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Trends in Axillary Surgery for Treating Ductal Carcinoma *In Situ*: A Korean Population-based Study

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Conflict of Interest
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ABSTRACT

Purpose: Ductal carcinoma *in situ* (DCIS) is common in South Korea. We evaluated the patterns of axillary surgery among patients with DCIS to highlight the need for compliance with the updated national guidelines. We also evaluated whether sentinel lymph node biopsy (SLNB) was performed in accordance with the national guidelines.
Methods: The Korean Health Insurance Review and Assessment Service-National Inpatient Sample database was searched for patients with DCIS (2009–2015) to identify axillary surgery patterns by breast surgery type, year of diagnosis, age at diagnosis, and the location and volume of surgeries for DCIS at the hospital. The rates of SLNB and axillary dissection were compared using descriptive statistics and univariate analyses. Analyses were also conducted using the chi-squared test and multiple logistic regression analysis.
Results: We identified 16,315 Korean women who underwent surgery for DCIS, including 11,292 cases of SLNB (69.2%) and 131 cases of axillary lymph node dissection (0.8%). Breast-conserving surgery (BCS) was performed in 10,323 patients (63.3%) with an SLNB rate of 56.0%, while total mastectomy (TM) was performed in 5,992 patients (36.7%), with an SLNB rate of 92.0%. During 2009–2015, the SLNB rate during TM increased from 88.23% to 92.80%. SLNB was influenced by hospital region and surgical volume, and hospitals performing low volumes of surgeries were significantly more likely to perform SLNB regardless of the surgery type (odds ratio, 1.372; 95% confidence interval, 1.265–1.488).
Conclusion: Although the Korean guidelines recommend SLNB for all TM procedures and select BCS procedures for DCIS, relatively high rates of SLNB were performed for BCS, and there was inter-hospital variability in performing SLNB. Improved compliance with the guidelines by the surgeons is critical for Korean patients with DCIS.

Keywords: Breast neoplasms; Ductal carcinoma *in situ*; Guideline; Sentinel lymph node biopsy

INTRODUCTION

According to the Korean Breast Cancer Society (KBCS), ductal carcinoma *in situ* (DCIS) accounted for 17.9% of all newly diagnosed neoplastic breast lesions in 2017 [1]. It has increased from 6.1% in 2000 to 17.9% in 2017 [1]. This increase was attributed to the national mammographic screening strategy and improvements in the diagnostic methods [2,3].

Author Contributions

Conceptualization: Choi YJ; Data curation: Shin YD, Kang G, Jang H, Choi YJ; Formal analysis: Shin YD, Kang G, Jang H, Choi YJ; Funding acquisition: Choi YJ; Investigation: Kang G; Methodology: Choi YJ; Project administration: Choi YJ; Resources: Kang G, Jang H; Software: Shin YD, Kang G, Jang H, Choi YJ; Writing - original draft: Choi YJ; Writing - review & editing: Shin YD, Kang G, Jang H, Choi YJ.

As a typically non-invasive malignancy, the proliferation of DCIS is generally confined to the epithelial basement membrane, and the rate of axillary lymph node metastasis in patients with only DCIS is reportedly 1%–6% [4,5]. Axillary surgery, including sentinel lymph node biopsy (SLNB), has a risk of long-term sequelae such as chronic pain, decreased strength, edema, and sensory disorders [6]. Therefore, patients with pure DCIS are usually not subjected to any axillary surgery. However, up to 38% of the patients with a preoperative histological diagnosis of DCIS are upstaged to invasive carcinoma after surgery, based on the pathological examination [7,8]. The predictors of upstaging to an invasive lesion are a large DCIS lesion, palpable tumor, mass-forming lesion detected during mammography, lack of hormone receptor expression, high nuclear grade, diagnosis via core-needle biopsy, and the non-cribriform subtype [9]. These patients require SLNB during the primary surgery to stage the axilla, avoid a second surgery and reduce the risk of missing the sentinel lymph nodes if a secondary procedure is necessary.

In 2019, the 8th Korean clinical practice guideline for breast cancer released by the KBCS indicated that SLNB was recommended during total mastectomy (TM) for DCIS, as well as during select cases of breast-conserving surgery (BCS) for DCIS lesions that are located near the axilla, or when the lesion is diffuse, large, palpable, has comedo necrosis, or has a high nuclear grade [10]. The National Comprehensive Cancer Network (NCCN) guidelines also do not recommend axillary lymph node evaluation for patients undergoing BCS. However, SLNB should be "strongly considered" with mastectomy or with "excision in an anatomic location compromising the performance of a future sentinel lymph node procedure" [11]. Therefore, the present study aimed to evaluate the breast and axillary surgery patterns among Korean patients with DCIS and to determine whether SLNB was being performed in accordance with the national guidelines. To the best of our knowledge, this is the first Korean study to evaluate the nationwide trends in axillary evaluation among DCIS patients according to the year, surgery type, patient age, and the hospital location and surgical volume.

METHODS

Ethical considerations

All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study evaluated de-identified registry-based data and therefore, was not subjected to review by an institutional review board in accordance with the BIOETHICS AND SAFETY ACT.

Informed consent

Patient-informed consent was not required as this study used existing data from the National Health Insurance Service in Korea, which are de-identified before being made available to researchers.

Data source

This registry-based study used data collected by the Health Insurance Review and Assessment Service (HIRA). HIRA is a neutral organization that evaluates the appropriateness of expenses charged by the medical institutions and provides recommendations regarding coverage to the National Health Insurance Corporation (NHIC). The Health Insurance Review and Assessment Service–National Inpatient Sample (HIRA-NIS) database provides annual

data for research purposes, which are obtained using a stratified randomized sampling of 13% of the patients who are admitted during each annual period. The HIRA-NIS also contains weighted scores for each patient, which facilitates extrapolation of the findings to the entire Korean population. For example, the 2009 data from the HIRA-NIS includes 246 patients with DCIS, which can be converted to 1,982 cases in the Korean population [12,13]. The present study evaluated the HIRA-NIS data from 2009–2015.

Patient selection

Diagnoses were coded based on the Korean Standard Classification of Diseases, 7th revision (KCD-7), adapted from the International Classification of Diseases (ICD), 10th revision. The KCD-7 code for DCIS is D05.1, and that for invasive breast carcinoma is C50.9. Patients who had both D05.1 and C50.9 codes simultaneously prior to curative breast and axillary surgery were excluded from the study. Related surgical procedures were identified based on the following procedure codes: N7121, N7122, N7133, N7131, N7135, P2121, P2122, P2123, and P2124. Related radiotherapy was identified based on the radiation therapy code (HD, HZ271). We categorized patients as having undergone BCS (N7121, N7122, or N7133) or TM (N7131 or N7134). Since N7135 includes radical surgery for breast cancer, including BCS and TM, we defined BCS as cases with the related radiation therapy code (HD, HZ271) within 90 days of breast surgery. Cases with an initial BCS code and a TM code within 30 days were assigned to the TM group. Cases with both a BCS code and a TM code during the same admission period were excluded. Cases with an initial TM code and a BCS code within 90 days were also excluded. The SLNB group was defined based on the codes for axillary surgery (P2121, P2123, or P2124), and axillary dissection (AD) was identified based on the related code (P2122). Cases with both AD and SLNB codes on the same day were assigned to the SLNB group (**Table 1**, **Figure 1**).

The parameters considered for evaluation included the year of diagnosis, patient age at treatment (≤ 19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and ≥ 70 years), combined age group (< 70 years, ≥ 70 years), type of breast surgery (BCS or TM), type of axillary surgery (SLNB, AD, or none), and type of hospital. The type of hospital was classified based on the geographic location (Seoul or non-Seoul), the number of beds (≤ 300, 301–550, 551–800, and ≥ 801), and annual surgical volume. To analyze the differences in the rate of SLNB based on the surgical volume, we subcategorized the hospitals as Type I (< 100 surgical procedures for DCIS patients annually [low volume] vs. ≥ 100 DCIS procedures annually [high volume]) and Type II (< 50 DCIS procedures annually [low volume] vs. ≥ 50 DCIS procedures annually [high volume]). To determine the differences in the rate of SLNB according to the region and surgical volume, we subcategorized the hospitals into four groups: Seoul-high volume, Seoul-low volume, non-Seoul-high volume, and non-Seoul-low volume.

Table 1. Surgery and treatment codes

Surgery code	Description	Category
N7121	Breast benign mass excision – single	Breast-conserving surgery
N7122	Breast benign mass excision – multiple	Breast-conserving surgery
N7133	Breast partial mastectomy	Breast-conserving surgery
N7135 with HD, HZ271	Breast radical mastectomy including radical breast-conserving surgery	Breast-conserving surgery
N7135 without HD, HZ271	Breast radical mastectomy including radical breast-conserving surgery	Total mastectomy
N7131	Breast simple mastectomy	Total mastectomy
P2122	Axillary lymph node dissection	Axillary dissection
P2121	Axillary lymph node excision	Sentinel lymph node biopsy
P2123	Axillary sentinel lymph node excision	Sentinel lymph node biopsy
P2124	Axillary sentinel lymph node excision (using radioactivity detector)	Sentinel lymph node biopsy

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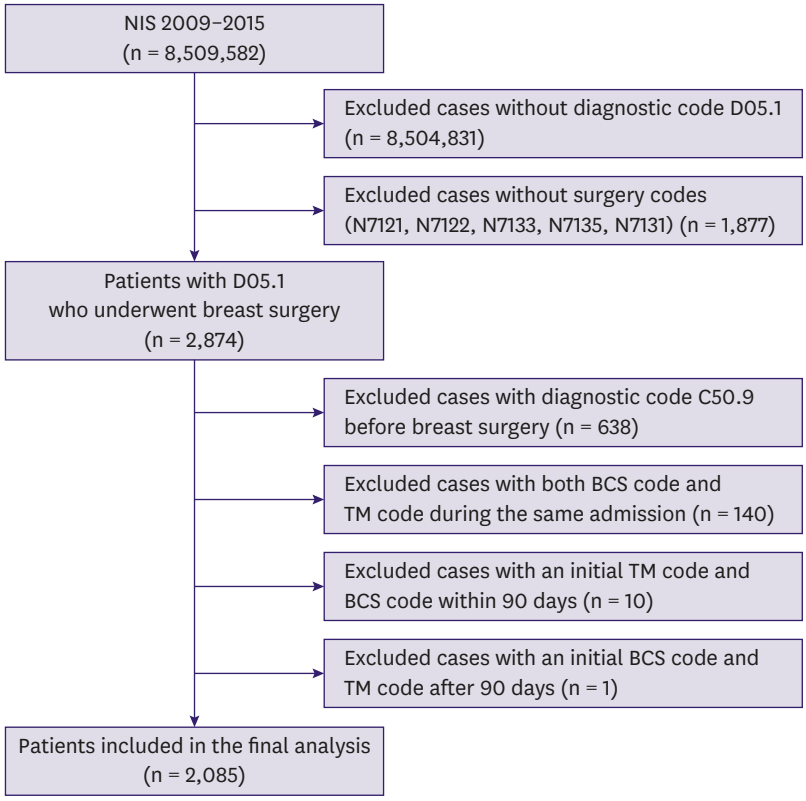

Figure 1. Study flowchart.
Fig. 1 details the process for exclusion and exclusion of patients in the study.
NIS = National Inpatient Sample; BCS = breast-conserving surgery; TM = total mastectomy.

Statistical analysis

The rates of SLNB and AD based on the various characteristics were compared using descriptive statistics and univariate analyses. The chi-squared test was used for analyses according to the year of diagnosis, patient age at treatment, surgical procedure, and type of hospital. Multiple logistic regression analysis was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for the probability of axillary evaluation. Differences were considered statistically significant at p-values of < 0.05. All statistical analyses were performed using SAS software version 9.4.

RESULTS

Between 2009 and 2015, the HIRA-NIS database incorporated the data of 8,509,582 patients, including 4,751 patients (0.06%) with the D05.1 diagnostic code for DCIS. Among these, 2,874 patients (60.49%) underwent breast surgery (N7121, N7122, N7133, N7135, or N7131), and we identified 2,085 DCIS patients who fulfilled the inclusion criteria (**Figure 1**). Based on this sample, the analyses were weighted for the Korean population, which indicated a sample of 16,315 cases, including 10,323 BCS cases (63.3%) and 5,992 TM cases (36.7%). No significant annual change was observed in the rates of breast surgery type (**Figure 2**). Among the weighted sample of 16,315 cases, the rate of axillary lymph node evaluation using SLNB or AD increased from 65.8% in 2009 to 70.9% in 2015. A total of 11,292 patients (69.2%) underwent SLNB, and the proportion of SLNB rate increased from 64.2% to 70.1% (p <

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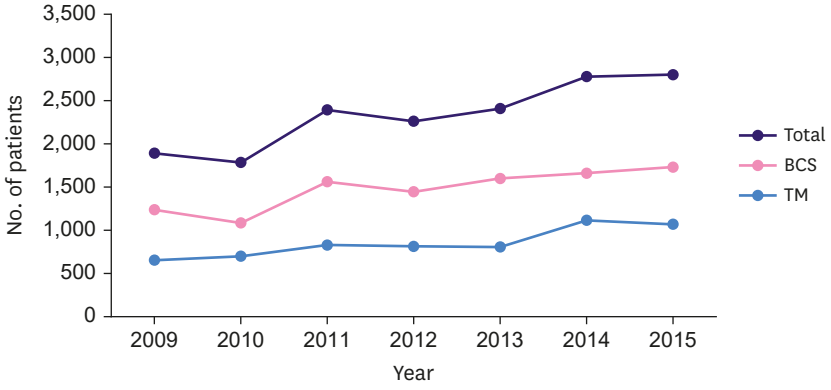

Figure 2. Trends of breast surgery types in patients with ductal carcinoma *in situ* according to year.
Between 2009 and 2015, no significant annual change was observed in the rates of breast cancer surgery according to surgery type (breast-conserving surgery or TM).
BCS = breast-conserving surgery; TM = total mastectomy.

0.001). On the other hand, a total of 138 patients (0.8%) underwent AD, and the proportion of AD decreased from 1.6% to 0.8% (**Figure 3**).

Table 2 shows the data for the year of diagnosis, patient age, surgery type, hospital region, hospital size, and volume of DCIS surgeries at the hospital, as well as their associations with SLNB and AD during surgery for DCIS between 2009 and 2015. Among the entire weighted cohort, the likelihood of SLNB during TM was higher than that during BCS (OR, 9.286; 95% CI; 8.382–10.287) and higher in low-volume hospitals than in high-volume hospitals (OR, 1.372; 95% CI, 1.265–1.488). There was no statistically significant difference in the rate of SLNB by age. Additionally, there was no significant difference in the rate of SLNB between the Seoul and non-Seoul regions. Although the sample size was extremely small, the likelihood of AD was higher in low-volume hospitals (< 100 and < 50 DCIS operations per year) than for other hospitals (OR, 2.628; 95% CI, 1.642–4.205 and OR, 3.255; 95% CI, 2.203–4.808, respectively).

Some differences in the rate of SLNB were observed according to the breast surgery type. The SLNB rate among all BCS cases was 55.96%, and the AD rate was 1.27%. The rate of

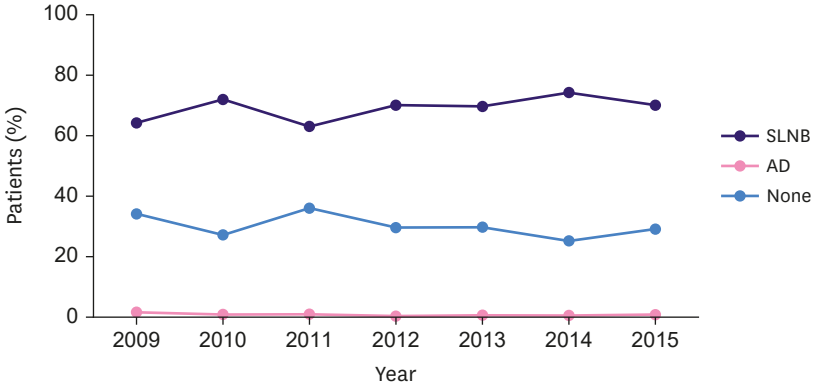

Figure 3. Trends of axillary evaluations in patients with ductal carcinoma in situ according to year.
Within the study period, the proportion of sentinel lymph node biopsy use increased while the proportion of axillary dissection use decreased.
SLNB = sentinel lymph node biopsy; AD = axillary dissection.

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Table 2. Patient, facility, and surgical characteristics for 21,223 Korean patients with ductal carcinoma in situ and their associations with axillary surgery particularly SLNB and AD between 2009–2015

Variables	Total	Weighted total	SLNB	AD	None	*p*-value	OR (SLNB)	95% CI	*p*-value	OR (AD)	95% CI	*p*-value
Year of diagnosis						< 0.001						
2009	246	1,982	1,215 (64.2)	31 (1.6)	646 (34.2)		1.000			1.000		
2010	232	1,785	1,285 (72.0)	15 (0.9)	485 (27.2)		1.341	1.151–1.561	0.002	0.553	0.296–1.036	0.065
2011	287	2,392	1,508 (63.0)	23 (1.0)	862 (36.0)		0.894	0.779–1.027	0.114	0.468	0.268–0.816	0.008
2012	294	2,262	1,585 (70.1)	8 (0.3)	669 (29.6)		1.292	1.121–1.49	< 0.001	0.182	0.082–0.404	< 0.001
2013	301	2,408	1,677 (69.6)	15 (0.6)	715 (29.7)		1.283	1.114–1.477	< 0.001	0.292	0.156–0.547	< 0.001
2014	361	2,777	2,062 (74.2)	15 (0.6)	700 (25.2)		1.441	1.254–1.657	< 0.001	0.274	0.146–0.512	< 0.001
2015	364	2,800	1,962 (70.1)	23 (0.8)	815 (29.1)		1.228	1.071–1.407	< 0.001	0.457	0.262–0.798	0.006
Age (yr)						< 0.001						
≤ 19	2	15	8 (50.0)	0 (0.0)	8 (50.0)		1.000			1.000		
20–29	26	200	85 (42.3)	0 (0.0)	115 (57.7)		0.371	0.129–1.066	0.065	0.0832	< 0.001, > 999.999	0.999
30–39	228	1,754	1,185 (67.5)	23 (1.3)	546 (31.1)		0.985	0.358–2.713	0.977	> 999.999	< 0.001, > 999.999	0.958
40–49	792	6,092	4,215 (69.2)	38 (0.6)	1,838 (30.2)		1.222	0.446–3.351	0.696	> 999.999	< 0.001, > 999.999	0.962
50–59	630	5,031	3,508 (69.7)	54 (1.1)	1,469 (29.2)		1.166	0.425–3.199	0.766	> 999.999	< 0.001, > 999.999	0.959
60–69	290	2,323	1,623 (69.9)	8 (0.3)	692 (29.8)		1.137	0.413–3.129	0.804	806.222	< 0.001, > 999.999	0.966
≥ 70	117	900	669 (74.4)	8 (0.9)	223 (24.8)		1.025	0.369–2.85	0.961	> 999.999	< 0.001, > 999.999	0.960
Combinde age						< 0.001						
< 70	1,968	15,415	10,623 (68.9)	123 (0.8)	4,669 (30.3)		1.000					
≥ 70	117	900	669 (74.4)	8 (0.9)	223 (24.8)		0.898	0.757–1.064	0.215	1.243	0.584–2.644	0.572
Surgery type						< 0.001						
BCS	1,306	10,323	5,777 (56.0)	131 (1.3)	4,415 (42.8)		1.000			1.000		
TM	779	5,992	5,515 (92.0)	0 (0)	477 (8.0)		9.286	8.382–10.287	< 0.001	< 0.001	< 0.001–116.904	0.216
Region						0.094						
Seoul	794	6,200	4,346 (70.1)	54 (0.9)	1,800 (29.0)		1.000			1.000		
Non-Seoul	1,291	10,115	6,946 (68.7)	77 (0.8)	3,092 (30.6)		0.972	0.898–1.052	0.477	0.795	0.552–1.147	0.220
Number of beds						< 0.001						
≤ 300	439	3,469	2,377 (68.5)	23 (0.7)	1,069 (30.8)		1.000			1.000		
301–550	231	1,777	1,269 (71.4)	8 (0.4)	500 (28.1)		1.193	1.039–1.37	0.012	0.563	0.246–1.289	0.174
551–800	425	3,361	2,315 (68.9)	46 (1.4)	1,000 (29.7)		1.187	1.06–1.33	0.003	1.209	1.209–3.375	0.007
≥ 801	990	7,708	5,331 (69.2)	54 (0.7)	2,323 (30.1)		1.186	1.0272–1.312	< 0.001	0.662	0.662–1.858	0.693
Type I volume*						< 0.001						
High volume	634	5,154	3,361 (65.2)	23 (0.4)	1,769 (34.3)		1.000			1.000		
Low volume	1,451	11,161	7,931 (71.1)	108 (1.0)	3,123 (28.0)		1.372	1.265–1.488	< 0.001	2.628	1.642–4.205	< 0.001
Type II volume						< 0.001						
High volume	1,218	9,646	6,592 (68.3)	46 (0.5)	3,008 (31.2)		1.000			1.000		
Low volume	867	6,669	4,700 (70.5)	85 (1.3)	1,885 (28.3)		1.065	0.984–1.153	0.120	3.255	2.203–4.808	< 0.001
Region + volume (type I)						< 0.001						
S-H	335	2,669	1,900 (71.2)	8 (0.3)	762 (28.5)		1.000			1.000		
S-L	459	3,531	2,446 (69.3)	46 (1.3)	1,038 (29.4)		1.073	0.944–1.219	0.283	4.205	1.889–9.36	< 0.001
NS-H	299	2,485	1,462 (58.8)	15 (0.6)	1,008 (40.6)		0.749	0.655–0.858	< 0.001	1.443	0.581–3.583	0.430
NS-L	992	7,631	5,485 (71.9)	62 (0.8)	2,085 (27.3)		1.210	1.076–1.361	0.002	2.810	1.269–6.225	0.011
Region + volume (type II)						< 0.001						
S-H	714	4,400	3,123 (71.0)	8 (0.2)	1,269 (28.8)		1.000			1.000		
S-L	309	1,800	1,223 (67.9)	46 (2.6)	531 (29.5)		0.911	0.795–1.044	0.180	19.013	8.590–42.082	< 0.001
NS-H	865	5,246	3,469 (66.1)	38 (0.7)	1,738 (33.1)		0.929	0.842–1.025	0.143	4.367	1.980–9.629	< 0.001
NS-L	814	4,869	3,477 (71.4)	38 (0.8)	1,354 (27.8)		1.060	0.951–1.182	0.290	5.657	2.532–12.642	< 0.001
Total	2,085	16,315	11,292 (69.2)	131 (0.8)	4,892 (30.0)							

Data are presented as number (%), unless otherwise indicated.
SLNB = sentinel lymph node biopsy; AD = axillary dissection; OR = odds ration; CI = confidence inerval; BCS = breast-conserving surgery; TM = total mastectomy; S-H = Seoul-high volume; S-L = Seoul-low volume; NS-H = non-Seoul- high volume; NS-L = non-Seoul-low volume; DCIS = ductal carcinoma *in situ*.
*Low volume and high volume as < 100 vs. ≥ 100 surgical procedures for DCIS patients annually; †Low volume and high volume as < 50 vs. ≥ 50 surgical procedures for DCIS annually.

SLNB in BCS cases remained fairly stable throughout the study period (**Figure 4**), although significant variations were observed between hospitals according to their surgical volumes for DCIS ($p < 0.001$, **Table 3**). The rate of SLNB during BCS was significantly higher in low-volume hospitals (< 100 DCIS operations per year) (OR, 1.349; 95% CI, 1.237–1.47; $p < 0.001$).

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However, the rate did not differ between institutions in the Seoul and non-Seoul regions. In a more detailed analysis combining the surgical volume and region of each hospital, the rate of SLNB during BCS was significantly lower in high-volume hospitals (> 100 DCIS operations per year) located in the non-Seoul region (OR, 0.573; 95% CI, 0.494–0.664; p<0.001).

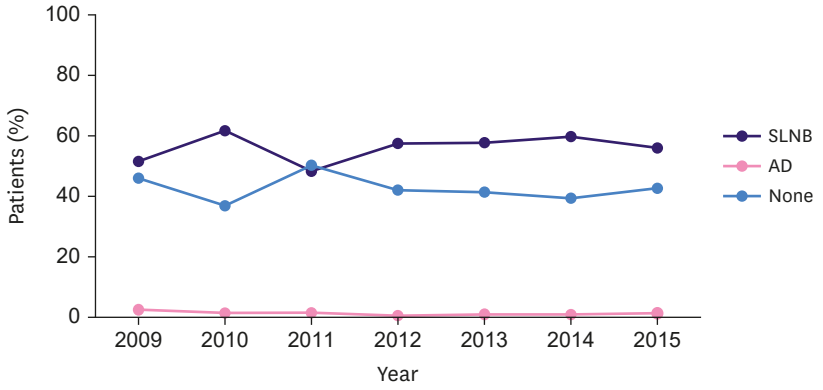

Figure 4. Trends of axillary evaluations in patients with ductal carcinoma in situ undergoing breast-conserving surgery according to year.
Among patients undergoing breast-conserving surgery, the use of sentinel lymph node biopsy remained fairly stable between 2009 and 2015.
SLNB = sentinel lymph node biopsy; AD = axillary dissection.

Table 3. Sentinel lymph node biopsy with breast-conserving surgery according to hospital type and surgical volume

Variables	Total	Weighted total	SLNB	AD	None	*p*-value	OR (SLNB)	95% CI	*p*-value
Age						0.030			
< 70	1,249	9,884	5,508 (55.72)	123 (1.25)	4,254 (43.03)		1.000		
≥ 70	57	438	269 (61.40)	8 (1.75)	162 (36.84)		1.210	0.993–1.475	0.059
Region						0.145			
Seoul	475	3,746	2,131 (56.88)	54 (1.44)	1,562 (41.68)		1.000		
Non-Seoul	831	6,577	2,646 (55.44)	77 (1.17)	2,854 (43.39)		0.931	0.855–1.013	0.097
Number of beds						< 0.001			
≤ 300	264	2,123	1,146 (53.99)	23 (1.09)	954 (44.93)		1.000		
301–550	142	1,092	600 (54.93)	8 (0.70)	485 (44.37)		0.969	0.835–1.124	0.679
551–800	276	2,215	1,262 (56.94)	46 (2.08)	908 (30.97)		1.205	1.066–1.361	0.003
≥ 801	624	4,892	2,769 (56.60)	54 (1.10)	2,069 (42.30)		1.096	0.983–1.222	0.100
Type I volume*						< 0.001			
High volume	389	3,269	1,685 (51.53)	23 (0.71)	1,562 (47.76)		1.000		
Low volume	917	7,054	4,092 (58.02)	108 (1.53)	2,864 (40.46)		1.349	1.237–1.471	< 0.001
Type II volume†						< 0.001			
High volume	772	6,215	3,408 (54.83)	46 (0.74)	2,761 (44.43)		1.000		
Low volume	534	4,108	2,369 (57.68)	85 (2.06)	1,654 (40.26)		1.162	1.067–1.265	< 0.001
Region + volume (type I)						< 0.001			
S-H	180	1,477	869 (58.85)	8 (0.52)	600 (40.63)		1.000		
S-L	295	2,269	1,262 (55.59)	46 (2.03)	962 (42.37)		0.872	0.759–1.003	0.055
NS-H	209	1,792	815 (45.49)	15 (0.86)	962 (53.65)		0.573	0.494–0.664	< 0.001
NS-L	622	4,785	2,831 (59.16)	62 (1.29)	1,892 (39.55)		1.021	0.898–1.160	0.756
Region + volume (type II)						< 0.001			
S-H	327	2,608	1,492 (57.23)	8 (0.29)	1,108 (42.48)		1.000		
S-L	148	1,138	638 (56.08)	46 (4.05)	454 (39.86)		0.986	0.851–1.143	0.852
NS-H	445	3,608	1,915 (53.09)	38 (1.07)	1,654 (45.84)		0.865	0.778–0.962	0.007
NS-L	386	2,969	1,731 (58.29)	38 (1.30)	1,200 (40.41)		1.080	0.961–1.213	0.196
Total	1,306	10,323	5,777 (55.96)	131 (1.27)	4,415 (42.77)				

Data are presented as number (%), unless otherwise indicated.
SLNB = sentinel lymph node biopsy; AD = axillary dissection; OR = odds ration; CI = confidence inerval; S-H = Seoul-high volume; S-L = Seoul-low volume; NS-H = non-Seoul- high volume; NS-L = non-Seoul-low volume; DCIS = ductal carcinoma *in situ*.
*Low volume and high volume as < 100 vs. ≥ 100 surgical procedures for DCIS patients annually; †Low volume and high volume as < 50 vs. ≥ 50 surgical procedures for DCIS annually.

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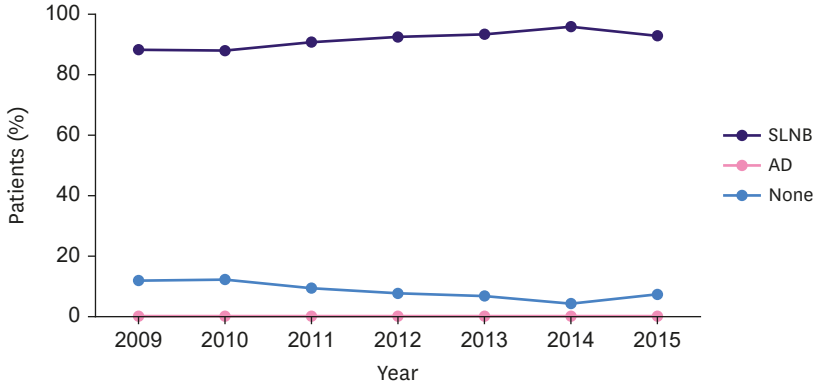

Figure 5. Trends of axillary evaluations in patients with ductal carcinoma in situ undergoing TM according to year. Among patients who underwent TM, the rate of sentinel lymph node biopsies increased from 2009 to 2015. SLNB = sentinel lymph node biopsy; AD = axillary dissection; TM = total mastectomy.

According to the age group, patients aged above 70 years underwent SLNB during BCS more frequently than those aged below 70 years, with a marginally significant difference (OR, 1.21; 95% CI, 0.993–1.475; $p = 0.059$).

The SLNB rate among all TM cases was 92.04%, showing an increase from 88.23% in 2009 to 92.86% in 2015 ($p < 0.001$, **Figure 5**). No patients underwent AD during TM in this study period. In contrast to cases of BCS, patients aged above 70 years had a significantly lower rate of SLNBs during TM than those below the age of 70 years (OR, 0.464; 95% CI, 0.346–0.662; $p < 0.001$). The rate of SLNB during TM also varied according to the hospital region and surgical volume (**Table 4**). Similar to that in BCS cases, the rate of SLNB during TM was likely to be significantly higher in low-volume hospitals (< 100 DCIS operations per year) (OR, 1.746; 95% CI, 1.397–2.181; $p < 0.001$). In addition, SLNB during TM was significantly more likely in facilities that were not located in the Seoul region (OR, 1.43; 95% CI, 1.157–1.767) ($p < 0.001$). In contrast to that seen in BCS cases, the rate of SLNB during TM was significantly lower in the high-volume hospitals (> 100 DCIS operations per year) located in the Seoul region ($p < 0.001$).

DISCUSSION

The present study evaluated the patterns of breast and axillary surgery among DCIS patients in Korea, using a national database. Although many international studies have evaluated the patterns of axillary surgery among patients with DCIS [14–18], we believe that this is the first Korean study to evaluate nationally representative data regarding the surgical management of DCIS. Among Korean women with DCIS, we found that BCS was more common than TM (59.9% versus 40.1%) between 2009 and 2015, and these proportions remained relatively stable. However, the rate of TM was higher than that in other countries [14,19,20]. The overall rate of axillary evaluation (including SLNB and AD) was 73.0% during the study period, which is also higher than the rates from previous studies [15,19,20], including rates of 61.2% between 2009–2011 reported by Mitchell et al. [19] and 54.3% between 2004–2015 reported by Holm-Rasmussen et al. [20]. We observed a general increase in the rate of SLNB in Korea, which might reflect increasing surgeon experience, and these findings are consistent with the results reported from other countries [14-16].

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Table 4. Sentinel lymph node biopsy with total mastectomy according to hospital type and surgical volume

Variables	Total	Weighted total	SLNB	AD	None	*p*-value	OR (SLNB)	95% CI	*p*-value
Age						< 0.001			
< 70	719	5,531	5,155 (92.49)	0 (0)	415 (7.51)		1.000		
≥ 70	60	462	400 (86.67)	0 (0)	62 (23.33)		0.464	0.346–0.622	< 0.001
Region						< 0.001			
Seoul	319	2,454	2,215 (90.28)	0 (0)	238 (9.72)		1.000		
Non-Seoul	460	3,538	3,300 (93.26)	0 (0)	238 (6.74)		1.430	1.157–1.767	< 0.001
Number of beds						< 0.001			
≤ 300	175	1,346	1,231 (91.43)	0 (0)	115 (8.57)		1.000		
301–550	89	685	669 (97.75)	0 (0)	15 (2.25)		5.504	3.17–9.556	< 0.001
551–800	149	1,146	1,054 (91.95)	0 (0)	92 (8.05)		1.270	0.949–1.699	0.107
≥ 801	366	2,815	2,562 (90.98)	0 (0)	254 (0.02)		1.493	1.133–1.969	0.005
Type I volume*						< 0.001			
High volume	245	1,885	1,677 (88.98)	0 (0)	208 (11.02)		1.000		
Low volume	534	4,108	3,838 (93.45)	0 (0)	269 (6.55)		1.746	1.397–2.181	< 0.001
Type II volume†						0.009			
High volume	446	3,431	3,185 (92.83)	0 (0)	246 (7.17)		1.000		
Low volume	333	2,562	2,331 (90.99)	0 (0)	231 (9.01)		0.614	0.492–0.766	< 0.001
Region + volume (type I)						< 0.001			
S-H	155	1,192	1,031 (86.45)	0 (0)	162 (13.55)		1.000		
S-L	164	1,262	1,185 (93.90)	0 (0)	77 (6.10)		2.787	2.025–3.836	< 0.001
NS-H	90	692	646 (93.33)	0 (0)	46 (6.67)		2.649	1.829–3.835	< 0.001
NS-L	370	2,846	2,654 (93.24)	0 (0)	192 (6.76)		2.765	2.075–3.683	< 0.001
Region + volume (type II)						< 0.001			
S-H	233	1,792	1,631 (90.99)	0 (0)	162 (9.01)		1.000		
S-L	86	662	585 (88.37)	0 (0)	77 (11.63)		0.665	0.483–0.915	0.012
NS-H	213	1,638	1,554 (94.84)	0 (0)	85 (5.16)		1.751	1.317–2.328	< 0.001
NS-L	247	1,900	1,746 (91.90)	0 (0)	154 (8.10)		1.010	0.764–1.334	0.944
Total	779	5,992	5,515 (92.04)	0	4,772 (7.96)				

Data are presented as number (%), unless otherwise indicated.
SLNB = sentinel lymph node biopsy; AD = axillary dissection; OR = odds ration; CI = confidence inerval; S-H = Seoul-high volume; S-L = Seoul-low volume; NS-H = non-Seoul- high volume; NS-L = non-Seoul-low volume; DCIS = ductal carcinoma *in situ*.
*Low volume and high volume as < 100 vs. ≥ 100 surgical procedures for DCIS patients annually; †Low volume and high volume as < 50 vs. ≥ 50 surgical procedures for DCIS annually.

The 3rd (2008) and 4th versions (2011) of the KBCS Korean clinical practice guidelines for breast cancer recommend SLNB for patients with diffuse DCIS, those with a possibility of invasive cancer, lesions located near the axilla, or in any case when mastectomy is planned [10]. The present study revealed that during the study period, SLNB was performed in 55.96% of BCS cases and 92.04% of TM cases. The rate of SLNB during TM also increased from 88.23% in 2009 to 92.86% in 2015, which is similar to the reported rates of 63.9–92.7% from other countries during similar periods [14,19,20]. In accordance with the national guidelines, the rate of SLNB in patients who underwent mastectomy was high and increased between 2009 and 2015. However, > 50% of the women who underwent BCS also received an axillary evaluation, despite the guidelines' recommendations against this practice. Thus, it appears that SLNB was overperformed in South Korean patients undergoing BCS. The rate of SLNB among BCS cases was also much higher than in previous studies during similar time periods, which revealed axillary evaluation rates of 17.7%–43.9% among DCIS patients undergoing BCS [14,19,20].

The rationale for performing axillary evaluation in women with DCIS is its potential to discover invasive cancer based on the final pathology report, which occurs in up to 38% of cases [7,8]. Therefore, both patients and surgeons might want to avoid a second surgery. However, the incidence of axillary node metastasis in DCIS is very low, with estimates ranging from 1% to 6% [4,5]. Furthermore, van Roozendaal et al. [17] reported

that SLNB revealed metastasis in only 5.6% of the patients with DCIS (3.5% for BCS and 7% for mastectomy), although 16.7% of these patients had invasive cancers. In this context, SLNB might help in identifying axillary metastasis via serial sectioning and additional immunohistochemical analysis. Nevertheless, the clinical significance of this metastasis is unknown, with multiple studies demonstrating no prognostic significance of micrometastasis based on long-term follow-up of women with invasive cancer [18,21]. Moreover, even among women with invasive cancer, completion of AD after positive SLNB does not lead to improved survival compared to patients who did not undergo further axillary surgery [22,23].

Better identification of women with DCIS and identifying the risk of axillary metastasis might reduce the number of patients requiring axillary evaluation. The predictors of upstaging to an invasive lesion are large DCIS lesion, palpable tumor, mass-forming lesion detected during mammography, lack of hormone receptor expression, high nuclear grade, a diagnosis via core-needle biopsy, and the non-cribriform subtype [9]. However, while these features are associated with invasive disease, they might not have a similar value for predicting axillary metastasis among women with DCIS, and there is currently no reliable method for identifying at-risk patients [24,25]. Individual surgeons or institutions might also have different rationales for SLNB depending on the tumor's location, size, and characteristics. In addition, patients undergoing primary oncoplastic surgery after BCS might benefit from SLNB by avoiding multiple surgeries. Unfortunately, we did not have access to data regarding the tumor size, location, pathological findings, or upstaging to invasive cancer, which precludes a clear conclusion regarding the indication for SLNB among Korean women undergoing BCS.

The Korean clinical practice guidelines for breast cancer strongly recommend SLNB during TM, as it cannot be performed later. In cases where the patient undergoes TM for DCIS without SLNB, it would be prudent to perform axillary staging via AD if the pathological examination reveals invasive cancer. Relative to SLNB, AD has higher rates of lymphedema (11%–75% vs. 6%) and paresthesia (19%–68%) [26]. Hence, the guidelines recommend SLNB for patients undergoing TM for DCIS. The present study revealed that SLNB was performed for 92.04% of all patients undergoing TM, and its rate increased from 2009 to 2015, which indicated good adherence to the guidelines relative to other studies [14,19,20].

International studies have found national variability in the surgical treatment of DCIS [27,28], with two UK survey-based studies revealing noticeable variability and lack of consistency regarding the indications for SLNB between regions and breast surgery units. Lack of consensus regarding the best practice for DCIS treatment could explain this variability. Moreover, a large international survey regarding the treatment of DCIS detected on screening revealed variability among multiple centers in Europe, Japan, and the United States [15]. The study reported that AD was performed to achieve the final diagnosis in 5% of the women who underwent BCS for DCIS, versus in almost 20% among women who underwent a mastectomy. Moreover, approximately one-third of the patients with patients, including many small or low-grade DCIS, had undergone SLNB, although the proportion of positive lymph nodes was low (0.6%).

We observed that SLNB in DCIS cases was influenced by the hospital region and surgical volume of DCIS. As Seoul is the capital of South Korea and has many hospitals, we divided the hospitals into Seoul and non-Seoul regions. Interestingly, hospitals in the Seoul region

were less likely to perform SLNB in TM cases, and that hospitals in non-Seoul regions were more compliant with the national guidelines for axillary evaluation in DCIS cases. Another finding was that SLNB was significantly more common in low-volume hospitals, regardless of BCS or TM. Unexpectedly, regardless of BCS or TM, a low rate of SLNB was observed in high-volume hospitals (> 100 DCIS surgeries per year). When we grouped the surgical volumes based on 100 surgeries per year or 50 surgeries per year, a higher proportion of SLNB was observed in low-volume centers with < 100 procedures per year, although no difference was seen for low-volume centers with < 50 procedures per year. Therefore, it appears that hospitals with 50–100 DCIS operations per year were relatively more likely to perform SLNB, regardless of whether the procedures involved BCS or TM. Based on breast cancer statistics from the Korean Breast Cancer Society [1], and assuming that DCIS accounts for 17% of total breast cancer cases, it would appear that hospitals with 300–600 breast cancer surgeries per year were more likely to perform SLNB, regardless of the BCS or TM procedure. In another analysis combining the region and surgical volume of hospitals, high-volume hospitals located in the Seoul region were more likely to perform SLNB in BCS cases and less likely to perform SLNB in TM cases.

A previous study found that SLNB was more common during TM in high-volume hospitals and more common during BCS in low-volume hospitals [20], which the authors attributed to better adherence to the national guidelines at high-volume hospitals. Another report also indicated that the practice type and facility location were associated with axillary evaluation [19]. A third study found that non-teaching hospitals and urban locations were associated with high rates of axillary evaluation during mastectomy, while low axillary evaluation rates during BCS were associated with surgeons performing a high volume of procedures, although such surgeons were more likely perform SLNB than AD [14]. Based on these results, the authors suggested that implementing or expanding multidisciplinary quality assurance teams might be necessary to ensure adherence to the guidelines.

The Society of Surgical Oncology recommends a 'Do not routinely use sentinel node biopsy in clinically node-negative women ≥ 70 years of age with early-stage hormonal receptor-positive, HER2 negative invasive breast cancer' in its 'Choosing Wisely Campaign' [29]. In this study population, we found that patients above 70 years of age had undergone more SLNBs than those below the age of 70 years. On further subgroup analysis according to the breast surgery type, more SLNBs were performed in BCS cases than in TM cases in patients aged above 70 years. There are limited data on the factors associated with high rates of SLNB in women aged 70 years or above. Smith et al. [30] reported that the barriers to implementation are surgeons' lack of familiarity with the recommendation to avoid sentinel-node biopsy in women ≥ 70 years of age and the influence of other collaborating oncology services providers as a justification for its continued use [30]. Usually, SLNB is considered to be less traumatic than AD, which could eliminate the need for a second surgery if invasive cancer was found in the final pathological examination. Therefore, it might be performed to reduce the risk of secondary surgery in older patients.

The present study has several limitations. For example, the HIRA-NIS data are not obtained by mandatory reporting and are not considered high-quality clinical data, as the database is intended to evaluate whether the costs are appropriate and should be covered by the NHIC. Thus, DCIS data might be underreported in the HIRA database. Another limitation is about the operation code of N7135. Although most DCIS patients undergoing BCS receive radiation therapy as standard treatment, lumpectomy alone can be performed in few patients with low-

risk of recurrence. Another challenge is that we could not distinguish between recurrent and primary DCIS in the various study groups. Patients who have been previously diagnosed with breast cancer and undergone axillary surgery often do not undergo another axillary surgery for recurrent DCIS. To reduce the impact of this confounding factor, we excluded patients who had concurrent D05.1 and C50.9 diagnostic codes prior to curative breast surgery. Although rare, patients who underwent surgery for malignant breast disease and relapsed DCIS might also have been included in the database, and it would be difficult to obtain accurate results if this group was included in the analysis. This might also be the reason for SLNB not being performed in patients undergoing TM for DCIS. In addition, among patients diagnosed with DCIS using an excisional biopsy, additional SLNB might not be performed at the discretion of the surgeon when additional TM is performed. Given the clinical findings of DCIS, which frequently involve clustered microcalcifications without a clear mass, excisional biopsy underwire localization could be the main diagnostic method. In such cases, SLNB might not have been performed during curative surgery, including TM and BCS. However, the data from this study cannot distinguish between the excision of a benign tumor located in another region and an excision performed for the examination of DCIS tissue. Another limitation is the retrospective design with limited data regarding the pathological DCIS subtypes that might warrant more aggressive surgical intervention. We also have no data regarding the clinical examination or intraoperative findings, which might have led surgeons to perform axillary evaluations regardless of the guideline recommendations. In addition, we do not have data regarding upstaging to invasive cancer or clinical information regarding tumor size, tumor location, or pathological findings.

Our study showed that SLNB was overperformed in patients undergoing BCS and that the rate of SLNB varied according to the hospital location and the surgical volume of DCIS cases. Further efforts are necessary to improve compliance with the guidelines, which might help in optimizing axillary surgery by decreasing unnecessary SLNB and morbidity in patients with DCIS. Since SLNB can cause surgical complications, including edema of the arm, surgeons must be careful when selecting SLNB for patients who are scheduled to undergo BCS for DCIS. Conversely, not performing SLNB might be considered as undertreatment for patients scheduled to undergo TM for DCIS. Thus, future research should aim to identify the risk factors for lymph node metastasis in DCIS cases, which might help customize the treatment. Moreover, the time and expense for SLNB suggest that adhering to the national guidelines might improve the economic outcomes. A survey-based study might be needed to understand the variability in performing SLNB during surgery for DCIS in Korea.

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