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Surgical Management of Lobular Carcinoma in Situ: Analysis of the National Cancer Data Base

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Abstract

Background—Current guidelines recommend counseling on risk reduction strategies, including lifestyles modification, endocrine therapy, and bilateral mastectomy, for patients with classic-type LCIS detected on core biopsy or surgical excision.¹ Importantly, current diagnosis and treatment guidelines for classic-type LCIS do not include unilateral mastectomy for primary treatment or risk-reduction.² Prior studies reporting national practice patterns suggest increasing use of mastectomy for management of LCIS with considerable variation by geographic region. However, these studies did not distinguish between unilateral and bilateral mastectomies. We sought to investigate national practice patterns and factors associated with unilateral mastectomy.

Methods—We used the National Cancer Database to identify women diagnosed with LCIS from 2004 to 2013. We used descriptive statistics to describe surgical treatment and multinomial logistic regression to identify temporal, patient and facility-level factors associated with receipt of unilateral and bilateral mastectomy.

Results—We identified 30,105 women with LCIS; 5.4% received no surgery, 84.8% surgical excision, 4.0% unilateral mastectomy, and 5.1% bilateral mastectomy. On adjusted analysis, young age, white race, having insurance, greater comorbidity, and geographic region ($p < 0.001$) were associated with receipt of both unilateral and bilateral mastectomy. Additionally, more recent year of diagnosis was associated with receipt of bilateral mastectomy. Unilateral mastectomy rates within geographic regions ranged from 2.7% in New England to 8.0% in the South.

Conclusions—Nearly as many patients underwent unilateral (4%) as bilateral mastectomy (5.1%), representing inappropriate care. These findings highlight an opportunity to reduce unnecessary care through improved provider and patient education regarding optimal management of LCIS.

Introduction

With the growing use of screening mammography, the incidence of lobular carcinoma in situ (LCIS) has increased in recent years.³ Commonly detected incidentally during needle biopsy

for a separate indication,^{4–7} classic-type LCIS is not considered a precursor lesion. However, LCIS is accepted to be an indicator of increased risk of malignancy; women diagnosed with LCIS have up to a 10-fold greater likelihood of developing breast cancer compared to the general population.^{8,9}

Current National Comprehensive Cancer Network (NCCN) guidelines recommend counseling on risk reduction strategies to reduce life-time risk of breast cancer for patients with classic-type LCIS detected on core biopsy or surgical excision.¹⁰ Accepted approaches include lifestyle modification (exercise, weight control, and limiting alcohol consumption), endocrine therapy, and bilateral mastectomy.¹ Importantly, current diagnosis and treatment guidelines for classic-type LCIS do not include unilateral mastectomy for primary treatment or risk-reduction.² While surgical excision is recommended for all patients with pleomorphic-type LCIS or LCIS that is non-concordant with imaging, further surgery for classic-type LCIS is not required if concomitant ductal carcinoma in situ or invasive carcinoma is not detected.

Prior studies reporting national practice patterns suggest increasing use of mastectomy for management of LCIS, with considerable variation by geographic region.³ However, this analysis did not distinguish between receipt of unilateral and bilateral mastectomy, making it difficult to assess whether the use of mastectomy in women with LCIS is appropriate for risk reduction or represents inappropriate care. The goal of the current investigation is describe the surgical treatment of LCIS using a nationally representative dataset and identify patient and facility-level factors associated with unilateral mastectomy.

Methods

Data Source and Cohort Selection

The National Cancer Data Base (NCDB) is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. It is a registry-based database that includes over 70% of newly diagnosed cases in the United States and Puerto Rico. Trained registrars abstract data from the medical records at each of approximately 1400 facilities across the U.S. using a standardized abstraction manual.¹¹ Registrars are required to follow their patients from diagnosis until death regardless of where they receive their follow-up care. Women were included in our study if they had a new histologic diagnosis of LCIS from 2004 to 2013 (n=44,646). We excluded men (n=147). We also excluded women with a prior history of malignancy (n=13,514), those who underwent surgery more than 120 days after the LCIS diagnosis (n=565), and those for whom definitive surgical management was unknown (n=315). The final sample size was 30,105 patients (Figure 1).

Measures

Our primary outcome was the type of definitive surgery performed as part of first course treatment. We categorized the NCDB provided surgical procedure codes into: 1) no surgery (code 00), 2) surgical excision (codes 20–24), 3) unilateral mastectomy (codes 30, 40, 41, 43–46, 50, 51, 53–56, 60, 61, 64–67, 70, 71, 80), and 4) bilateral mastectomy (codes 42, 47–

49, 52, 57–59, 62, 63, 68, 69, 72–76).¹² We additionally evaluated whether patients underwent removal of lymph nodes, and whether they received endocrine therapy. Patient demographics included year of diagnosis, age, race, insurance status, and Charlson Comorbidity Index. System-level factors included facility type and geographic region (West, Midwest, South, New England, and South Atlantic).

Statistical Analysis

We used descriptive statistics to summarize demographic characteristics and trends in first course of surgical treatment for women diagnosed with LCIS during the study period. We assessed for differences in patients characteristics across the defined categories of definitive surgery using Chi square tests. A multinomial logistic regression model was then used to identify temporal, patient and facility-level factors associated with receipt of unilateral mastectomy versus no surgery/surgical excision, and bilateral mastectomy versus no surgery/surgical excision. Analyses were performed using Stata 12.1 (StataCorp, College Station, TX).

This project is considered to be exempt by the University of Wisconsin Institutional Review Board.

Results

Overall, women with LCIS were a median 52 years (range 21–90) of age. 85.5% of women were white and 76.4% privately insured. Over one- third of women received definitive treatment for their LCIS at an academic institution.

Of the total cohort, 5.4% did not receive surgery, 84.8% underwent surgical excision, 4.0% underwent unilateral mastectomy, and 5.1% underwent bilateral mastectomy as the definitive surgical treatment (Table 1). Patients treated with surgical excision were unlikely to undergo lymph node examination (4%). However, 49% of patients undergoing unilateral mastectomy and 44% of patients undergoing bilateral mastectomy received lymph node examination. Overall, 24% of women received endocrine therapy. This was most significantly more common ($p<0.001$) for patients treated with surgical excision (25%) or no surgery (22%) than in patients treated with mastectomy (13% unilateral and 6% bilateral).

On our multinomial analysis, patients were more likely to undergo either unilateral or bilateral mastectomy (compared with no surgery or surgical excision) if they were younger, white race, insured, or with greater comorbidity ($p<0.01$ for all) (Table 2). The type of treatment facility was not significantly associated ($p=0.3$) but geographic region of the reporting facility ($p<0.001$) was a strong predictor of receipt of mastectomy (Figure 2). In particular, facilities in the Southern United States were associated with over 4-fold greater odds of mastectomy (OR 3.5, 95% CI 3.0–4.3 for unilateral and OR 5.3, 95% CI 4.4–6.4 for bilateral) compared to New England. More recent year of diagnosis was associated with receipt of bilateral, but not unilateral, mastectomy; compared to 2004 to 2005, adjusted odds ratio for women treated between 2012 and 2013 was 1.25 (95% CI 1.09–1.43). Overall, the effect size of each variable tended to be greater for use of bilateral compared with unilateral mastectomy.

Discussion

Using a large, nationally-representative cohort of women with LCIS, we were able to demonstrate that the majority of women received appropriate surgical management, with the vast majority of women either receiving no surgery or undergoing surgical excision. While a substantial proportion underwent mastectomy (9%), over half of these were bilateral procedures and, therefore, reflect an appropriate risk-reduction strategy for women with LCIS. However, a substantial proportion of women continue to undergo unilateral mastectomy (4%), with significant geographic variation; rates ranged from 2.7% in New England to 8.0% in the South.

Our results are concordant with reported findings of Portschy³ and Wong¹³, each of whom used Surveillance, Epidemiology, and Results (SEER) data to examine rates of mastectomy (combined unilateral or bilateral) for LCIS. Reported rates of mastectomy in these studies were 18% (Portschy, et al. in 2009) and 10.3% (Wong, et al. in 2013). Portschy, et al. also observed substantial variation in the receipt of mastectomy between geographic regions, with a low of 12% in Connecticut to a high of 24% in the Greater Georgia area. Similar to our results, these authors found young age and white race to be predictive of mastectomy. However, neither study distinguished between receipt of a unilateral versus bilateral procedure.

For patients with LCIS, NCCN guidelines advocate for counseling regarding risk-reduction strategies with risk reducing medical therapy as the preferred approach.² Yet, for patients who desire surgical treatment, prophylactic bilateral mastectomy may be considered for women with certain genetic mutations such as BRCA 1 or 2, significant family history, or history of prior thoracic radiation at age less than 30 years. Institutional data suggest that these criteria apply to approximately 5% of patients with LCIS,¹⁴ which is similar to the percentage of patients in our total cohort who received bilateral mastectomy.

Importantly, our results add to the existing literature by assessing trends in and predictors of bilateral procedures. In our cohort, the rising use of bilateral mastectomy in the management of patients with LCIS mirrors increasing rates of contralateral prophylactic mastectomy (CPM) in women with unilateral DCIS or early-stage invasive cancer in the United States.^{15–20} In the setting of malignancy, King and colleagues¹⁵ report only 13% of patients who underwent CPM had documented evidence of being at high risk for contralateral breast cancer based on genetic mutations or history, suggesting that factors other than increased risk are driving the rise in bilateral mastectomy. Indeed, previous studies have identified an association between CPM, younger age, white race, and socioeconomic factors including higher education level,^{17–19,21} similar to the patient characteristics associated with receipt of a bilateral as opposed to unilateral mastectomy in our cohort.

Patient preference is believed to be a significant driver in the decision to pursue bilateral surgery for unilateral breast cancer^{16,22} and likely plays a key role in decision making for patients with LCIS as well. Rosenberg and colleagues report that emotional factors such as patient anxiety and the perception that treatment decisions were patient-driven, as opposed to physician-driven or shared, were associated with CPM for women with early-stage breast

cancer.²² While the long-term malignant potential of LCIS is poorly understood, the elevated risk for developing breast cancer in patients with LCIS compared to the average population may also drive some patients to be pro-active. Recent work by King and colleagues¹⁴ analyzing a prospectively maintained institutional database from 1980 to 2009 found the rate of cancer development in women with LCIS to be approximately 2% per year, equating to a cumulative rate of 26% at 15 years. This risk is the same for both breasts. A similar rate was reported using SEER data, with a cumulative incidence of 11.3% at 10-years and 19.8% at 20 years.¹³ These data offer valuable information for surgeons to incorporate when counseling patients with LCIS about their preferences, risk for future cancer and potential benefits/risk associated with bilateral mastectomy.

A significant upgrade rate of LCIS detected on core biopsy to ductal carcinoma in situ or invasive cancer underlies current practice guidelines recommending surgical excision for pleomorphic LCIS or lesions non-concordant with imaging.^{23,24} However, patients who were found to have either ductal carcinoma in situ or invasive cancer were excluded from our study, and cannot explain the observed rate of unilateral mastectomy.² Adjusted analyses demonstrated striking geographic variation that cannot be easily explained. As such, these results suggest an opportunity to reduce unnecessary care through education at both a provider and patient level. Based on our findings, efforts to bolster provider knowledge are best targeted to specific geographic regions rather than types of facilities and should focus on specific vulnerable patient populations.

While the NCDB advances prior investigation by offering analysis of a large, nationally representative cohort, it is not without limitation. In particular, the NCDB does not collect information regarding the patient's family history, prior radiation exposure, or genetic mutations such as BRCA 1 or 2. The NCDB also does not discriminate between pleomorphic and classic LCIS. Current guidelines do not necessitate excisional biopsy for all patients with classic-type LCIS on core biopsy, but do recommend surgical excision to negative margins for pleomorphic LCIS. However, pleomorphic subtype represents a very small proportion of LCIS (<6%).²⁵ Furthermore, the use of unilateral mastectomy would represent overuse even in the setting of pleomorphic rather than classic-type LCIS. Finally, we do not have details of the imaging characteristics that may have led to selection of a specific treatment plan or provider level data to assess variation based on practices of individual surgeons.

Conclusion

This population-based analysis demonstrates that nearly as many patients underwent unilateral (4%) as bilateral mastectomy (5.1%), representing inappropriate care. These findings highlight an opportunity to reduce unnecessary care through improved provider and patient education regarding the natural history and optimal management of LCIS.

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Synopsis

Nearly as many patients underwent unilateral (4%) as bilateral mastectomy (5.1%), representing inappropriate care. These findings highlight an opportunity to reduce unnecessary care through improved provider and patient education regarding optimal management of LCIS.

Figure 1.

Figure 2.

Table 1
 Characteristics Of Women Diagnosed with LCIS from 2004–2013 by Type of Definitive Surgical Management*

Variable	Overall cohort N=30,105	No Surgery n (%) N=1,627	Surgical Excision n (%) N=25,799	Unilateral Mastectomy n (%) N=1,136	Bilateral Mastectomy n (%) N=1,543
Age, years					
45	5,959	246 (4.1%)	5,009 (84.1%)	254 (4.3%)	450 (7.6%)
46–55	13,361	739 (5.5%)	11,365 (85.1%)	482 (3.6%)	775 (5.8%)
56–65	6,355	339 (5.3%)	5,515 (86.8%)	248 (3.9%)	253 (4.0%)
>65	4,430	303 (6.8%)	3,910 (88.3%)	152 (3.4%)	65 (1.5%)
Race					
White	25,730	1,357 (5.3%)	21,959 (85.3%)	999 (3.9%)	1,415 (5.5%)
Non-white	4,375	270 (6.2%)	3,840 (87.8%)	137 (3.1%)	128 (2.9%)
Insurance status					
Uninsured/Medicaid	1,844	128 (6.9%)	1,601 (86.8%)	50 (2.7%)	65 (3.5%)
Private	22,979	1,166 (5.1%)	19,607 (85.3%)	878 (3.8%)	1,328 (5.8%)
Medicare/other govt	5,282	333 (6.3%)	4,591 (86.9%)	208 (3.9%)	150 (2.8%)
Charlson-deyo score					
0	27,351	1,518 (5.6%)	23,445 (85.7%)	999 (3.7%)	1,389 (5.1%)
1	2,754	109 (4.0%)	2,354 (85.5%)	137 (5.0%)	154 (5.6%)
Facility type					
Community	2,619	164 (6.3%)	2,242 (85.6%)	104 (4.0%)	109 (4.1%)
Comprehensive community	15,673	879 (5.6%)	13,343 (85.1%)	607 (3.9%)	844 (5.4%)
Academic	10,660	549 (5.2%)	9,235 (86.6%)	385 (3.6%)	491 (4.6%)
Unknown	1,153	2.2 (3.0%)	979 (84.9%)	40 (3.5%)	99 (8.6%)
Facility location					
New England	11,462	473 (4.1%)	10,367 (90.5%)	309 (2.7%)	313 (2.7%)
South Atlantic	5,526	335 (6.1%)	4,644 (84.0%)	235 (4.3%)	312 (5.7%)
Mid-west	6,424	409 (6.4%)	5,390 (83.9%)	244 (3.8%)	381 (5.9%)

Variable	Overall cohort n N=30,105	No Surgery n (%) N=1,627	Surgical Excision n (%) N=25,799	Unilateral Mastectomy n (%) N=1,136	Bilateral Mastectomy n (%) N=1,543
South	2,133	159 (7.5%)	1,565 (73.4%)	171 (8.0%)	238 (11.2%)
West	3,455	217 (6.3%)	2,899 (83.9%)	138 (4.0%)	201 (5.8%)
Unknown	1,105	34 (3.1%)	934 (84.5%)	39 (3.5%)	98 (8.9%)

* Statistically significant differences where observed across types of definitive surgical management for all variables

Table 2

Multinomial adjusted analysis comparing receipt of mastectomy (unilateral or bilateral) versus No surgery/
Surgical Excision as definitive surgical management of LCIS

Variable	Unilateral mastectomy vs. No surgery/Surgical Excision	Bilateral mastectomy vs. No Surgery/Surgical Excision
	OR (95% CI)	OR (95% CI)
Age, years		
>65	Reference *	Reference *
55–65	1.4 (1.1–1.8)	3.1 (2.3–4.2)
45–55	1.4 (1.1–1.8)	5.1 (3.7–6.9)
≤45	1.8 (1.4–2.4)	6.9 (4.9–9.2)
Race		
Non-white	Reference *	Reference *
White	1.3 (1.1–1.6)	2.0 (1.6–2.4)
Insurance status		
Uninsured/medicaid	Reference *	Reference *
Private	1.5 (1.1–2.0)	1.7 (1.3–2.2)
Medicare/other government	1.8 (1.3–2.6)	1.9 (1.4–2.6)
Charlson-deyo score		
0	Reference *	Reference *
1	1.4 (1.2–1.7)	1.3 (1.1–1.5)
Facility type		
Academic	Reference	Reference
Comprehensive community	0.9 (0.8–1.1)	1.0 (0.9–1.1)
Community	1.0 (0.8–1.2)	0.8 (0.7–1.1)
Unknown	0.5 (0.1–3.6)	0.3 (0.0–2.3)
Facility location		
New England	Reference *	Reference *
South Atlantic	1.7 (1.4–2.0)	2.3 (2.0–2.4)
Mid-west	1.5 (1.2–1.7)	2.3 (2.0–2.7)
South	3.5 (3.0–4.3)	5.3 (4.4–6.4)
West	1.6 (1.3–1.9)	2.3 (1.9–2.7)
Year of diagnosis		
2004–2005	Reference	Reference *
2006–2007	1.0 (0.8–1.2)	1.1 (0.9–1.3)
2008–2009	0.8 (0.7–1.0)	1.1 (1.0–1.4)

Variable	Unilateral mastectomy vs. No surgery/Surgical Excision	Bilateral mastectomy vs. No Surgery/Surgical Excision
	OR (95% CI)	OR (95% CI)
2010–2011	0.9 (0.7–1.1)	1.4 (1.1–1.6)
2012–2013	0.9 (0.7–1.1)	1.5 (1.2–1.8)

* Significant at $p < 0.01$