

The adaptation process of a teaching and research hospital to changing trends in modern breast surgery

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ABSTRACT

Objective: Minimally invasive surgery is increasingly gaining importance in breast surgery parallel to other surgical branches. Sentinel lymph node biopsy (SLNB) is a method that has radically changed the approach to breast surgery in the last decade of the 20th century. In this study, we aimed to evaluate the adaptation process to these alterations in breast surgery at our clinic.

Material and Methods: Patients who underwent surgery with a diagnosis of breast cancer in our clinic between April 2010 and November 2013 were retrospectively evaluated in terms of demographic characteristics, the number of operations and type of surgical methods applied according to years, SLNB performance rate, and results of frozen section and histopathological analysis. The first year of SLNB practice was accepted as part of the learning curve, and 24 patients who were operated during that period underwent routine axillary dissection.

Results: The median age of 198 patients who were included in the study was 55 years (25-89). It was detected that the number of cases who underwent surgery for breast cancer increased in years, that the SLNB application rate increased from 37% to 66% between 2010 and 2013 ($p=0.01$), and SLNB staining rates increased from 70% to 94% ($p=0.03$). When only results from the last four years were evaluated, the mean staining rate in patients with SLNB ($n=105$) was 88% ($n=92$), with positive histopathology in 32% of these cases ($n=30$). Despite a decreasing trend over the years, a metastatic axillary lymph node was detected in paraffin block evaluation in spite of negative frozen section examination of SLNB in five cases, and 5 patients (5%) out of 97 patients who underwent breast conserving surgery required re-excision. The histopathological diagnosis was invasive ductal carcinoma in 84% ($n=167$) of patients.

Conclusion: It was observed that during the four-year period of adaptation, the application rate of breast conserving surgery and SLNB reached accepted standards, and that both the technical problems encountered in SLNB and the requirement for re-excision after breast conserving surgery significantly decreased with increasing case volume and experience.

Key Words: Breast-conserving surgery, sentinel lymph node biopsy, lymph node dissection, mastectomy

INTRODUCTION

Today, breast cancer is the most commonly seen type of cancer among women (1). It is stated that breast cancer-related mortalities can be reduced by 21% with the frequent use of screening methods (2).

When the surgical methods applied for malignant breast diseases are put in a historical perspective, it is seen that the requirement to remove the organ was defined by Leonides in 180s and the method he proposed remained in practice for 1500 years. Then, in the sixteenth century, Marcus Aurelius Severinus recommended the removal of axillary lymphatic nodes. The method of radical mastectomy, which was described by Halsted towards the end of the nineteenth century, has become the first globally recognized surgical intervention. The advent of radiotherapy (RT) and chemotherapy (CT) in 1950s paved the way for the use of less radical techniques (3). In the studies conducted as of 1970s, no significant differences were observed between cases who received breast-conserving surgery (BCS) and those who underwent mastectomy in terms of survival (3).

With the gradually increasing importance of minimally invasive surgery in breast surgery as in all branches, and the possibility to diagnose the disease at early stages with the development of technology, minimally invasive methods for the axilla in addition to the breast-sparing approaches have become a point of discussion. In that context, the term sentinel lymph node (SLN) emerged and Giuliano et al. (4) clearly demonstrated for the first time in the year 1994 that the sentinel lymph node was the first lymphatic node where the primary breast tumor drained into the axilla. There are also publications comparing axillary dissection (AD) and SLN biopsy in patients with negative SLN biopsy, among cases diagnosed with early stage breast cancer and demonstrating that there were no significant differences in terms of survival (5). The presence of metastatic lymph node in the axilla is important in determining the prognosis of breast cancer (6). In the literature, the false negativity

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rates of sentinel lymph node biopsy (SLNB) have been stated to be 5-9.8% (7). Among patients whose sentinel lymph node biopsy was found negative and who did not receive AD, the local-regional recurrence rates have been reported as 0.1-1.5% (4). American Society of Clinical Oncology and National Comprehensive Cancer Network (NCCN) have recommended performance of AD in SLNB-positive cases as a consensus decision (4).

All these developments have targeted at ensuring maximum survival and minimum morbidity rates with minimally invasive methods. In this study, we have planned to relate the process of adaptation to minimally invasive methods and the performance of SLNB in breast surgery as in all surgical branches at our clinic.

MATERIAL AND METHODS

At our clinic, the decision to routinely perform SLNB in breast cancer cases was made in 2010. It was also decided that breast surgery operations would be conducted by 3 general surgeons, who would care only for breast cancer patients as of the year 2012. In this process, routine AD was applied to the first 24 cases who received SLNB, considering that both the surgical team and the pathologists were in a learning curve. The cases were evaluated before the operation by a multidisciplinary oncology council consisting of general surgery, radiation oncology, medical oncology, pathology and radiology specialists. Before the procedure, a computer-assisted cancer program (Memorial Sloan Kettering Cancer Center Breast Cancer Nomogram for SLNB positivity) was used to determine SLNB positivity. The nomogram was used to not only create a standard for the learning curve but also to be employed at a currently ongoing clinical study. Written informed consent forms were received for all cases. At the end of the learning curve, SLNB was routinely applied at our clinic.

The files of cases operated on at our clinic with a diagnosis of breast cancer between April 2010 and November 2013 were extracted and their information was registered at a Microsoft Excel 2007 data sheet. The cases whose diagnoses were made and verified by our clinic, whose decisions for surgery were taken by the multidisciplinary council, who were operated on by the surgical team designated for breast surgery and whose histopathological assessment and follow-up or additional treatment processes were managed by the multidisciplinary council were included in the study. Eight cases whose data were accessed but did not meet the inclusion criteria were excluded from the study. The demographic data, diagnosis, number of operations sorted by year and the rates of methods administered, rate of SLNB administration, frozen section examination and histopathological results of the cases included in the study were examined and retrospectively evaluated.

All the cases who would undergo surgery were assessed via physical examination in terms of applicability of BCS and the status of axilla by the breast surgery team before the operation.

For sentinel lymph node biopsy, the staining method with 5 mL methylene blue diluted at 1% was used. The methylene blue was injected in the subareolar site. Then, massage was applied towards the axilla for 5-10 minutes. The axilla incision

was performed either 1 cm under the axillary hair line in a separate incision or along the axillary edge of the quadrantectomy or lumpectomy incision for outer quadrant tumors. The lymph node or nodes removed after the sentinel lymph node biopsy were sent to the pathology clinic for frozen section examination. According to the pre-operative decision, standard mastectomy or BCS was performed. Depending on the frozen section result, AD was added for SLNB-positive cases apart from those within the learning curve process. Negative pressurized drains were placed to the axilla and under the flaps in cases that underwent modified radical mastectomy (MRM). No drains apart from the axilla were used in patients receiving BCS.

Statistical Analysis

The data were assessed by the Statistical Package for the Social Sciences 15 for Windows (SPSS® Inc. Chicago, IL, USA) statistical software program. For the parametric definitions, mean \pm standard deviation was used. For categorical calculations, χ^2 was used; for the comparison of continuous variables, the Student t-test was used for parametric data and the Mann-Whitney U test was used for the non-parametric data. A P value below 0.05 was considered statistically significant.

RESULTS

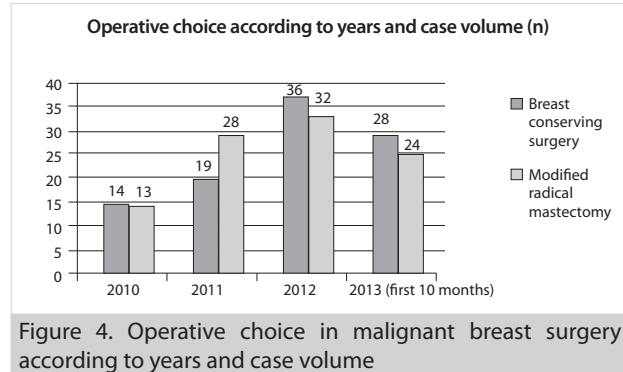
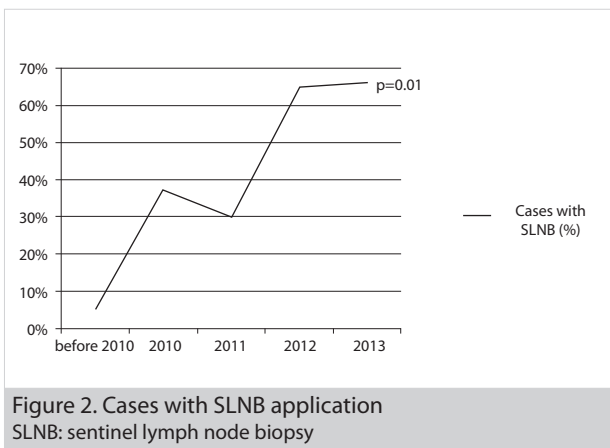
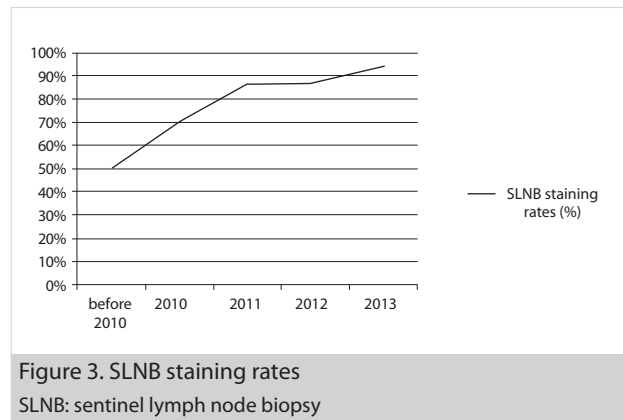
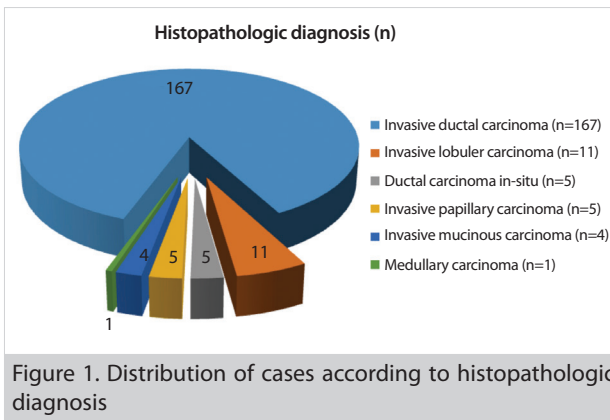
For the patients included in the study (n=198), the median age was identified as 55 (25-89). Among the cases that were operated on, 64% had a mammography result of BIRADS 4 and above. In terms of histopathological diagnosis, 84% (n=167) of the cases had invasive ductal carcinoma with three cases being bilateral (Figure 1). Twenty seven cases had received neo-adjuvant treatment before the operation and 96% (n=26) of these cases received BCS+AD. When the cases were reviewed as per year, it was seen that the surgical case volume for malignant breast tumor increased (Table 1). All cases who were identified to have lymph nodes upon imaging and physical examination between 2010 and 2011, whose SLNB positivity possibility was calculated and saved in the computer environment with the nomogram program, and who received SLNB (n=24) underwent AD considering that both the surgical and pathological clinics were in the learning process. Among patients who underwent AD, 6 cases had a negative SLNB frozen section result whereas they had axillary involvement on histopathological examination.

It was observed that the number of cases who received sentinel lymph node biopsy significantly increased by year (p=0.01) (Figure 2). The average staining rate of cases who received SLNB (n=105) was 87 (n=92), and positive histopathology was identified in 32 of these cases. In the final year of the study, it was observed that the SLNB staining rate reached 94%, which was significant (p=0.03) (Figure 3). Apart from the learning curve period, the paraffin examination result was positive in 5 cases with negative frozen section examination, with one having micrometastasis. It was determined that the number of patients who were reported to have a negative SLNB but were identified to have a positive result according to paraffin block examination significantly decreased in time (p=0.04) (Table 1).

It was seen that BCS/Mastectomy ratio increased, although it was not statistically significant (p=0.93) (Figure 4). Re-excision

Table 1. The rate and results of minimal invasive procedure in malignant breast tumor surgery according to years

	Total		BCS			Simple mastectomy*		MRM		SLNB application		SLNB staining		SLNB (+)		SLNB (-) Paraffine (+)		AD in BCS ^b		Re-excision due to (+) margin on BCS	
	n	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	n	%	
Years																					
2010	27	14	52	-	0	13	48	10*	37	7	70	1	3 ^b	30		14		2	14		
2011	47	19	40	-	0	28	60	14*	30	12	86	7	4 ^b	28		17		1	5		
2012	71	36	51	3	4	32	45	46	65	40	87	12	3	7		12		1	1		
2013 (first 10 months)	53	28	53	1	2	24	45	35	66	33	95	12	2	6		12		1	4		
Total	198	97	49	4	2	97	49	105	53	92	88	32	5 ^a	5		55		5	5		
P	BCS/MRM: 0.93 [†]					0.01 [†]					0.03 [‡] -		0.04 [‡]		-		0.2 [‡]				
*Cases without completion MRM due to (-) SLNB																					
^b AD was applied routinely in the first 24 cases between 2010-2011 regardless from SLNB result due to learning period																					
^c Cases without routine AD after the learning curve period																					
^{a-y} p values were obtained by comparing the years 2010 and 2013																					
[†] with Student-t test																					
[‡] with Mann-Whitney U test (non-parametric data)																					
BCS: breast conserving surgery; MRM: modified radical mastectomy; SLNB: sentinel lymph node biopsy; AD: axillary dissection																					



was performed in 5 (5%) out of 97 cases who underwent breast conserving surgery. Similarly, it was seen that the re-excision rates had decreased in BCS cases when the baseline and the final year of the study were compared ($p=0.2$) (Table 1).

DISCUSSION

Within the past 20 years, there has been a rapidly increasing tendency towards minimally invasive methods in the field of breast surgery as in other surgical interventions (8). In a randomized study, no significant differences in terms of

recurrence were seen in the 10-year and 20-year follow-ups of cases who underwent BCS and mastectomy (9). Especially, the development of RT and CT treatment regimens, identification of similar local recurrence and long-term survival rates for both BCS+RT and MRM, and the low rate of local recurrence in BCS (1% per year) have increased the tendency towards BCS (10, 11). In a randomized clinical trial published by Guiliano et al. (12) in 2011, patients with T_1 and T_2 tumors and 1 or 2 positive SLNs were included in the study, and BCS+RT were routinely performed. Patients were randomized into either AD or no additional surgery groups, and were followed up for 6.3 years on average. In conclusion, no significant dif-

ferences were seen between the two groups with respect to survival.

Complications such as lymph-edema, limitation in arm movements and hematoma are seen more frequently in axillary dissection as compared to SLNB. Therefore, SLNB is being used at an increasing frequency, and the axillary complication rate among primary breast cancer patients is decreasing (13). Furthermore, in a study comparing mastectomy and BCS + axillary surgery, patients who received breast conserving surgery were reported to have lower mortality and morbidity rates (14). Another reason is that loss of self-image was lower in patients who received BCS and they had significantly better sexual life, although no differences were noted between the two surgical groups in terms of impairment of psychological conditions in the post-operative period (15-18).

The American Society of Breast Surgeons accepted the number of procedures for completion of SLNB learning curve as 20 (19). False negativity rate was reported to be less than 5%, and SLN identification was not less than 85% after this limit (19). Furthermore, a 'short learning curve' that defined performing 8 consecutive positive SLNBs as adequate and acceptable was also reported in the literature (19). Similarly, the first 24 cases in our clinic were considered to be part of the learning curve, and all those cases received AD. There are studies in the literature stating that the administration site of methylene blue in the peritumoral site or subareolar site was not significant in terms of positive node identification rate, however, there are also studies reporting that false positivity rates have not yet been clearly demonstrated (20). At our clinic, methylene blue was routinely administered to the subareolar site.

There are publications in the literature reporting re-excision rates in the range of 9-50% following BCS (21, 22). We think that the reason why the re-excision rate of 4% in our series was lower as compared to similar publications was that the number of our cases was low.

The main limitations of the study are as follows: low case-volume due to our clinic not yet being a reference center for breast surgery, increase in malignant cases especially after the establishment of the breast outpatient clinic, the new multidisciplinary standardization and consequently, the design of the study.

CONCLUSION

Based on an evaluation of the 4-year-long period in our study, it was seen that the BCS and SLNB administration rates approached acceptable standards. After implementation of the multidisciplinary oncology council at our hospital, it was seen that the technical problems encountered in SLNB and requirement for re-excision following BCS were remarkably decreased, owing to the increasing case volume and experience.

Ethics Committee Approval: Due to the retrospective design and anonymized data of patient charts, ethical approval has not been questioned.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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