Impact of the Society of Surgical Oncology-American Society for Radiation Oncology Margin Guidelines on Breast-Conserving Surgery and Mastectomy Trends

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BACKGROUND: In 2014, the Society of Surgical Oncology and American Society for Radiation Oncology guidelines defined negative margin for stage I and II breast cancer as "no tumor on ink." We hypothesized that repeat operation rates have decreased since the guideline introduction and would be associated with changes in overall surgical trends.

STUDY DESIGN: The National Cancer Database was used to identify women who underwent initial breast-conserving surgery (BCS) for stage I and II breast cancer from 2004 to 2015.

RESULTS: Of 521,578 patients that underwent initial BCS, 82.7% had BCS alone and 17.3% had repeat operation: 67% with BCS followed by another BCS, 24% with BCS followed by unilateral mastectomy, and 9% with BCS followed by bilateral mastectomy (BM). The repeat operation rate decreased from 16.2% in 2004 to 14.0% in 2015 ($p < 0.01$). Breast-conserving surgery with repeat BCS decreased from 12.8% to 9.7%, and BCS followed by BM increased from 0.7% in 2004 to 1.9% 2013, then decreased to 1.4% in 2015. Trends for all surgical patients regardless of initial procedure showed a BCS rate of 64.0% in 2013 that increased to 67.6% in 2015. The BM rate increased from 4.6% in 2004 to 13.6% in 2013, then decreased to 12.8% in 2015 ($p < 0.05$). Adjusted multivariable regression found independent predictors of repeat operation to be diagnosis before 2014 (odds ratio [OR] 1.25), age younger than 50 years (OR 1.70), Her2neu receptor-positive tumors (OR 1.61), and lobular histology (OR 1.61).

CONCLUSIONS: Repeat operation rates are decreasing after 2014, which is also associated with a rise in BCS and decrease in BM rates. Dissemination of margin guidelines for early-stage breast cancer might be impacting overall surgical trends. (J Am Coll Surg 2019;229:104−114. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Optimal margin width for a negative margin in breast-conserving surgery (BCS) has been a long-debated topic. Positive margins are associated with increased locoregional recurrence in breast cancer. A meta-analysis of surgical margins and recurrence in early-stage breast cancer demonstrated that although increasing the distance threshold for positive margin was weakly associated with decreasing odds of local recurrence, the use of multimodality therapy completely negated this effect.[1] In the modern era of multimodality therapy for breast cancer, margin width is likely less important than other modalities, such as radiation or endocrine therapy, to decrease locoregional recurrence.

The publication of the Society of Surgical Oncology (SSO) and American Society for Radiation Oncology

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Abbreviations and Acronyms

ASTRO = American Society for Radiation Oncology
BCS = breast-conserving surgery
BM = bilateral mastectomy
Her2 = Her2neu receptor
HR = hormone receptor
NCDB = National Cancer Data Base
OR = odds ratio
SSO = Society of Surgical Oncology
UM = unilateral mastectomy

(ASTRO) margin guidelines for stage I to II breast cancer in 2014[2] standardized negative margins for invasive breast cancer as "no tumor on ink." These guidelines have been widely accepted and adopted in the US, with endorsement from national societies, such as the American Society of Clinical Oncology and the National Comprehensive Cancer Network, as well as pathology laboratories.[3-5] In addition, these guidelines have been widely accepted into practice. A recent nationwide survey of 866 pathology laboratories found that 94% routinely define positive margins as "tumor on ink."[6] The implementation of these guidelines has resulted in described reduction of re-excision rates of 4% to 6% at single institutions,[7-9] and up to 28% in one study.[10] A multi-institutional study of 252 providers from the American Society of Breast Surgeons mastery database demonstrated an absolute reduction in re-excisions by 3.7% after guideline publication, with a 13.8% decrease in re-excisions for close margins.[11] A survey study of 488 surgeons found that >60% endorsed no tumor on ink as an acceptable margin regardless of hormone receptor status of the tumor.[12] Studies have even shown that these decreased re-excision rates have significant potential impact on decreasing healthcare costs when applied widely.[13-15]

However, it is not clear if the margin guidelines have impacted surgical decision making, particularly for mastectomy. Re-excisions can lead to mastectomy, as patients might not have clear margins after a re-excision and might need a mastectomy to remove all disease. Patients can also choose mastectomy instead of BCS to avoid the uncertainty of a re-excision. Among patients who were told they needed mastectomy, one study showed that patients undergoing contralateral prophylactic mastectomy were 1.7 times as likely to have had a previous re-excision procedure compared with patients not undergoing contralateral prophylactic mastectomy.[16] A recent survey of patients found that patient-reported rates of BCS as final operation went from 52% to 65%, and bilateral mastectomy (BM) decreased from 21% to 16%.[12] However, no studies have examined BCS and mastectomy rates from a large oncology data set and compared trends around the time of margin guideline publication with those of the past decade. To assess practice patterns across the US, we used the National Cancer Data Base (NCDB) to examine the impact of the SSO-ASTRO guidelines on BCS and mastectomy rates. The NCDB does not contain a specific variable for re-excision operation; however, time to first and definitive operation is included. Using this time to operation variable as a surrogate for "re-excision" or what we term *repeat operation*, we examined national rates of repeat operations after initial BCS in stage I to II breast cancer. We then examined overall surgical trends for BCS, unilateral mastectomy (UM) and BM during the study period. We hypothesized that repeat operation rates have decreased nationally after publication of the SSO-ASTRO consensus guidelines, and would be associated with a shift in overall trends for BCS and mastectomy.

METHODS

Data source

The NCDB is a joint project of the American Cancer Society and the American College of Surgeons Commission on Cancer that captures approximately 70% of new cancer diagnoses nationwide. Data are de-identified and compliant with the Health Insurance Portability and Accountability Act.[17] Our IRB granted a waiver for approval for this study as the collected information was de-identified, no protected health information was reviewed, and the analysis was retrospective. The American Cancer Society and Commission on Cancer have not verified and are not responsible for the methodology used in this study or the conclusions drawn by the investigators.

Patient selection criteria

The 2015 breast cancer Participant User File of the NCDB was used to identify women with unilateral, American Joint Committee on Cancer 7th edition[18] stage I to II breast cancer from 2004 to 2015. Our study was limited to stage I to II breast cancer because this was the population addressed in the SSO-ASTRO margin guidelines. To capture repeat operation rates, inclusion criteria required a biopsy-proven diagnosis of breast cancer and BCS as the initial operation. The NCDB defines a diagnostic biopsy as incisional, needle, or aspiration biopsy. Patients diagnosed through an excisional biopsy were excluded, as were patients with positive margins at definitive operation (positive margins defined as

microscopic or macroscopic residual tumor). Neoadjuvant therapy patients and those with missing information on staging or operation, as well as those not treated at the reporting facility, were also excluded from the study. There were 521,578 women eligible for analysis (Fig. 1) after exclusions.

Patient covariates

Patient covariates included age (younger than 50 years, 50 to 70 years, older than 70 years), race, comorbidity index, insurance status, and socioeconomic status. Facility covariates included type of cancer center (community, comprehensive, academic, or integrated network), and region of the country. Tumor covariates included stage, grade, histology (ductal, lobular, mixed), and subtype (hormone receptor [HR]$^{+}$Her2neu receptor [Her2]$^{-}$, HR^{-}Her2^{-}, HR^{+}Her2^{+}, HR^{-}Her2^{+}). Subtype data are only available for years 2010 to 2015, as Her2 was not included as a variable in the NCDB until 2010.

Repeat operation

Repeat operation was defined using the NCDB variable of time from diagnosis to date of first operation and time from diagnosis to date of definitive operation. If the time to first operation was less then the time to definitive operation, then a repeat operation occurred. These patients who had either UM or BM as definitive operation were assumed to have BCS as their first operation. Those patients who had BCS as their definitive operation were assumed to have BCS as their first operation. If time to first operation was the same as time to definitive operation, then no repeat operation occurred. All patients had to have had their definitive operation within 90 days. The type of first operation is not specifically defined in the NCDB, nor is the number of repeat operations. Stringent selection criteria were used in an attempt to ensure that the repeat operations captured were truly repeat cancer operations (Fig. 1). This methodology has been used previously to define repeat operation in the NCDB.[19]

Statistical analysis

All covariates were analyzed as categorical variables. Patient, facility, and tumor characteristics were compared between patients undergoing repeat operations and no repeat operations after initial BCS using chi-square tests. Trends in repeat operation rates after initial BCS from 2004 to 2015 were examined for the entire cohort, as well as for the subgroups identified with higher rates of repeat operation. We compared operation trends for stage I to II patients undergoing initial BCS with those for all stage I to II patients from 2004 to 2015, regardless of their first operation. Univariable and multivariable logistic regression were used to examine the odds of undergoing repeat operation compared with BCS without repeat operation, adjusting for patient factors (age, race, comorbidity index, insurance, and socioeconomic status), facility factors (type of cancer center and location), and tumor factors (stage, grade, histology, and subtype). Odds ratio (OR) >1 signified higher odds of repeat operation. All CIs were reported at a 95% significance

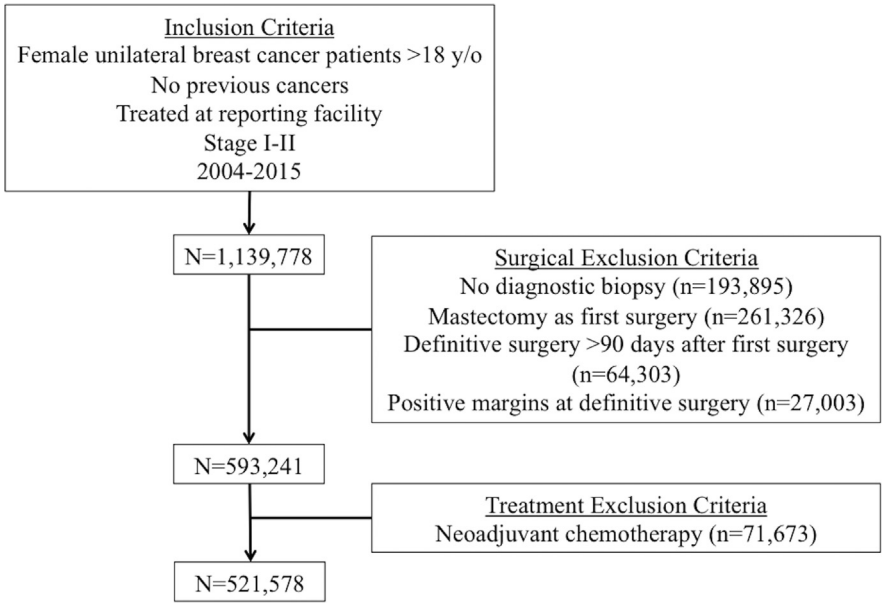

Figure 1. Selection criteria.

level. All p values <0.05 were considered statistically significant. All analysis was performed using SPSS software, version 19.0 (IBM Corp).

RESULTS

Cohort characteristics

There were 521,578 patients that underwent initial BCS for unilateral American Joint Committee on Cancer 7th edition stage I to II biopsy-proven breast cancer at 1,335 facilities and 90,245 (17.3%) had a repeat operation. Of those who had repeat operation, 60,703 (67.3%) had another BCS, 21,402 (23.7%) had UM, and 8,140 (9.0%) had BM. Patients that had repeat operations after initial BCS were more likely to be younger (24.9% vs 17.1% younger than 50 years; $p < 0.01$), have private insurance (58.8% vs 51.7%; $p < 0.01$), stage II disease (37.0% vs 25.8%; $p < 0.01$), grade 3 disease (25.6% vs 22.9%; $p < 0.01$), and lobular histology (10.2% vs 6.9%; $p < 0.01$) than patients who did not undergo repeat operation (Table 1).

Surgical trends in stage I to II breast cancer undergoing initial breast-conserving surgery

Patients undergoing initial BCS without repeat operation decreased from 83.9% in 2004 to 81.3% in 2011, slightly increased to 82.8% in 2013 and continued to increase to 86.0% in 2015. Patients undergoing repeat BCS after initial BCS increased from 10.7% in 2004 to 12.8% in 2011, and decreased to 9.7% in 2015. Patients undergoing repeat operation with UM after initial BCS decreased from 4.8% in 2004 to 2.9% in 2015. Patients undergoing repeat operation with BM after initial BCS increased from 0.7% in 2004 to 1.9% in 2013, then decreased to 1.4% in 2015 (all, $p < 0.01$) (Fig. 2A). There was an absolute reduction of 3.6% in repeat operation after initial BCS between 2004 to 2013 and 2014 to 2015. Repeat operation trends in women younger than 50 years were similar to overall trends, with BCS after initial BCS increasing from 13.8% in 2004 to 14.7% in 2010 and decreasing to 11.7% in 2015 and BM after initial BCS increasing from 2.2% in 2004 to 5.4% in 2013 then decreasing to 4.3% in 2015 ($p < 0.01$) (data not shown).

When repeat operation trends were examined by facility, there was a downward shift in repeat operation rates from 2014 to 2015 (post-guideline) compared to 2004 to 2013 (pre-guideline) (Fig. 3).

Surgical trends for breast-conserving surgery and mastectomy

Surgical trends of all patients that underwent operations for stage I to II breast cancer, including those that underwent initial UM or BM, were also examined for 1,110,654 patients during the same timeframe. The rate of BCS decreased from 67.5% in 2004 to 63.8% in 2012, then increased to 67.6% in 2015. The rate of UM steadily decreased from 27.9% in 2004 to 19.6% in 2015. The rate of BM increased from 4.6% in 2004 to 13.6% in 2013, and then decreased to 12.8% in 2015 (all, $p < 0.01$) (Fig. 2B).

Subgroup analysis of patients with the highest repeat operation rates after initial breast-conserving surgery

The subgroups that had the highest rates of repeat operations after initial BCS were women younger than 50 years (23.4%), those with lobular histology (23.6%), HR-Her2$^+$ subtype (25.3%), and stage II disease (23.1%) Repeat operation rates for each of these subgroups decreased after 2013 (all, $p < 0.01$). In all subgroups, the greatest rate of decrease was from 2013 to 2015 (Fig. 4A). The absolute decrease in repeat operation after initial BCS was 2.8% for age younger than 50 years, 4.9% for lobular histology, 2.1% for stage II, and 6.0% for HR-Her2$^+$ subtype between 2004 to 2013 and 2014 to 2015.

When examining the rates of BM after initial BCS for these subgroups, all subgroups had a rise in rates of BM after initial BCS until 2012 to 2013, followed by a decrease by 2015 ($p < 0.01$) (Fig. 4B).

Predictors of repeat operation after initial breast-conserving surgery

Multivariable analysis examining predictors of repeat operations after initial BCS was done, adjusting for patient, tumor, and facility factors. Year of diagnosis before 2014 (OR 1.25; 95% CI 1.22 to 1.27), younger age (OR 1.69; 95% CI 1.65 to 1.74 for younger than 50 years; OR 1.27; 95% CI 1.24 to 1.30 for 50 to 70 years), Asian race (OR 1.27; 95% CI 1.22 to 1.33), stage II disease (OR 1.52; 95% CI 1.50 to 1.55), lymphovascular invasion (OR 1.35; 95% CI 1.32 to 1.39), Her2$^+$ subtype (OR 1.26; 95% CI 1.21 to 1.31 for HR$^+$Her2$^+$; OR 1.60; 95% CI 1.52 to 1.69 for HR$^-$Her2$^+$), and lobular histology (OR 1.64; 95% CI 1.59 to 1.68) were the strongest factors associated with increased odds of repeat operation after initial BCS (Table 2).

DISCUSSION

In this nationwide facility-based study of more than 500,000 patients who underwent initial BCS for early-stage breast cancer, we saw an absolute decrease in repeat operation of 3.6% since publication of the SSO-ASTRO

Table 1. Cohort Characteristics

Characteristic	BCS without repeat operation (n = 431,333)		BCS with repeat operation (n = 90,245)		p Value
	n	%	n	%	
Age					<0.01
Younger than 50 y	73,648	17.1	22,502	24.9	
50–70 y	239,935	55.6	49,421	54.8	
Older than 70 y	117,750	27.3	18,322	20.3	
Race					<0.01
Caucasian	358,938	83.2	72,857	80.7%	
African American	37,867	8.8	9,144	10.1%	
Hispanic	20,633	4.8	4,565	5.1%	
Asian	11,578	2.7	3,189	3.5%	
Insurance					<0.01
Private	223,202	51.7	53,095	58.8	
Medicare	177,327	41.1	30,363	33.6	
Medicaid	19,492	4.5	4,602	5.1	
Uninsured	6,017	1.4	1,318	1.5	
Cancer center type					<0.01
Community	42,361	9.8	7,742	8.6	
Comprehensive	209,499	48.6	40,891	45.3	
Academic	123,978	28.7	27,921	30.9	
Integrated network	46,907	10.9	10,345	11.5	
Cancer center location					<0.01
Northeast	95769	22.2	21500	23.8	
Midwest	108968	25.3	22828	25.3	
South	142422	33.0	27951	31.0	
West	75586	17.5	14620	16.2	
Stage					<0.01
I	320,031	74.2	56,891	63.0	
II	111,302	25.8	33,354	37.0	
Lymphovascular invasion					<0.01
No	213,448	49.5	39,892	44.1	
Yes	28,375	6.6	8,805	9.8	
Unknown (2004–2009)	189,510	43.9	41,648	46.1	
Molecular subtype					<0.01
$HR^{+}Her2^{-}$	215,078	49.9	41,714	46.2	
$HR^{-}Her2^{-}$	24,956	5.8	4,372	4.8	
$HR^{+}Her2^{+}$	13,379	3.1	3,611	4.0	
$HR^{+}Her2^{-}$	5,734	1.3	1,943	2.2	
Unknown (2004–2009)	172,186	39.9	38,605	42.8	
Grade					<0.01
1	128,211	29.7	20,576	22.9	
2	183,878	42.6	40,731	45.1	
3	98,712	22.9	23,068	25.6	
Histology					<0.01
Ductal	339,191	78.6	66,527	73.7	
Lobular	29,902	6.9	9,221	10.2	
Mixed	59,212	13.7	13,781	15.3	

BCS, breast-conserving surgery; Her2, Her2neu receptor; HR, hormone receptor.

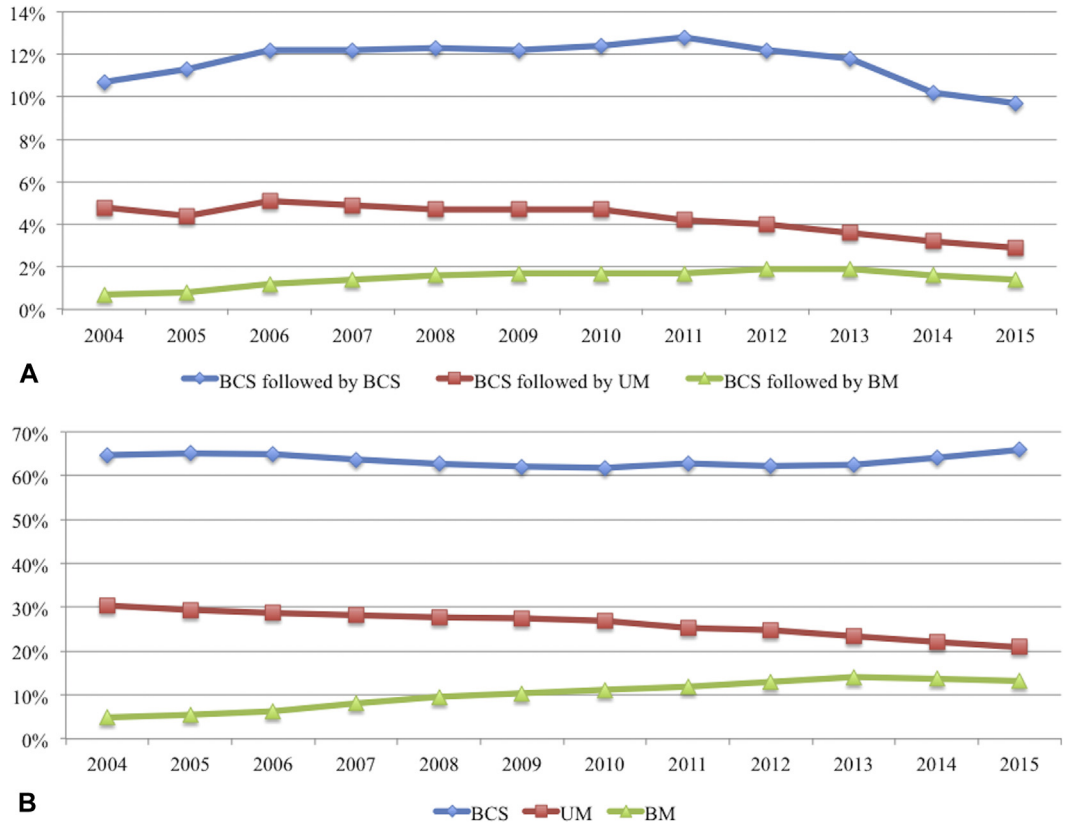

Figure 2. Operation rates over time, 2004 to 2015. (A) Repeat operation for patients undergoing initial breast-conserving surgery (BCS) and (B) overall operation trends for stage I and II breast cancer patients. BM, bilateral mastectomy; UM, unilateral mastectomy.

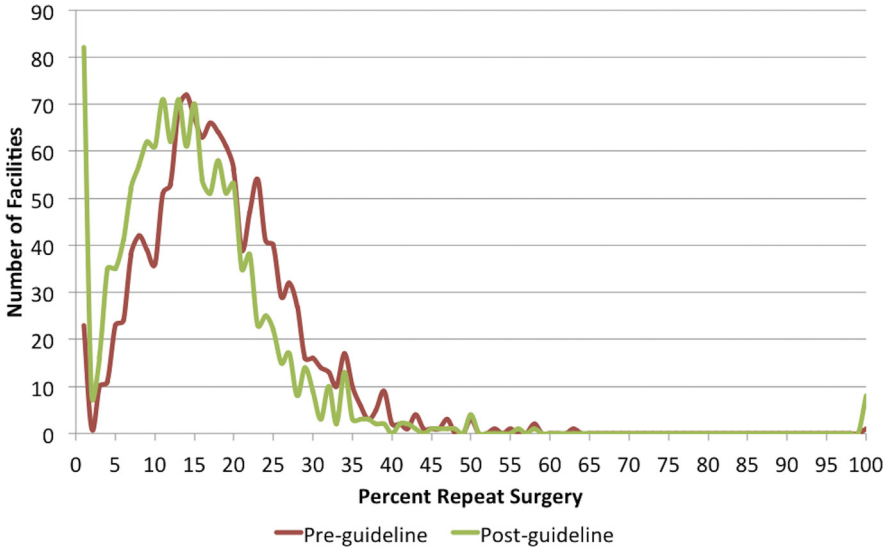

Figure 3. Repeat operation rates pre- (2004 to 2013) and post- (2014 to 2015) Society of Surgical Oncology and American Society for Radiation Oncology guideline publication by facility.

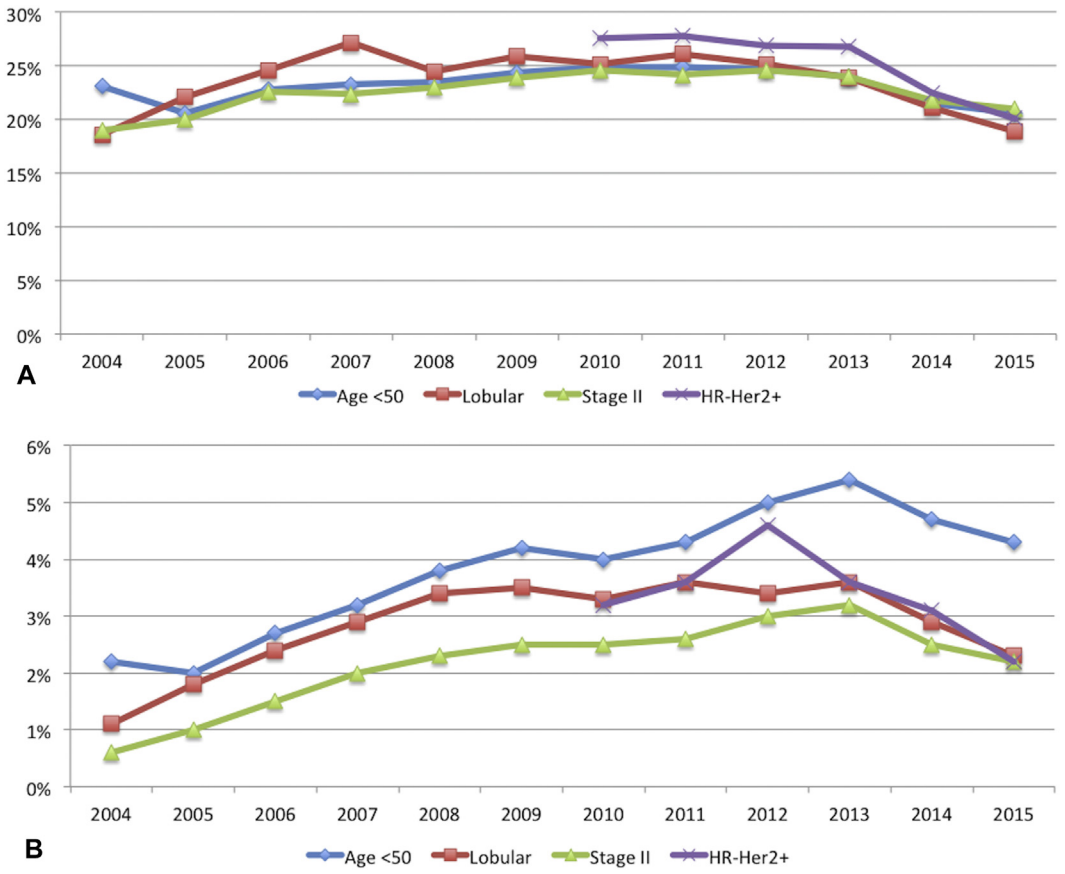

Figure 4. Repeat operation rates stratified by tumor characteristics, 2004 to 2015. (A) Overall repeat operation rates in patients undergoing initial breast-conserving surgery (BCS) and (B) rates of patients undergoing bilateral mastectomy after initial BCS. $HR^{-}Her2^{+}$, hormone receptor negative-Her2neu receptor-positive.

margin guidelines. In addition, we saw an increase in BCS rates and a slight decrease in BM rates when we examined all patient regardless of whether they underwent BCS as initial operation or not. Although our study can only show an association between the margin guidelines and changes in BCS and mastectomy rates, the absence of any other clinical trial or large study on margins during the same time period makes it more likely that these trends have some link to the dissemination of the SSO-ASTRO margin guidelines.

Our study is not the first to show the impact of the SSO-ASTRO guidelines on repeat or re-excision operation. Rosenberg and colleagues[8] reported on the Memorial Sloan Kettering experience, which demonstrated a 6% decrease in re-excision for negative margins and a 7% decrease in re-excision for close margins after guideline publication. A study of the Cedars-Sinai experience of 845 patients by Chung and colleagues[9] found a 7% decrease in re-excision rates after guideline publication, and the re-excision rate for negative margins decreased from 30% to 22%. Patten and colleagues[7] analyzed 954 patients at a single institution and reported a significant decrease in the close/positive margin rate after the margin guidelines from 30% to 10%, although this was associated with only a 4% decrease in re-excision rate and did not reach statistical significance. Heelan Gladden and colleagues[20] examined 863 patients and found no significant difference before and after guideline implementation (12% vs 11%). A study of 257 patients by Bhutiani and colleagues[10] found a 28% decrease in re-excision rates after guideline implementation, although the mean tumor size was also smaller in the post group. A retrospective multi-institutional study of 252 surgeons in the American Society of Breast Surgeons mastery database also demonstrated a 3.7% decrease in re-excisions after publication of the guidelines, similar to our experience. In the American Society of Breast Surgeons mastery study, there was also a 13.8% decrease in re-excisions for close margins.[11] This study also showed wide variation in practice patterns in re-excision rates among surgeons, ranging anywhere

Table 2. Multivariable Regression Predicting Repeat Operation after Initial Breast-Conserving Surgery

Characteristic	Univariate OR	p Value	Multivariate OR	p Value
Year				
2014–2015	Reference	—	Reference	—
2004–2013	1.31 (1.28–1.33)	<0.01	1.25 (1.22–1.27)	<0.01
Age				
Younger than 50 y	Reference	—	Reference	—
50–70 y	1.32 (1.30–1.35)	<0.01	1.27 (1.24–1.30)	<0.01
Older than 70 y	1.96 (1.92–2.01)	<0.01	1.69 (1.65–1.74)	<0.01
Race				
Caucasian	Reference	—	Reference	<0.01
African American	1.19 (1.16–1.22)	<0.01	1.11 (1.08–1.14)	0.40
Hispanic	1.09 (1.06–1.13)	<0.01	1.01 (0.98–1.05)	<0.01
Asian	1.36 (1.30–1.41)	<0.01	1.27 (1.22–1.33)	<0.01
Insurance				
Private	Reference	—	Reference	—
Medicare	0.72 (0.71–0.73)	<0.01	0.91 (0.89–0.93)	<0.01
Medicaid	0.99 (0.96–1.03)	0.66	0.93 (0.90–0.96)	<0.01
Uninsured	0.92 (0.87–0.98)	0.01	0.85 (0.80–0.90)	<0.01
Cancer center type				
Community	Reference	—	Reference	—
Comprehensive	1.07 (1.04–1.10)	<0.01	1.06 (1.04–1.09)	<0.01
Academic	1.23 (1.20–1.27)	<0.01	1.16 (1.13–1.20)	<0.01
Integrated	1.21 (1.17–1.25)	<0.01	1.20 (1.16–1.24)	<0.01
Cancer center location				
Midwest	Reference	—	Reference	—
Northeast	1.07 (1.05–1.09)	<0.01	1.03 (1.01–1.05)	<0.01
South	0.94 (0.92–0.96)	<0.01	0.93 (0.91–0.94)	<0.01
West	0.92 (0.90–0.95)	<0.01	0.91 (0.88–0.93)	<0.01
Stage				
I	Reference	—	Reference	—
II	1.69 (1.66–1.71)	<0.01	1.52 (1.50–1.55)	<0.01
Lymphovascular invasion				
No	Reference	—	Reference	—
Yes	1.67 (1.62–1.71)	<0.01	1.35 (1.32–1.39)	<0.01
Molecular subtype				
$HR^{+}Her2^{-}$	Reference	—	Reference	—
$HR^{-}Her2^{-}$	0.90 (0.87–0.93)	<0.01	0.81 (0.78–0.84)	<0.01
$HR^{+}Her2^{+}$	1.39 (1.34–1.45)	<0.01	1.26 (1.21–1.31)	<0.01
$HR^{+}Her2^{-}$	1.74 (1.66–1.84)	<0.01	1.60 (1.52–1.69)	<0.01
Grade				
1	Reference	—	Reference	—
2	1.37 (1.35–1.40)	<0.01	1.26 (1.24–1.28)	<0.01
3	1.45 (1.42–1.48)	<0.01	1.22 (1.19–1.25)	<0.01
Histology				
Ductal	Reference	—	Reference	—
Lobular	1.57 (1.53–1.61)	<0.01	1.64 (1.59–1.68)	<0.01
Mixed	1.21 (1.11–1.31)	<0.01	1.25 (1.23–1.28)	<0.01

Her2, Her2neu receptor; HR, hormone receptor; OR, odds ratio.

from 0% to 100% pre-guideline and 0% to 54% post-guideline. A survey study by Morrow and colleagues[12] of patients and surgeons in cancer registries in Georgia and Los Angeles found a 16% decrease in repeat operations after initial BCS between 2013 and 2015. This study also noted that surgeons with a higher breast cancer volume were more likely to adopt the margin guidelines. In addition, a 2015 survey of American Society of Breast Surgery members found 92% of respondents to be familiar with the guidelines[21] and a 2018 survey of pathology laboratory practices demonstrated that 94% define positive margins as "tumor on ink."[6] Our findings are in line with these studies and confirm that the SSO-ASTRO margin guidelines have impacted practices across the country. The strength of our study is the fact that our study includes more than 1,300 facilities and a large volume of patients.

Our study also found that patients younger than 50 years old, those patients with lobular carcinomas, American Joint Committee on Cancer Stage II disease, and $HR^{-}HER2neu^{+}$ tumors had repeat operation rates of approximately 25%. There was an absolute decrease of 2% to 6% across these groups after the guidelines were published. Other studies have shown that these same tumor factors have been associated with tumor-positive margins, so it is not surprising that these groups would have the highest repeat operation rates. A retrospective study of lobular cancers found that tumor size and multifocality were associated with positive surgical margins after initial BCS and that positive, but not close, surgical margins were associated with increased locoregional recurrence.[22] A large national study from The Netherlands found positive margins, young age, multifocality, lobular subtype, tumor size >2 cm, grade and $Her2^{+}$ status, and presence of ductal carcinoma in situ to be associated with positive margins after BCS.[23] However, in the Dutch experience, re-excision for focally positive margins, and associated with decreased ipsilateral breast recurrence, was not associated with improved disease-free or overall survival.[24] A retrospective multi-institutional study out of New England found that in addition to positive margins, non-luminal A subtypes, younger age, and nodal disease have all been associated with increased odds of locoregional recurrence after BCS.[25] We are not able to examine locoregional recurrence or long-term oncologic outcomes in our study because the NCDB does not contain local recurrence information. Additionally, we do not have long enough follow-up to examine how the guidelines have impacted other outcomes, such as overall survival.

Our study noted a subtle increase in repeat operation rates in African-American and Asian patients that persisted on multivariate analysis. None of the aforementioned single-institutional studies on margin re-excisions specifically analyzed race. A few previous NCDB studies have consistently found that African-American and Asian patients have higher repeat operation rates[19] and that African Americans are more likely to have persistently positive margin status after definitive operation.[26] An analysis using Surveillance, Epidemiology, and End Results Program data found that compared with Caucasian race, African-American race was associated with less mastectomy and other race (including Asian race) was associated with more mastectomy.[27] These racial differences in surgical trends cannot be fully explained by these large data registries and additional studies are needed to better understand the association between race and type and number of breast operations.

Similar to a previous study from our group, there is still substantial variation in repeat operation rates across facilities. In our previous study, rates varied from 14% to 30%, and our study shows rates of 18.1% to 14.5% after the guidelines were published.[19] Tracking of re-excision rates has long been debated as a quality measure, but concerns about the negative consequences of instituting this measure have prevented this.[28] Development of devices to test margins intraoperatively and use of different technique to assess margins can help decrease high re-excision rates at those institutions with higher than average repeat rates. Simple tracking of re-excision rates by physicians within institutions might be just as effective in lowering rates as purchasing a new device. It will be up to the surgical community to decide what the highest acceptable rate of re-excision should be.

Limitations of our study are due mainly to the retrospective nature of the study and the data set. Although the NCDB captures a large proportion of the country, it is not a true population-based data set. It collects data on centers with Commission on Cancer accreditation only. Additionally, there are many clinical factors that can influence repeat rates that we do not have access to with the NCDB. The use of MRI, the number of repeat operations, repeat imaging for second opinions, multifocality of tumors, and technique to assess margins are all factors that could influence repeat operation rates. Our definition of repeat operation is not exact, as we do not know with certainty the intent or rationale of the repeat operation, only suggest that the most likely reason is related to margin positivity. Although we have attempted to exclude excisional biopsies in our selection criteria, it might not be possible to completely eliminate them in our selection criteria, as it is not a specifically coded field in the NCDB. This might contribute a degree of selection

bias to our data set. Additionally, margins are defined as positive or negative by the data set, but the NCDB does not specify what margin distance is considered positive or negative. Different surgeon and institutional practices, such as the use of intraoperative margins or sending separate shave margins cannot be accounted or controlled for in our study and can contribute to institutional variability.

CONCLUSIONS

Rates of repeat operation after BCS are decreasing, which correlates with the implementation of the SSO-ASTRO margin guidelines of "no tumor on ink" published in 2014. Additionally, rates of repeat operation with BM after initial BCS are decreasing, starting in 2014. These trends are reflected in overall operation rates of BM plateauing and a rise in BCS in all patients with stage I to II breast cancer. It appears that the SSO-ASTRO margin guidelines are contributing to changing surgical trends for early-stage breast cancer.

Author Contributions

Study conception and design: Kantor, Yao
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Analysis and interpretation of data: Kantor, Pesce, Kopkash, Barrera, Winchester, Kuchta, Yao
Drafting of manuscript: Kantor, Pesce, Kopkash, Barrera, Winchester, Yao
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Discussion

DR INGRID MESZOELY (Nashville, TN): Margin status remains a nemesis for surgeons in nearly all cancer procedures, given its association with risk of recurrence and poorer outcomes. Breast cancer is no exception. The goal of a negative margin often results in reoperation including re-excision or unilateral or bilateral mastectomy, frequently leading to increased surgeon frustration, increased patient anxiety, possible decrease in optimal cosmetic outcome, and increase in health care expenditure.

When the National Surgical Adjuvant Breast and Bowel Project-B06 was published in 1989, the study that demonstrated that mastectomy provided no survival benefit over breast conservation in women with invasive breast cancer, the definition of a negative margin was "no tumor on ink." Since then, there has been significant confusion and inconsistent definitions of what constitutes a negative margin from institution to institution and even surgeon to surgeon, until the Surgical Oncology–American Society for Radiation Oncology (SSO/ASTRO) consensus guideline was published in 2014. Based on systematic review of the literature, the guideline states "no tumor on ink" is an appropriate margin.

Since the guideline publication, multiple studies have shown the impact of the SSO/ASTRO guidelines, with an absolute reduction in re-excision rates of 3.7% to 28%. In addition, the study published by Morrow and colleagues in *JAMA Oncology* in 2017, using Surveillance, Epidemiology, and End Results data with 7,000 patients, showed similar trends, with an increase in lumpectomy rates and a decrease in unilateral and bilateral mastectomies as the final surgical procedure between the years 2013 and 2015.

This review from the National Cancer Database (NCDB) representing more than 500,000 patients from the Commission on Cancer accredited sites, of whom 90,000 underwent reoperation, is the largest study to date. As in earlier studies, it confirmed that the consensus guidelines have influenced reoperation rates, although somewhat more modestly, with an absolute reduction of 3.6%. This study also confirmed that patients are increasingly likely to undergo re-excision and commit to breast-conserving surgery (BCS) vs mastectomy, whether unilateral or bilateral, as a definitive surgical procedure for stage I and stage II breast cancers. These trends suggest that there may be increasing confidence in the effectiveness of breast conservation in an era in which the definition of an adequate margin has reached a consensus. We could extrapolate from this that as we develop clear consensus guidelines in the practice of surgery, there will be more consistency in practice patterns, and patients will subsequently have more confidence in our recommendations.

I noticed that the trends of decrease in lumpectomy re-excisions and decrease in mastectomies seem to begin before the actual publication of the guidelines. Can you comment on causality vs association? Why do you think there was such a rapid adoption of these guidelines compared with other practice-changing breakthroughs such as sentinel lymph node biopsy and American College of Surgeons Oncology Group Z-011, which appeared to have taken many years before most practices considered this standard of care? Who do you believe is the driving force behind choosing re-excision vs mastectomy after a positive margin is identified by lumpectomy? Is it patients or is it surgeons? Are surgeons, with the recent guideline changes, more confident about achieving appropriate margins and therefore encouraging patients to commit to BCS as opposed to mastectomy?

DR KATHARINE YAO (Chicago, IL): As has been mentioned with many NCDB papers, this is a trend and an association, not necessarily a causation that we are showing with our data. There could be other factors responsible for why we are seeing a plateau, if not a decrease, in bilateral mastectomy rates.

The first question asked about the trend, and it seems to be occurring before actual publication of the guidelines. I think there are several reasons for that. There was a publication of a paper in *JAMA* by a group that looked at re-excision rates across several different medical centers and several different surgeons, along with an editorial published in 2012 by Dr Monica Morrow, and I think that raised a lot of awareness for surgeons about re-excision rates, and probably a lot of surgeons and centers started to focus on their re-excision rate after that paper came out. Also, the SSO/ASTRO guidelines were presented in October 2013, and actually, the official press release was in February 2014. I think