44 years were grouped into Northeastern, North Central, South, and West regions used in the MarketScan data set, the variation between regions in the rate of stage IIA/B and IIIB breast cancers was not significant (n=28,957; *P*=.371).

Discussion

In this national assessment of postoperative imaging variations in patients with breast cancer who received care compatible with early-stage disease, we found wide geographic variation in imaging use and frequency between MSA regions for both dedicated breast imaging and nonbreast tomographic imaging, presumed to represent surveillance imaging for the detection of recurrent or metastatic disease (Figures 1–3). No MSA-level correlation was observed between rates of breast and nonbreast imaging.

Delivering appropriate screening while avoiding unnecessary postoperative imaging in the millions of US patients with breast cancer has significant clinical, ethical, and economic ramifications.[1] Oncology imaging costs are increasing at twice the rate of total cancer care, accounting for 4.6% of the $32.1 billion in Medicare cancer expenditures in 2009.[20–22]

Expert guidelines support routine mammography or, depending on age and other factors, dedicated breast MRI for all patients with a personal history of breast cancer.[2–6] Our study demonstrates a high geographic-based variability regarding whether patients actually receive dedicated breast imaging after treatment for a primary breast cancer.

On the other hand, other nonbreast surveillance imaging to detect recurrent or metastatic disease has consistently shown no benefit in terms of survival or quality of life for patients with stage I–III (nonmetastatic) disease.[8–13] A recently published meta-analysis of outcomes for patients with early-stage breast cancer showed that recurrences continued at a similar rate through 20 years and that the risk of distant metastasis ranged from 10% to 41%, correlating with the original T and N status.[23] Pursuing a surveillance strategy apart from dedicated breast imaging early after completion of primary therapy in early-stage cancer with low T and N status does not make sense, particularly when the patient may require symptom-driven imaging studies for 20 years after completion of 5 years of tamoxifen. Depending on treatment and geographic location, our study found that 18% to 46% of patients received high-cost tomographic imaging within the

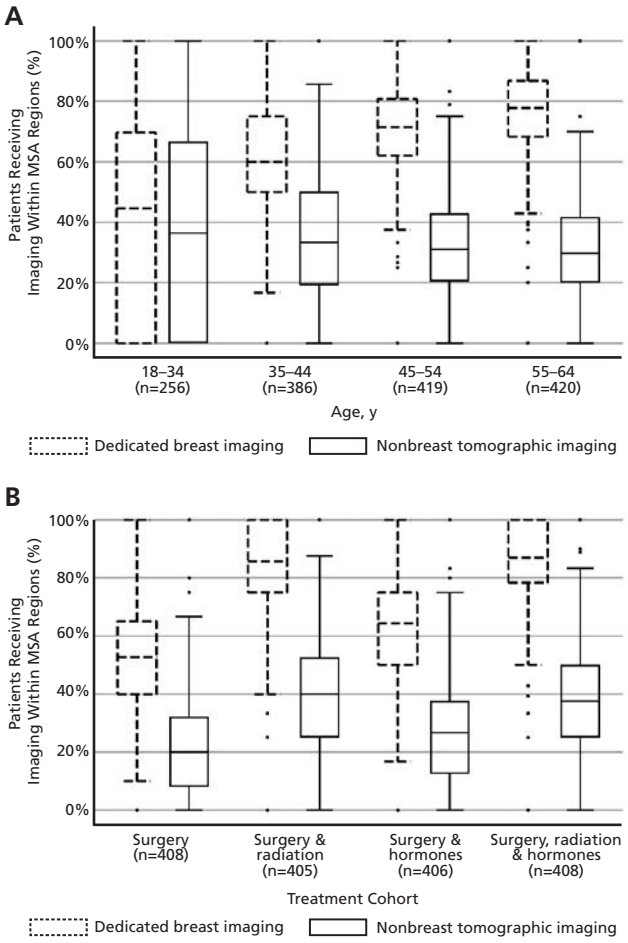

Figure 2. Proportion of patients imaged within metropolitan statistical area (MSA) regions by modality category, grouped by (A) age and (B) treatment cohort.

18 months after surgery. National data on patients with early-stage breast cancer diagnosed in 1998–2003 showed that 40% had at least one advanced imaging test (eg, CT or PET) in the 4 years after diagnosis.[24] Findings from recent smaller studies suggest even higher rates of nonbreast surveillance testing.[25,26] In some cases, young women may be subject to overly aggressive monitoring strategies because of the presumed risk of age rather than a specific genotype, a practice discouraged by oncology experts.[27]

Surveillance strategies can present medical and financial harms to patients. False-positives can result in unnecessary workup, which can in turn lead to patient anxiety and risk of additional procedures and radiation exposure.[28–33] As many as 0.4% of all cancers are estimated to be caused by radiation from imaging, with the time between radiation exposure and clinical detection of a cancer being ≥25 years in some cases.[34,35]

With the aim of improved cancer screening and follow-up, some systems of care have made significant efforts to coordinate care between primary care providers and oncologists, the results of which have yet to be determined.[36,37] Fear of cancer recurrence in certain patient populations may decrease recommended breast imaging activities or increase high-cost whole-body imaging in early-stage breast cancer, both potentially ameliorable through education.[38]

Limitations, Caveats, and Strengths

Staging information was unavailable, but care was taken to identify only patients with treatment consistent with early-stage disease. Many tumor and patient characteristics contribute to the overall perceived risk of future recurrence or contralateral malignancy, and thereby reflect the type of initial treatment, arguably more so than merely stage alone.[39–48]

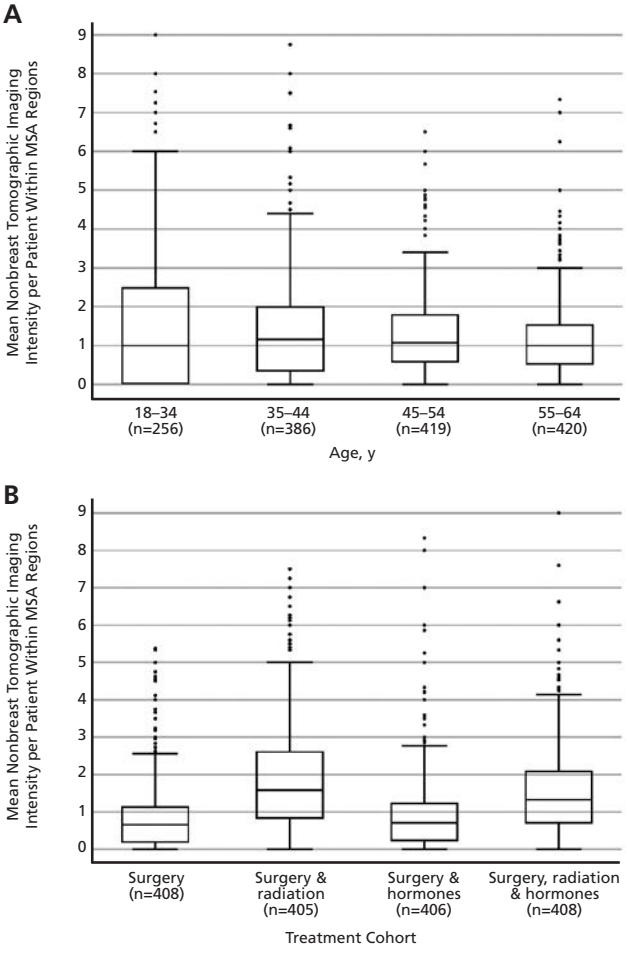

Figure 3. Mean patient nonbreast tomographic imaging intensity (annualized number of imaging examinations per imaged patient) within metropolitan statistical area (MSA) regions, grouped by (A) age and (B) treatment cohort.

Claims data do not provide information about patients' conditions leading to imaging, and therefore high-cost body imaging in some patients may have been indicated by symptoms and not simply represent whole-body surveillance scanning, or may have been conducted for reasons unrelated to cancer in some cases. We know of no reasons that these conditions would be unevenly distributed geographically, suggesting that our findings are likely relevant despite this limitation.

Conclusions

The large geographic variation we observed in rates of both postoperative breast imaging and high-cost imaging for detection of recurrent or metastatic disease suggests that some patients are not receiving beneficial screening and that high-cost imaging may not be targeted to the groups most likely to benefit. Some patients are likely receiving excessive amounts of high-cost whole-body imaging, which is not typically indicated in low-risk disease.

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