

Oncoplastic Surgery and Outcome prediction deserve Axillary Lymph Node Dissection – Treatment results of 51 cases of breast cancer.

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Article Received 01-08-2021 / Article Accepted 06-09-2021 / Article Published 10-09-2021

Abstract

Background: The current trend of early breast cancer (BC) management is to conserve axillary lymph nodes (ALNs) with the idea that ALN dissection (ALND) has no therapeutic value. Owing to wide individual variations of number of ALNs, lymph node ratio (LNR) could predict recurrence and death ('Incident') better and ALND is in need for LNR expression. ALND invite lymphedema thus oncoplastic surgery (OPS) along with ipsilateral ALND might cause enlargement of reconstructed breast resulting in spontaneous symmetrization. The aim of this study was to determine role of LNR for prediction of 'Incident' of BC and spontaneous symmetrization of breasts of OPS as a new concept through utilization of ALND. The objectives of study of ALND were to assess LNR categories to predict 'Incident' of BC patients, and outcome of ipsilateral ALND for spontaneous breast symmetrization of OPS.

Methods: This prospective study was conducted on 51 consecutive BC patients treated and under follow-up study. Patients' information was collected using research instrument after obtaining informed consent of patients and approval of Institutional Ethical Board.

Results: The median age, weight of patients and number of LNs were 48 years, 59 kg and 12 LNs respectively. Postmenopausal and ALND negative were 67% and 26% respectively. Follow-up study indicated 12% patients had 'Incident'. The difference of 'Incident' and LNR categories was significant ($p < 0.001$). Spontaneous enlargements of all OPS breasts were observed.

How to Cite:

Mostaque, A., A. A. Mamun, M., Kamal, M., Shariful Alam, A., Chowdhury, I. U., & Mamun, M. (2021). Oncoplastic Surgery and Outcome prediction deserve Axillary Lymph Node Dissection – Treatment results of 51 cases of breast cancer. International Invention of Scientific Journal, 5(09). Page: 25-37. Retrieved from <https://iisj.in/index.php/iisj/article/view/344>



Conclusions: High-risk LNR has strong association with recurrences and deaths. Ipsilateral axillary lymph node dissection with oncoplastic surgery lead to lymphedema of the operated cancer bearing breast and should be a routine procedure to have enlargement of operated-breast to achieve 'spontaneous breasts symmetrization' instead of current practice of 'iatrogenic breasts symmetrization'. This discovery will be well accepted by patients desiring oncoplastic surgery of cancer bearing breasts but unwilling reduction mammoplasty of contralateral normal breasts.

Key words: Oncoplastic surgery axillary lymph node dissection; breast cancer surgery spontaneous operated breast enlargement; axillary lymph node ratio breast cancer outcome prediction.

Introduction

The current trend in treating early breast cancer (BC) is to preserve ipsilateral axillary lymph nodes (ALNs) with the idea that axillary lymph node dissection (ALND) has no definite therapeutic value. In contrast, importance is being given on extensive lymphadenectomy in GIT (Zhang & Yang, 2020) and esophageal cancers because of it would increase duration of progression free survival (PFS) and overall survival (Matsuda, Takeuchi, Kawakubo, & Kitagawa, 2017). ALND has reliably been identifying number of nodal metastasis and maintain regional control, but its therapeutic value is unclear (Giuliano et al, 2011). It has also been observed that in T1 and T2 BC patients with 1-2 positive LNs from sentinel LN biopsy have an equivalent PFS and OS to ALND (Martin et al, 2018). LN status does not play any role in planning neoadjuvant chemotherapy (NAC). Rather, adjuvant radiotherapy and systemic treatment is planned according to tumor biology (Reimer, Engel, Schmidt, Offersen, Smidt, & Gentilini, 2018). In BC an increase in number of positive ALNs is associated with poorer clinical outcomes and increased of BC patients by determining lymph node ratio (LNR) i.e. ratio of total number of positive nodes to ALNs removed (Soran, Ozmen, Salamat, Soybir, & Johnson, 2019). The TNM classification for BC emphasizes on absolute number of positive LNs possibly with the assumption that number of ALNs is constant in humans. In fact variations in the number of ALNs has been observed and ranging from 5 to >30 (Nall, 2019). No clear data about the 'adequate' number

of ALNs to be dissected has been observed, and studies indicate no significant difference of PFS and OS among patients with ≥ 10 LNs dissected comparing patients with < 10 LNs dissected (Nabil, maklad, Elyamany, Goma, & Ali, 2019). An important issue to be noted is counting absolute number of positive ALNs for staging purpose could not express magnitude of tumor burden and regional progression of cancer for example 20 positive LNs out of 20 ALNs examined should be something else than that of pN3 stage. ALN staging in BC is the only node-related factor for BC staging and predictor for recurrence and survival (Li, Holnes, Shah, Albuquerque, Szpaderska, & Ersahim, 2012) recognized by American Joint Committee on Cancer (AJCC). It might possible that LNR offers a better option to predict recurrence and death ('Incident') and ALND is a prerequisite for LNR expression. ALND invite lymphedema to the ipsilateral upper limb, chest wall and breast by impairing lymphatic drainage. Thus oncoplastic surgery (OPS) along with ipsilateral ALND might cause continued spontaneous enlargement of the reconstructed breast. Enlargement of the treated breast could be controlled to a desired size by physical means resulting in spontaneous symmetrization.

The aim of this study was to determine scope of LNR to predict 'Incident', and spontaneous symmetrization of breasts of BC patients after OPS through utilization of ALND as a new concept. The objectives of this study of ALND were to assess LNR categories leading to prediction of 'Incident' of BC

patients and outcome of routine ipsilateral ALND for breast symmetrization as a part of OPS.

Materials and Methods

This prospective study was conducted on 51 consecutive BC patients admitted and treated under Surgical Oncology Department of Ahsania Mission Cancer and General Hospital, Dhaka, Bangladesh. Institutional Ethical Board approval and informed consent of the patient were obtained. Study period was from August 2016 through December 2019. Patients who underwent BC surgery with regular follow-up from the date of enrolment were included and those who had BC with distant metastasis at the time of diagnosis or dropped-out from follow-up were excluded. No patient was lost from follow-up. Patient's information was collected from the hospital registry using a research instrument form and after obtaining informed consent of OPS cases and approval of Institutional Ethical Board. Particulars of the patients were recorded including age, address, telephone number, body weight and height for BMI, date of diagnosis and of starting treatment, type of surgery, number and size of the tumor, number of ALNs dissected and number of positive LNs obtained, histological type, immunohistochemistry (ER, PR, and Her-2/neu), TNM stage, stage grouping and quarterly follow-up. The patients were divided into premenopausal (≤ 44 years) and postmenopausal (> 44 years) age groups (Ringa, 2000), and according to schedule of treatment 'Surgery-First' (those underwent surgery as initial treatment) and 'NAC-Surgery' (those had neoadjuvant chemotherapy and then surgery) groups. BMI was calculated and categorized as underweight (< 18.5), healthy (18.6-24.9), overweight (25-29.9) and obese (≥ 30). Date of diagnosis was counted from the date of cytology or histological confirmation of BC. Types of surgery performed were modified radical mastectomy (MRM) i.e. mastectomy including skin, nipple-

areolar complex and pectoral fascia along with ipsilateral (level I, II, and III) ALND, MRM with ipsilateral pedicle latissimus dorsi myocutaneous flap reconstruction in locally advanced BC, OPS (up to 30% breast tissue excision with tumor having safe tumor free margin and reconstruction of breast) with ALND. Outcome of surgery was recorded along with duration of PFS and OS. Staging of BC were done according to AJCC cancer staging manual (7th edition).

ALND is defined as a surgical procedure which identified and removed ALNs between axillary vein superiorly, the serratus anterior medially and the latissimus dorsi muscle laterally with dissection of level I, II and III LNs (Ebner et al, 2019). Complete ALND is defined as removal and examination of ≥ 6 ALNs and 6 LNs is the minimum number needed to adequately assess the extent of nodal involvement in the axilla (Katz, 2008).

Patients surviving without any evidence of disease progression after surgery were defined as 'No-Incident' and with evidence of recurrence and deaths as 'Incident'. Recurrence was defined as the recurrence of breast cancer after surgery to regional LNs, chest wall, and metastasis to distant organs or second primary breast cancer. Follow-up time was calculated from the date of diagnosis to end of September, 2020 or death. PFS is defined as the length of time of survival in months from date of operation to date of diagnosis of recurrence. OS is defined as the length of time in months from the date of diagnosis to death of a treated BC patient. 'Spontaneous symmetrization' of breasts was defined as controlled enlargement of the operated breast secondary to lymphedema of ALND.

LNR was calculated as the total number of positive LNs divided by the total number of LNs dissected out of ALND. If ALN contains metastatic deposit, it was then called LN positive and if free of malignant deposits then LN negative. Patients were divided in 3 were low- (≤ 0.20), intermediate- (0.21-0.65), and

high-risk (>0.65) LNR (Bansal & Bright, 2018). During analysis of LNR pN0 was incorporated with pN1 group.

Statistical analysis was performed using IBM SPSS version 24. Mean was expressed as mean \pm SD (minimum-maximum). Median values were recorded to provide an accurate picture of distributions. Chi-square, T-test, ANOVA, and nonparametric tests were used as indicated to assess significance; *p* values < 0.05 with 95% confidence interval (CI) considered statistically significant.

Result

Total number of patients were 51 of which females 50 (98%) and male 1 (2%). Number of patients of pre- and post-menopausal age groups were 17 (33.33%) and 34 (66.67%) respectively. In premenopausal age group of low-, intermediate-, and high-risk LNR were 10 (53.82%), 4 (23.53%), and 3 (17.65%), and those of postmenopausal age were 14 (41.18%), 15 (44.12%), and 5 (14.79%) respectively. The differences was not significant (Kruskal-Wallis test, *p* = 0.315).

The median and mean age of the patients was 48 and 47.29 \pm 9.84 (28 - 75) years respectively. The

median and mean age of pre- and post-menopausal group was 38, 36.29 \pm 4.25 (28 - 40), and 48, 52.79 \pm 6.66 (45 - 75) years respectively.

The median and mean body weight was 59 and 59.16 \pm 10.59 (35-103) kg, and of BMI was 25.43 and 25.71 \pm 4.47 (14.2 - 40.23) kg/m² respectively. In underweight (*n* = 3), 1 (1.96%) of each were pN1, pN2 and pN3 respectively. The pN0, pN1, pN2, and pN3 of healthy weight (*n* = 17) were 0, 6 (11.76%), 5 (9.8%), and 6 (11.76%), in overweight (*n* = 23) were 5 (9.8%), 9 (17.65%), 8 (15.69%), and (1.96%), and in obese group (*n* = 8) 2(3.92%), 1(1.96%), 3(5.88%), and 2 (3.92%) respectively. The differences was not significant (Chi-Square Test, *p* = 0.342). All the underweight cases belonged to intermediate-risk LNR. Among healthy weight cases low-, intermediate-, and high-risk LNR were of 11 (64.72%), 4 (23.53%), and 2 (11.76%), for overweight cases were of 10 (43.48%), 11 (47.89%), and 2 (8.7%), and for obese were of 3 (37.5%), 1 (12.5%), and 4 (50%) respectively (Table 1). The difference was significant and (Chi-Square test, *p* < 0.014).

Table 1: Summary statistics of patient's BMI, pN stages and LNR.

Variable Name	Number of Subject (%)	<i>p</i> value	
Underweight			
pN1	1 (1.96)		
pN2	1 (1.96)		
pN3	1 (1.96)		
Healthy weight			
pN0	6 (11.76)		
pN1	5 (9.8)		
pN2	6 (11.76)		
Overweight			
pN0	5 (9.8)	<i>0.342</i>	
pN1	9 (17.65)		
pN2	8 (15.69)		
pN3	1 (1.96)		
Obese			
pN0	2 (3.92)		
pN1	1 (1.96)		
pN2	3 (5.88)		
pN3	2 (3.92)		
Underweight			
Intermediate-risk LNR	3 (5.88)		<i>0.013</i>
Healthy weight			
Low-risk LNR	11 (21.57)		
Intermediate-risk LNR	4 (7.84)		
High-risk LNR	2 (3.92)		
Overweight			
Low-risk LNR	10 (19.61)		
Intermediate-risk LNR	11 (21.57)		
High-risk LNR	2 (3.92)		
Obese			
Low-risk LNR	3 (5.88)		
Intermediate-risk LNR	1 (1.96)		
High-risk LNR	4 (7.84)		

BMI: Basal metabolic rate, pN: Pathological node, LNR: Lymph node ratio.

The ALND negative cases were 13 (25.5%) and positive were 38 (74.5%). The median number of ALNs dissected was 12 LNs. The median number of LNs of ALN negative and positive groups were 12 LNs each. The difference was not significant (t-test, $p = 0.491$). The median ALNs removed in 'Surgery-First' and 'NAC-Surgery' were 12 and 13.5 LNs

respectively (Table 2). The difference was not significant (Kolmogorov-Smirnov Z test, $p = 0.98$). Number of ALNs removed within the range of 6 – 9 LNs was 11 (21.6%), 10 – 15 LNs was 27 (53.1%), 16 – 20 LNs was 7 (13.73%), and 21 – 26 LNs was 6 (11.76%) respectively (Table 2).

Table 2: Summary statistics of axillary lymph nodes.

Variable Name	Number of Subjects (%)	Mean \pm SD (minimum-maximum)	<i>p</i> value
LN's dissected ALND negative ALND positive	51 (100) 13 (25.5) 38 (74.5)	13.33 \pm 5.23 (6-26) 12.48 \pm 4.59 (6-20) 13.24 \pm 5.06 (6-26)	0.491
Number of positive LN's		4 \pm 5.42 (0-20)	
Number of LN's dissected 'Surgery-First' group 'NAC-Surgery' group	41 (80.39) 10 (19.61)	13.07 \pm 5.12 (6-25) 14.4 \pm 5.8 (7-26)	0.98
LN range 6-9 10-15 16-20 21-26	11 (21.6) 27 (53.1) 7 (13.73) 6 (11.76)		
Number of Positive LN's 'Surgery-First' group 'NAC-Surgery' group	41(80.39) 10 (19.61)	3.61 \pm 4.41 (1-20) 5.8 \pm 5.49 (1-19)	<0.001
pN status 'Surgery-First' group N0 N1 N2 N3 pN status 'NAC-Surgery' group N0 N1 N2 N3	12 (29.27) 13 (31.7) 13 (31.7) 3 (7.32) 1 (10) 3 (30) 5 (50) 1 (10)		0.183

LN: Lymph node, ALND: Axillary lymph node dissection, NAC: Neoadjuvant chemotherapy, pN: Pathological lymph node, N: node

The median number of positive ALNs was 4 (Table 2). The median number of positive ALNs in 'Surgery-First' and 'NAC-Surgery' groups were 3 and 4.5 nodes respectively. The difference was significant (Mann-Whitney test, $p < 0.001$). Number of pN0, pN1, pN2, and pN3 in 'Surgery-First' group were 12 (29.27%), 13 (31.7%), 13 (31.7%) and 3 (7.32%) respectively and those of 'NAC-Surgery' group were 1(10%), 3 (30%), 5 (50%) and 1 (10%) respectively (Table 2). The difference was not significant (Jonckheere-Terpstra test, $p = 0.183$).

According to LNR number of patients of low-, intermediate- and high-risk categories were 24 (47.06%), 19 (37.25%), and 8 (15.68%) respectively. The median ALNs dissected of low-, intermediate-, and high-risk LNR was 13, 11, and 11.5 LN's respectively. The difference was not significant (Kruskal-Wallis test, $p = 0.384$). The mean number of positive ALNs in low-, intermediate- and high-risk categories were 1.08 \pm 1.53 (0 – 5), 4.58 \pm 2.87 (2-15), and 11.63 \pm 5.48 (7 – 20) respectively. The difference was significant (Kruskal-Wallis test, $p < 0.001$). The pN0, pN1, pN2, and pN3 of low-risk LN

were 13 (54.17%), 8 (33.33%), 3 (12.5%), and 0 respectively, in intermediate-risk LNR were 0, 8 (42.11%), 10 (52.63%), and 1(5.26%) respectively,

and in high-risk LNR were 0, 5 (62.5%), and 3 (37.5%) respectively (Table 3). The difference was significant (Kruskal-Wallis test, $p < 0.001$).

Table 3: Distribution of LNR and pN stage.

Variable Name	Number of Subjects (%)	Median LNs	Mean \pm SD (minimum-maximum) LNs	<i>p value</i>
LNR groups				
Low-risk	24 (47.06)	13	14.75 \pm 6.08 (6-26)	0.384
Intermediate-risk	19 (37.25)	11	11.79 \pm 3.79 (7-25)	
High-risk	8 (15.68)	11.5	12.75 \pm 4.77 (8-20)	
LN positive LNR group				
Low-risk			1.08 \pm 1.53 (0-5)	<0.001
Intermediate-risk		4	4.58 \pm 2.87 (2-15)	
High-risk		8	11.63 \pm 5.48 (7-20)	
pN stage in LNR group				
Low-risk				<0.001
pN0	13 (54.17)			
pN1	8 (33.33)			
pN2	3 (12.5)			
Intermediate-risk				
pN1	8 (42.11)			
pN2	10 (52.63)			
pN3	1 (5.26)			
High-risk				
pN2	5 (62.5)			
pN3	3 (37.5)			

LNR: Lymph node ratio, pN: pathological node.

Out of 51 treated BC patients 6 (11.76%) had 'Incident'. Distant metastasis to liver, lungs and sacrum occurred 1 (1.96%) of each respectively and 3 (5.88%) cases died with mean PFS and OS of 13.42 and 22.16 months respectively. In pre- and post-menopausal groups 'Incident' were 2 (3.92%) and 4 (7.84%) respectively (Table 4). The differences was not significant (Fisher's Exact Test, $p = 1.00$). The pN0 and pN1 had no 'Incident', and those of pN2, and pN3 had 4 (66.67%), and 2 (33.33%) respectively. The difference was not significant (Wilcoxon Signed Rank test, $P = 0.369$). Low-risk LNR had no 'Incident', intermediate-risk LNR had 1 (1.96%) and high-risk LNR had 5 (9.8%) respectively.

The difference was significant (Kruskal-Wallis test, $p < 0.001$). In 'Surgery-First' group number of 'Incident' of pN0, pN1, pN2, and pN3 were 0, 0, 2 (4.88%), 1 (2.44%) respectively (Table 4). The difference was not significant (Kruskal-Wallis Test, $p = 0.109$) and those of low-, intermediate- and high-risk LNR were 0, 1(2.44%) and 2 (4.88%) respectively. The difference was significant (Kruskal-Wallis Test, $p = 0.002$). In 'NAC-Surgery' group number of 'incident' of pN0, pN1, pN2 and pN3 were 0, 0, 2(20%) and 1 (10%) respectively. The differences was not significant (Wilcoxon Signed Rank test, $p = 0.18$). In 'NAC-Surgery' group 'Incident' was 3 (30%) and 'Incident' of low-,

intermediate-, and high-risk LNR were 0, 0, and 3(30%) respectively (Table 4). The difference was significant (Wilcoxon Signed Rank test, $p = 0.008$).

Table 4: Distribution of recurrences and deaths ('Incident') of breast cancer patients.

Variable Name	Number (%)	<i>p value</i>
Total number	6 (11.76)	
Recurrences	3 (5.88)	
Deaths	3 (5.88)	
Premenopausal age group	17(33.33)	
'No-incident'	15 (29.41)	
'Incident'	2 (3.92)	
Postmenopausal group	34 (66.67)	<i>1.00</i>
'No-incident'	30 (58.82)	
'Incident'	4 (7.84)	
According to pN stage		
pN0	0	
pN1	0	
pN2	4 (66.67)	<i>0.369</i>
pN3	2 (33.33)	
According to LNR categories		
Low-risk	0	
Intermediate-risk	1 (16.67)	<i><0.001</i>
High-risk	5 (83.33)	
Of 'Surgery-First' group		
'No-incident'	38 (92.68)	
'Incident'	3 (7.32)	
According to pN stage		
pN0	0	
pN1	0	
pN2	2 (4.88)	<i>0.109</i>
pN3	1 (2.44)	
According to LNR categories		
Low-risk	0	
Intermediate-risk	1 (2.44)	<i>0.002</i>
High-risk	2 (4.88)	
Of 'NAC-Surgery' group		
'No-incident'	7 (70)	
'Incident'	3 (30)	
According to pN stage		
pN0	0	
pN1	0	
pN2	2 (20)	<i>0.18</i>
pN3	1 (10)	
According to LNR categories		
Low-risk	0	
Intermediate-risk	0	<i>0.008</i>
High-risk	3 (30)	

N: node, LNR: Lymph node ratio, NAC: Neoadjuvant chemotherapy, pN: Pathological node.

MRM were performed in 46 (90.2%), OPS and ipsilateral ALND 4 (7.84%), and MRM with ipsilateral latissimus dorsi myocutaneous pedicle flap reconstruction in 1 (2%) cases. Pre- and post-menopausal OPS with ipsilateral ALND was 1 (25%) and 3 (75%) respectively, the median and mean weight was 62 kg, healthy weight and obese was 1 of each and 2 were overweight. All OPS patients had single tumor, the median and mean tumor size was 2.5 cm, and 2 of each were T1 and T2 stage. The median and mean number of LNs dissected was 11 and 11 ± 4.16 (6 - 16), and LNs involved was 1 and 1 ± 0.82 (0 - 2) respectively. All were belonged to low-risk LNR category. The median and mean follow-up time was 17.38 and 16.58 ± 1.71 (14 - 17.5) months. There was progressive enlargement of all OPS breasts. OPS and

contralateral normal breast attained grade – II ptosis with minimum upper limb lymphedema (**Figure 1A, 1B, 2A and 2B**).

Figure 1A: Appearance of the left breast 12 months of oncoplastic surgery with ipsilateral axillary lymph node dissection of a 50 years old woman. Patient had pathological T1N0Mx stage tumor, ER and PR positive, Her-2 negative infiltrating ductal carcinoma at 1-2 O'clock position. Operated breast was swollen and unmatched with normal counterpart.

Figure 1B: Appearance of breasts of figure 1A 17.5 months after oncoplastic surgery with ipsilateral axillary lymph node dissection. Operated breast is prominent with minimum edema of the left upper extremity and chest.



Figure 1A:



Figure 1B:



Figure 2A

Figure 2A: Appearance of left breast 4.5 months after oncoplastic surgery with ipsilateral axillary lymph node dissection of a 38 years old woman. Patient had pathological T1N1Mx tumor stage, ER and PR positive, Her-2 negative, infiltrating ductal carcinoma at 2-3 O'clock position of the breast. Operated breast was swollen and larger the normal counterpart. Nipple areolar complexes were almost at same levels.

Figure 2B: Appearance of breasts figure 2A 23 months of oncoplastic surgery with axillary lymph node dissection. Patient received adjuvant chemo- and radiation-therapy and antihormone therapy. There was 'spontaneous symmetrization' of the breasts. Patient was abstaining from wearing bra for one month. Left breast mound was prominent than normal counterpart.

Discussion

Significant and strong positive association was observed between BMI and LNR categories in this

Figure 2B

study. Similar strong association was also reported in other studies (Kaviani, Neishaboury, Damavandi, & Jamal, 2012). The etiology of increased number of positive axillary lymph nodes in overweight and obese patients might be due to increased level of estradiol in the peripheral adipose tissue which is an important factor for development of easy ALN metastasis (wang, Cai, Yu, Ping, & Liu, 2020).

ALND were performed in all cases of this study. In one study ALND is indicated in 30% of breast cancer cases and considered in other cases as overtreatment because of ALN negative early breast cancer (Qiu, 2016). This study observed median and mean number of dissected LNs after ALND were 12 and 13.33 respectively. A similar result was observed in another study with median and mean LNs of 11 and 14.29 (El-Bary, Tawfik, El-ghani, Shaltout, & Hussein, 2017). No significant differences observed of number of ALNs dissected between 'Surgery-First' and 'NAC-Surgery' groups.

Similar result was presented in other study (Boughery, Donohue, Jakub, Lohse, & Degnim, 2010) but another study observed significantly low number of ALNs (<10 LNs) dissected out in NAC patients (Neuman, et al, 2006).

This study observed 21.6% of BC patients had 6 - 9 ALNs. Other observed 34.5% BC patient had 7 – 9 ALNs (El-Bary, Tawfik, El-Ghani, Shaltout, & Hussein, 2017). Though number of ALNs ranging from 5 to >30 (Nall, 2019), it is important to determine proportion of population having < 10 ALNs. One study indicated that at least 6 LNs should be dissected out of axilla for examination (Katz, 2008) whereas another study indicated 10 ALNs should be examined for TNM staging (Nabil, maklad, Elyamany, Goma, & Ali, 2019). But it has been observed that there is no significant difference of PFS/OS between patients having >10 and <10 LNs excised. But quality of life is better among less axillary LN dissected patients from low prevalence of lymphedema (Ebner et al, 2019).

This study observed 75.5% BC cases with positive ALNs. One study found 64% BC patients presented with positive ALNs (Somner, Dixon, & Thomas, 2004). This study observed overall median and mean number of positive ALNs were 3 and 4.1 ± 4.7 respectively. Similar result was observed in other study (Somner, Dixon, & Thomas, 2004).

This study observed significant differences of number of positive ALNs between 'Surgery-First' (3.61 LNs) and 'NAC-Surgery' (6.1 LNs) groups ($p < 0.001$). One study observed decreased number of positive ALNs in BC patient having NAC (Neuman et al, 2006). Increased number of positive ALNs among 'NAC-Surgery' group could be due to very long surgical treatment delay time (median of 305 days) observed indicating sufficient time to regain regional tumor progression. This study indicated that 10% 'NAC-Surgery' patients attained pathologically node-negative status after NAC. One study observed 37% patients attained

pathologically node-negative status after NAC (Fisher et al, 1997).

This study observed 47% of patients were in low-risk, 37.25% in intermediate-risk, and 15.68% in high-risk LNR group. Almost similar result was reproduced in one UK study (Bansal & Bright, 2018). The distribution of 'Incident' observed no difference among menopausal age groups, also observed in another study (Mahmood, Faheem, Mahmood, & Sadiq, 2015). The distribution of 'Incident' and pN stage were of no significant difference, also observed in one study (Li, Holnes, Shah, Albuquerque, Szpadarska, & Ersahim, 2012). This study observed significant difference of distribution of 'Incident' and LNR categories ($p < 0.001$) with majority 'Incident' observed in high-risk LNR. Similar result was observed in another study (Ebner et al, 2019). Significant differences of 'Incident' and LNR categories were observed in 'Surgery-First' ($p = 0.002$) and 'NAC-Surgery' group ($p = 0.008$), also observed in other studies (Soran, Ozmen, Salamat, Soybir, & Johnson, 2019). Spontaneous enlargements of the operated breasts after OPS with ipsilateral ALND were observed in all cases indicating definite therapeutic role of ALND though one study observed no clinical benefit (Kuhn, 2018) and as overtreatment in ALN negative patients (Qiu, 2016). The therapeutic value of ALND should be reintroduced as a simple, sound, and secured concept of OPS. Breasts symmetry can be maintained by wearing tight bra and exercise. Routine ALND will simplify OPS and avoid unnecessary surgery of the opposite normal breast for symmetrization. Current OPS depict operation of bilateral breasts. If ipsilateral ALND is introduced then operation will be confined to only affected breast for removal of the cancer and as well as symmetrization. Ipsilateral ALND should be a routine technique in OPS. This modality of surgery will be applicable to patients who do not want reduction mammoplasty of the opposite normal

breast as a requirement of 'symmetrization'. The nipple-areolar complex of the operated breast observed mildly elevated than that of normal breast after long term follow-up (Fig 1A, 1B, 2A and 2B).

Conclusions:

High-risk LNR has strong association with recurrences and deaths of breast cancer. Ipsilateral axillary lymph node dissection with oncoplastic surgery has therapeutic value in surgical management of breast cancer and should be a routine procedure irrespective of lymph node status because it causes spontaneous enlargement of operated-breast thus achieving spontaneous symmetrization, eliminating the need of ethically unsound complicated reduction mammoplasty of opposite normal-breasts for iatrogenic symmetrization of the breast of BC patients. This discovery will be well accepted by patients desiring oncoplastic surgery of cancer bearing breasts but unwilling reduction mammoplasty of contralateral normal breasts.

Disclosure:

The authors have declared no conflict of interest. There was no financial interest or connection with this work.

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