Original Research Article

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Surgical management of axilla: controversy and care

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ABSTRACT

Background: Surgical staging of the axilla has traditionally provided the best prognostic information about breast cancer. However, the morbidity of a complete axillary clearance outweighs the therapeutic and prognostic benefits of the procedure. Authors observed the types of axillary lymph node dissection (ALND) performed in authors' institute and the magnitude of morbidities of a complete ALND.

Methods: This observational study was conducted at the Cancer Institute of Himalayan Institute of Medical Sciences for a period of one year. Sequelae of ALND was observed at 1, 3 and 6 months in all female patients undergoing axillary dissection as part of surgery for breast cancer.

Results: Out of 150 patients 53 (35.33%) presented with locally advanced disease, and 84 (56%) had palpable axillary nodes. All patients with palpable nodes underwent level II-III dissection. 32 patients underwent sentinel node dissection using blue dye only. Tumour size correlated positively with grade of tumour (r = 0.36, P < 0.001) and number of positive lymph nodes (r = 0.34; P < 0.001). There was significant difference in incidence of lymphedema at 6 months in patients who underwent level III dissection (27.38%) as opposed to those who did not (8.92 %) (p < 0.05). The incidence of seroma was also more at 1 month in these patients (57.14%) vs (39.28%), (p < 0.05). Post-operative pain/ wound infection/Restriction of motion were not statistically significant.

Conclusions: Higher stages of presentation require higher levels of axillary dissection. Unwarranted dissection can be avoided by tailoring the surgery during initial clinical assessment.

Keywords: Axillary lymph node dissection, Invasive breast carcinoma, Lymphedema, Post-operative pain, Seroma

INTRODUCTION

The incidence of breast cancer in India is on the rise and is rapidly becoming the number one cancer in females pushing the cervical cancer to the second spot.¹

In India 5% women are likely to suffer from breast cancer during their lifetime. Even though the rise is only evident in the metropolitan cities, it can be safely said that many patients in rural India go unobserved and because of lack of knowledge and ignorance such patients present in a late stage of the disease.²

Surgery for cancer of the breast was pioneered by William S. Halstead, who advocated en bloc removal of the breast, axillary nodes and part of the chest wall.³ Called the radical mastectomy, this procedure became the unquestionable path that generations of surgeons followed with diligence. Although it often resulted in significant morbidities, it increased the 20 years survival rate from 10 to 50%.

Axillary node involvement is the single most important prognostic variable in patients with breast cancer.⁴ It was established that when the axillary lymph nodes came out

to be positive for metastatic disease, the complete elimination of nodal metastases might help in contributing to the surgical cure of the patient. Hence axillary dissection became a mandatory part of the surgery for breast cancer for more than a century. Axillary dissection is mainly responsible for morbidities such as post-operative neuralgia, seroma formation, lymphedema and restriction of movements in the ipsilateral arm. Therefore, questions about the therapeutic value of axillary clearance have cropped up over the years and quest for alternative less radical procedures on the axilla have been proposed in recent times.

The introduction of sentinel node concept in the nineties brought a paradigm shift in surgical staging of the axilla.⁵ Multiple studies over the decade confirmed that it was ontologically safe to say that a completion axillary clearance was not necessary where sentinel lymph node biopsy was negative, thereby reducing the morbidities associated with this procedure such as lymphedema, pain and shoulder dysfunction.⁶

However, a clinically positive axilla continued to be offered a complete clearance, the level of clearance depending on the surgeon's choice and expertise in the procedure rather than standard guidelines or institutional policies.

With this background, the present study was done to evaluate and investigate the prevalence of the standard sequelae of complete axillary lymph node clearance such as pain, neuralgia, lymphedema, seroma, range-of-motion restriction, and wound dehiscence in all female patients with biopsy proven breast cancer who underwent axillary surgery as part of surgical treatment at our Institute.

METHODS

An observational study was conducted at the Cancer Institute and Department of Surgery of the Himalayan Institute of Medical Sciences for a period of one year (2017-2018). Out of 182 patients fulfilling the enrollment criteria, 32 were not available for the proposed follow up at one, three and six months and had to be excluded from the study. A total of 150 patients chosen were observed from the date of their admission to surgical wards to the requisite follow up period. Consent was taken from all patients and University Research committee and Ethics committee approval was taken before accrual of patients.

Inclusion criteria

All female patients with biopsy/cytology proven breast cancer breast planned for surgery of breast including axilla were included in the study.

Exclusion criteria

 Patients who underwent any surgery in the same axilla in the past and patients having axillary

- metastasis due to primary malignancy other than carcinoma breast.
- 32 patients fulfilling the criteria were unable to be followed up for the requisite time period and had to be excluded from the study.

Research tools

Post-operative pain

Recorded as present or absent. No pain scores were used.

Lymphedema (arm swelling)

The upper arm circumference (in cm) at 15cm proximal to the lateral epicondyle ipsilateral to the axilla surgery site was compared with the contra lateral upper arm circumference, just as described by Veronesi et al. Lymphedema was defined as a difference of more than 2cm in the upper arm circumference between the arm ipsilateral to the axillary dissection and the contra lateral arm.

Seroma

Recorded as per documentation in clinic, OPD and day care and was recorded as present or absent.

Wound infection

Recorded as per documentation in OPD and IPD.

Restriction of arm movement

Patients demographic profile, tumor stage, and surgery performed were also documented. Patients were followed up at 1, 3 and 6 months from the date of surgery.

Statistical analysis

Statistical analysis was conducted with the Statistical Package for the Social science System version SPSS 22 and Microsoft Excel 2007 Continuous variables were presented as Mean±SD or median (IQR) for non-normally distributed data.

Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using ANOVA. Data being dichotomous in nature (i.e.; non-metric), application of non-parametric test was most suitable. Therefore, Spearman's Rank correlation was also used, to study the correlation.

The data was statistically tested in SPSS at 5% significance level. For all statistical tests, a p value < 0.05 was taken to indicate a significant difference and value ≤ 0.01 was considered as highly significant

RESULTS

Most of the patients (30%) belonged to the age group between 46-55 years with median age of 50.83 years. 58% patients had breast cancer on left side, 41.30% had involvement of right breast and only 1 patient (0.67%) had bilateral involvement.

Twenty-six patients (17.33%) underwent breast conserving surgery (BCS). 120 patients (80.00%) underwent modified radical mastectomy while simple mastectomy was performed in 2 patients. 2 patients underwent toilet mastectomy for palliation.

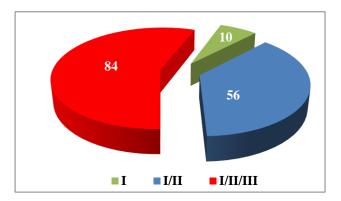


Figure 1: Level of axillary dissection (n = 150).

Eighty four patients out of 150 (56%) underwent axillary dissection up to level III, 56 patients (37.33 %) underwent axillary dissection up to level II and 32 patients underwent SLNB. Out of them the sentinel node was found negative on frozen section evaluation in 10 patients and no axillary clearance was done (Figure 1).

Table 1: Correlation of tumor size with number of positive lymph nodes.

T classification	No of positive lymph nodes			Total no. of patients (%)		
	0	<3	>3			
T1a	0	0	2	2 (1.33%)		
T1b	2	1	2	5 (1.33 %)		
T1c	4	0	1	5 (3.33%)		
T2	41	18	23	82 (54.67%)		
T3	8	6	19	33 (22.00%)		
T4	5	8	10	23 (15.33%)		

Fifty three patients (35.33%) were staged as locally advanced breast cancer (LABC) and included stages IIIB, III C and IV. Tumor size (T classification) correlated positively with grade (r =0.36, P <0.001) and the number of positive lymph nodes (r = 0.34; P <0.001) shown in Table 1.

Evaluation of post-operative sequelae was done at 1, 3 and 6 months for all patients. Pain was assessed subjectively by asking the patients, lymphedema was

assessed by measurement according defined criteria. Wound infection and seroma were noted by clinical examination and restriction of arm movement was clinically evaluated as mild moderate and severe (Table 2).

There was significant difference seen in the incidence of lymphedema at 6 months of follow up between patients who underwent level III clearance (27.38 %) as opposed to those who did not (8.92 %) (p <0.05). It was also observed that the incidence of seroma at one month was seen more in patients who underwent Level III clearance (57.14 %) as opposed to those who did not (39.28 %) (P value <0.05).

There was no evidence of lymphedema (0%) or restriction of arm movement (0%) at 1, 3 or 6 months follow up in SLNB negative patients (P=0.289) who did not undergo axillary clearance (Table 3). Interestingly the incidence of post-operative pain / wound infection/Restriction of arm movement was not found statistically different in between level II and level III axillary dissection.

There was statistically significant difference seen in incidence of lymphedema between patients who underwent up to level II (I/II) and up to Level III (I/II/III) clearance at 6 months of follow up.

Incidence of Lymphedema in patients who underwent up to level III clearance was 27.38 % as opposed to 8.92 % seen with those who underwent up to Level II dissection (p <0.05). However, there was no statistically significant difference seen in incidence of lymphedema between level II (I/II) and level III (I/II/III) clearance at 1 months or 3 months of follow up (Figure 2).

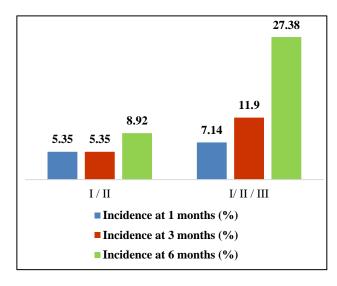


Figure 2: Incidence of lymphedema.

The incidence of seroma formation at one month from the time of surgery was seen more in patients who underwent up to level III (I/II/III) axillary lymph node dissection

(57.14%) than in those who underwent up to level II (I/II) axillary lymph node dissection (39.28%). This was statistically significant (p value <0.05). The incidence of Seroma gradually decreased over the course of follow up.

At 3 months, level III (21.42%) as compared to level II (16.07%) and at 6 months, level III (3.57%) as compared to level II (8.92%) (Figure 3).

Table 2: Sequelae of axillary dissection.

Level of axillary node dissection (II) (n=56)									
	1 month			3 months			6 months		
	No. of patients	%	Mean±SD	No. of patients	%	Mean±SD	No. of patients	%	Mean±SD
Post-operative pain	41	73.2%	1.27±0.447	19	39.92%	1.66±0.478	7	12.5%	1.87±0.334
Lymphedema	3	5.35%	1.95±0.227	3	5.35%	1.95±0.227	5	8.92%	1.91±0.228
Seroma formation	22	39.28%	1.41±0.496	9	16.07%	1.79±0.414	0	0%	1.96±0.187 ±0.187
wound infection	12	21.4%	1.79±0.414	4	7.14%	1.93±0.260	0	0%	2.00±0.000
Restriction of arm movement	11	19.64%	1.80±0.401	14	25%	1.75±0.437	14	25%	1.75±0.437
Level of axilla	Level of axillary node dissection (III) (n=84)								
	1 month		3 months			6 months			
	No. of patients	%	Mean±SD	No. of patients	%	Mean±SD	No. of patients	%	Mean±SD
Post-operative pain	63	75%	1.25±0.436	28	33.3%	1.67±0.474	8	9.52%	1.9±0.295
Lymphedema	6	7.14%	1.93±0.259	10	11.9%	1.88±0.326	23	27.3%	1.73±0.449
Seroma formation	48	57.14%	1.63±0.485	18	21.14%	1.86±0.352	3	3.57%	1.99±0.109
Wound infection	12	14.28%	1.85±0.364	3	3.57%	1.96±0.187	2	2.38%	1.98±0.153
Restriction of arm movement	10	11.9%	1.88±0.326	16	19.04%	1.81±0.395	24	28.57%	1.71±0.454

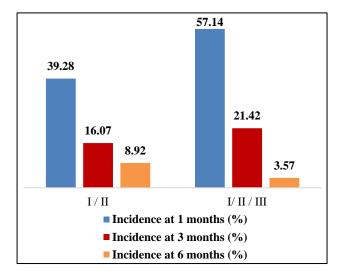


Figure 3: Incidence of seroma.

Table 3: Follow up of sentinel lymph node biopsy patients (SLNB - negative (n = 10)).

SLNB dissection			
Morbidity	1 month	3 month	6 month
Post-operative pain	30.00%	10.00%	10.00%
Lymphedema	0.00%	0.00%	0.00%
Seroma formation	0.00%	10.00%	0.00%
Wound infection	0.00%	0.00%	0.00%
Restriction of arm movement	0.00%	0.00%	0.00%

ANOVA (p value =0.289)

DISCUSSION

This study reports a median age of 50.83 years which is consistent with the survey carried out by Indian council of medical research (ICMR) from 1982 to 2005 that

showed that in India, women with breast cancer are found a decade younger as compared to the west, the reason for this is unknown as yet.

Out of 150 patients 53 patients (35.33%) were seen to be locally advanced clinically at diagnosis (stage IIIB, IIIC, and IV). There was a significant relation between tumor size and the number of positive lymph nodes (r=0.34; P < 0.001) (Table 1). As Danforth has emphasized, one of the reasons to perform ALND is to accurately stage the tumour.⁸

Surgical treatment of axilla has become a source of controversy owing to the fact that it is the major cause of morbidity associated with breast surgery.9 The NSABP B04 trial reported that axillary recurrence rates were without adequate axillary approximately 18.6% clearance, though this notion has been challenged in recent studies. 10 The reason axillary clearance is performed in node positive disease is to avoid the difficulties in treating axillary recurrence and in enforcing intensive follow-up. 11,12 Authors found no recurrent axillary disease in any patient within the follow-up period. Although current recommendations suggest a level II axillary dissection to be performed in a node positive axilla, level III dissection is still carried out in many centers.¹³ Authors followed a similar practice in our institution, with out of 150 patients taken up for this study, 84 (56%) underwent level III dissection and 56 (37.33%) Level II dissection as shown in Figure 1.

As per the current recommendations in clinically node negative patients' axillary dissection should be carried out only if the Sentinel lymph node biopsy (SLNB) is positive. This can also be carried out during the index operation if the sentinel node can be analyzed intra operatively using frozen section (as used in this study) imprint cytology, or molecular-based assays. Authors performed SLNB in 32 patients out of which 10 came out to be node negative on frozen section examination. 59.37% (19 patients) out of these were found to have sentinel node positive on frozen section and underwent a complete axillary clearance.

As per the current literature, SLNB is associated with lower morbidity rates as compared to ALND (64). This was further proven by the ALMANAC trial which stated that the rates of arm morbidity are less with SLNB as compared to standard axillary lymph node dissection (65). The results were similar in our study there was no evidence of lymphedema or restriction of arm movement at 1, 3 or 6 months of follow up in SLNB negative cases (Table 3).

Previous studies have stated that the extent of dissection is directly proportional to the rate of complications of ALND, which was similar to observations in this study. Post-operative pain / neuralgia at 1 month was seen in 73.21% cases who underwent level II dissection as compared to 73.81% undergoing Level III dissection (p

value = 0.938). Incidence of post-operative pain decreased with time. At 6 months post-operative pain /neuralgia was seen in 12.50% of patients undergoing Level II dissection and 9.52 % in Level III dissection (p value =0.580).

Lymphedema is one of the most serious and difficult complication to treat as it has a high effect on the quality of life of the patient. Its incidence varies widely in the literature, this can be attributed to the different techniques of measurement and also the varied intervals between surgery and measurement of arm circumference. Larson et al, reported that the risk of arm edema was 37% when Level III was carried out, compared with 8% when a Level II dissection was performed. DiSipio et al, observed a 21.4% lymphedema incidence after analyzing 30 prospective cohort studies. In this study incidence of Lymphedema in patients who underwent level III clearance was 27.38% as opposed to 8.92% seen in level II dissection (p <0.05).

Seroma formation most frequently occurs after mastectomy and axillary surgery. There are further difficulties in prolonged drainage such as increase in risk of infection which can delay adjuvant therapy. On detailed analysis of the use of drains it was seen that use of single or multiple drains, early or late removal, and drains with or without suction do not significantly influence the incidence of seroma. In our study all axillary dissections were drained using a closed suction system. Drains were kept in place for an average of 4 to 5 days and were removed at the time when serous drainage was invariably <50cc per 24 hours.

It was also observed that the incidence of seroma at one month was seen more in patients who underwent level III clearance (57.14 %) as opposed to those who did not (39.28 %) (P value <0.05). The incidence of seroma gradually decreased over the course of follow up. At 3 months, Level III (21.42%) as compared to level II (16.07%) p value = 0.435. All patients who developed seroma after removal of the suction drain were managed by repeated transcutaneous needle aspiration. As per the reported literature seroma aspiration is necessary in 10% to 80% of ALND. Various studies demonstrated the range-of-motion restriction to be 28.57% and 25% in the patients, who underwent Level III and Level II dissection respectively. The range-of-motion restriction was assessed as per defined criteria. Various studies demonstration was assessed as per defined criteria.

In conclusion, the results of this study showed that the lymphedema and seroma prevalence, two of the most detrimental ALND side effects, were more in patients who underwent level III axillary dissection as compared to those who underwent level II axillary dissection.

CONCLUSION

The aim of this study was to observe and evaluate the sequelae/morbidities in patients who undergo axillary

node dissection as part of surgery for breast cancer. As per world literature, the incidence of morbidities increases with higher levels of axillary clearance. The results of our evaluation showed a similar trend. However, authors also saw that a majority of patients require a complete axillary clearance that might be explained because most of them were in a higher stage group as compared to other studies. Unwarranted dissection of axilla can be avoided by tailoring the surgery in initial clinical assessment and incorporating imaging of axilla. The breast surgeon should have the complete repertoire of axillary surgeries his/her armamentarium, starting from a good sentinel node dissection to a complete level III clearance with minimum morbidity. The surgeon should also ensure that a proper follow up evaluation at predefined intervals should be done to audit the sequelae of axillary dissection in breast cancer patients so that the information gathered from it can be used to guide further protocols.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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