ORIGINAL RESEARCH PAPER

Volume - 12 | Issue - 10 | October - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ROLE OF LOW AXILLARY SAMPLING IN TREATMENT OF CARCINOMA BREAST.

Breast Surgery

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ABSTRACT

Background: Low axillary sampling (LAS) was defined as excision of all fibrofatty tissue overlying the second digitation of serratus anterior below the intercostobrachial nerve. The present study was undertaken to study the role of LAS in a consecutive series of clinically axillary node negative patients undergoing surgery for primary breast cancer at our institution. **Method:** A total of 31 patients admitted in surgery ward undergoing surgery for primary breast cancer with cytology or histology proved cases of- clinically node-negative operable breast cancer and down staged patients of locally advanced breast cancer (LABC) and large operable breast cancer (LOBC) were included in the study. **Results:** The most common presenting complaint was lump in the breast (100%). Majority of patients had right side involvement (64.51%) and upper outer quadrant involvement (51.61%). Most of the patients had stage 2 tumour (64.51%), stage N0 tumour (87.09%) and most belongs to stage II a (64.51%). In maximum cases (67.74%) 4 lymph nodes were harvested in LAS. Out of 31 cases, 09(29.03%) patients were positive in LAS and rest of axillary lymph nodes were positive in 7(22.58%) patients. The sensitivity of 85.71% specificity of 87.5% PPV of 66.66%, NPV of 95.45 % and diagnostic accuracy of 87.09% for LAS of axilla amongst all the patients. A sensitivity of 100%, specificity of 95%, PPV of 87.5%, NPV of 100 % and diagnostic accuracy of 83.87 % for LAS of axilla, among operable breast cancer patients having node negative axilla. **Conclusion:** LAS is easy, less-time-consuming procedure which is a reliable alternative to sentinel node biopsy for axillary nodal prediction in clinically node-negative primary breast cancer.

KEYWORDS

Low axillary sampling; Lump; Carcinoma; Breast; Sensitivity; Specificity

INTRODUCTION

Breast cancer is the most common cancer in women both in developed and less developed world. A woman who lives to age 90 has a one in eight chance of developing breast cancer. It is as ironic and tragic that a neoplasm arising in an exposed organ, readily accessible to self-examination and clinical surveillance, continues to exact such a heavy toll [1].

In any breast carcinoma treatment consist of two things i.e., breast and axilla. Since axillary lymph node involvement is the most important prognostic marker for breast cancer, axillary lymph node dissection (ALND) has been considered an essential component of breast cancer management. But the important and common complications associated with ALND are injury to axillary vessels, injury to brachial plexus, seroma, wound infection resulting in delayed wound healing, restriction of shoulder movement, intercostobrachial nerve syndrome (paraesthesia of the axilla, shoulder, and upper arm), lymph edema predisposing to cellulitis, rarely lymphangio-sarcoma [2].

Several alternative ways have been studied to reduce possible complications of the dissection and to spare the increasing proportion of patients without axillary metastases [3]. The alternative available for ALND are sentinel lymph node biopsy and axillary sampling (AS). Sentinel lymph node biopsy has been incorporated into standard guidelines as an appropriate initial alternative to routine staging ALND for patient with early-stage breast cancer with clinically negative axillary lymph nodes. Sentinel lymph node biopsy requires gamma camera and radioactive agent. High cost of gamma probe and need for radio-colloid have limited its widespread acceptance in developing countries [3].

AS entails the removal of a sufficient number of suspicious lymph nodes with the aim of detecting the presence of lymph nodal metastasis. Many centres in UK, and Japan have tested and adapted, as an alternative to targeted SNB, 4 node axillary sampling as standard procedure for axillary prediction in clinically node negative operable breast cancer. The anatomically defined, low axillary sampling (LAS) ensures the procedure is less subjective more standardized and uniform with low inter-observer variability [3, 4]. LAS were performed in this research work for predicting axillary nodal metastasis in operable breast cancer by completing ALND in all cases. An anatomically guided LAS removes the lower level I axillary fat with lymph nodes and the method was validated by completing axillary clearance in all women. The present study was undertaken to study the role of LAS in a consecutive series of clinically axillary node negative patients undergoing surgery for primary breast cancer at our institution and in the patients with post neoadjuant chemotherapy.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients, this hospital based prospective interventional study was conducted in the Department of Surgery at Tertiary Care Teaching Centre during a period from February 2021 to November 2022. A total of 31 patients admitted in surgery ward undergoing surgery for primary breast cancer with cytology or histology proved cases of - clinically node-negative operable breast cancer and down staged patients of locally advanced breast cancer (LABC) and large operable breast cancer (LOBC) were included in the study. Any patient with a prior axillary nodal biopsy, metastatic carcinoma breast, recurrent carcinoma breast and patients not giving consent for this study were excluded.

Socio-demographic data was collected from IPD records of patients. Detailed history was noted. A thorough General, systemic, and local examination was carried out. Diagnosis was confirmed by cytology or core cut biopsy. Patients were subjected for routine blood tests, coagulation profile, Complete hemogram, KFT, LFT, blood group, HIV, HBs-Ag, ECG and The Metastatic work up included - Chest X-ray, X-ray spine-AP and lateral views, USG abdomen and pelvis and serum Alkaline phosphatase estimation. Histopathology specimens were screened for HER2 status, HR (ER and /or PR) status (positive or negative).

Pre-anesthetic check-up was done, and patients were posted for

surgical intervention. LAS was done through a 3-4 cm long incision in the middle-third of the standard axillary clearance incision in case of breast Conservation surgery and through the lateral part of the upper flap incision in case of modified radical mastectomy.

The extent of LAS excision was anatomically defined.

a) Posteriorly - The lateral border of the latissimus dorsi muscle,
b) Anteriorly - The lateral border of the pectoralis major muscle
c) Superiorly -The intercostobrachial nerve
d) Medially - The second digitation of the serratus anterior muscle,
e) Base - The subscapularis muscle and the pedicle of the latissimus dorsi.

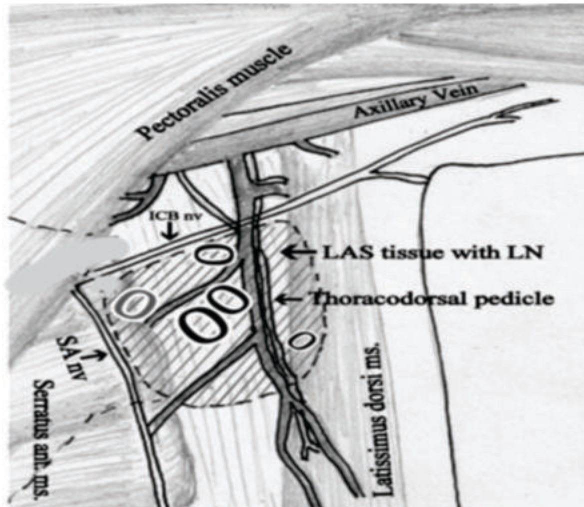

Figure 1: Schematic Anatomical illustration of the area in axilla defining the boundaries of low axillary sampling [5]

The LAS specimen was excised and confirmed that it had at least 4 lymph nodes. If the tissue did not contain the required lymph nodes, additional larger palpable lymph nodes was resected in level 1 so as the sample has at least 4 lymph nodes and the obtained sample sent for histopathological examination. All patients had a complete ALND, and the lymph nodes obtained during ALND were sent separately for histopathological examination. The sampled lymph nodes were compared with the remaining axillary nodes for reliability of predicting axillary nodal status. Patients were continuously monitored, and data was collected for prospective study. If patient was sent for chemoradiotherapy to oncology department, Patient was followed up in surgical OPD during post -operative periods every 15 days.

Statistical analysis

The data were collected and entered in Microsoft Excel sheet and then statistically analyzed using SPSS Version 20.0. Continuous variables were expressed as mean ± SD and categorical variables were summarized as frequencies and percentages.

OBSERVATIONS AND RESULTS

A total of 31 patients were enrolled in the study. Most of the patients were in the age group of 40 to 60 years (67.74%) with mean age of patients was 52.74±10.25 years, ranging from 30 to 74 years. The most common presenting complaint was lump in the breast (100%) followed by lump with pain (51.61%). Maximum (61.29%) patients presented with a history of 2-6 months duration. 64.51% of patients had right side involvement for carcinoma and the upper outer quadrant involvement was the most prevalent owing to 51.61%. Most of the patients had stage 2 tumour (64.51%), 87.09% had stage N0 tumour and by clinical staging most of the patients belong to stage II a (64.51%), (Table 1). The average size of the tumour being 4.2 cms.

Table 1: Patient and Tumor Characteristics (N = 31)

Characteristics		No. of patients	Percentage
Age group (Years)	30 to 40	03	9.67
	41 to 50	12	38.70
	51 to 60	09	29.03
	61 to 70	06	19.35
	>70	01	3.22
Symptoms	lump	31	100.0
	Lump + pain	16	51.61
Duration of symptoms	2 to 6 months	19	61.29
	7 to 12 months	09	29.03
	>12 months	03	9.67
Side involvement	Right	20	64.51
	Left	11	35.48
Site involvement (Quadrant involved)	UOQ	16	51.61
	UIQ	07	22.58
	LOQ	05	16.12
	RA	03	9.67
	LIQ	00	0.0
Lump size (T stage)	T1	02	6.45
	T2	20	64.51
	T3	05	16.12
	T4	04	12.90
Lymph node status (N stage)	N0	27	87.09
	N1	03	9.67
	N2	01	3.22
Clinical stage	I a	02	6.45
	I b	00	0.0
	II a	20	64.51
	II b	05	16.12
	III a	00	0.0
	III b	04	12.90

Upper outer quadrant (UOQ); Upper inner quadrant (UIQ); Lower outer quadrant (LOQ); Retro areolar (RA); Lower inner quadrant (LIQ)

In maximum cases (67.74%) 4 lymph nodes were harvested in low axillary sample followed by 5 lymph nodes (22.58%) as depicted in figure 2. The median number of lymph nodes in the LAS was 3 and mean lymph nodes harvested in LAS was 4.5±0.91.

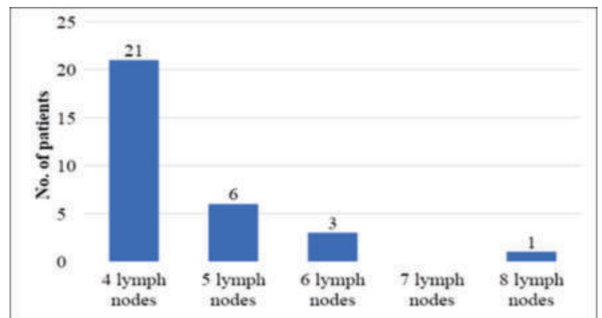

Figure 2: No. of lymph nodes harvested in low axillary sample (LAS)

Out of 31 cases, 09 (29.03%) patients were positive in low axillary sample and the rest of axillary lymph nodes were positive in 7 (22.58%) patients as shown in table 2.

Table 2: Distribution of subjects according to LAS and rest of axillary node status

Lymph nodes status		No. of patients	Percentage
Low axillary sample	Positive	09	29.03
	Negative	22	70.96
Rest of axillary lymph nodes	Positive	07	22.58
	Negative	24	77.41

9 patients had low axillary sampling positive for malignancy, out of this rest of axillary lymph nodes were positive in 7 patients. At the same time, low axillary sampling was negative in 22 patients and rest of axillary lymph nodes were found to be negative in 24 patients. LAS was negative, but rest of axillary lymph nodes was positive in only 1 patient, (Table 3).

Table 3: LAS validation as compared with rest of the axilla (n=31)

LAS	Rest of axillary lymph nodes		Total
	Positive	Negative	
Positive	06(TP=A)	03(FP=B)	09
Negative	01(FN=C)	21 (TN=D)	22
Total	07	24	31

Among the operable breast cancer with node negative axilla, in whom low axillary sampling was performed, it was observed that, rest of axillary lymph nodes were positive for malignancy in 7 patients and in 8 patients LAS was positive for malignancy. While the rest of axillary lymph nodes were negative for malignancy in 20 patients out of these, 19 patient's LAS was also negative for malignancy, (Table 4).

Table 4: LAS as compared to rest of axillary lymph nodes in operable breast cancer with clinically node negative status (n=27).

LAS	Rest of axillary lymph nodes		Total
	Positive	Negative	
Positive	07	01	08
Negative	00	19	19
Total	07	20	27

The present study observed sensitivity, specificity, PPV, NPV and diagnostic accuracy of 85.71%, 87.5%, 66.66%, 95.45% and 87.09% respectively for low axillary sampling of axilla amongst all the patients. Whereas sensitivity, specificity, PPV, NPV and diagnostic accuracy of 100%, 95%, 87.5%, 100% and 83.87% respectively for low axillary sampling of axilla, among operable breast cancer patients having node negative axilla, (Table 5).

Table 5: Diagnostic accuracy of LAS compared in total number of study patients and operable breast cancer with clinically node negative status.

Diagnostic accuracy parameter	Values (%)	
	Total number of study patients (N=31)	Operable breast cancer with clinically node negative status (N=27)
Sensitivity	85.71%	100%
Specificity	87.5%	95%
PPV	66.66%	87.5%
NPV	95.45%	100%
Diagnostic accuracy	87.09%	83.87%

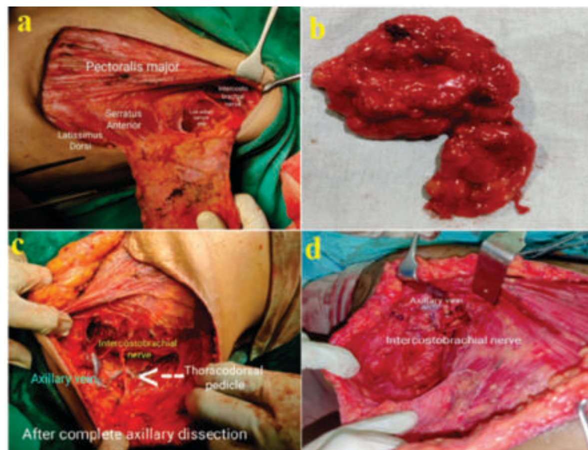

Figure 3: a) Axillary dissection showing area of low axillary sampling; b) Excised low Axillary Sample; c & d) After complete axillary dissection.

DISCUSSION

At our tertiary care hospital, we adapted an improvement over the palpable axillary nodal sampling procedure by carrying out a lower-level sampling of the axillary fat and lymph nodes by a dissection guided by strict anatomical landmarks. The anatomically defined, LAS ensures that the procedure is less subjective, more standardized and uniform, with lower inter-observer variability [6, 7]. In the present study, the maximum number of patients (39%) were from the age group of 41 and 50 years followed by 51 to 60 years (29.03%). This shows that the perimenopausal age group are more susceptible with breast cancer. Overall, the mean age of patients was 53.69±9.93 years, ranged from 35 to 74 years. These findings are comparable with the previous studies [5, 8, 9]. The most common presenting complaint was lump in the breast (100%) followed by lump with pain (51.61%). Maximum patients (61.29%) presented with a history of 2-6 months duration with the mean duration from detection of lump was 6.16±3.61 months. These findings are in accordance with the study conducted by Surakasula et al [10].

Out of 31 patients, about 20 (64.51%) patients had right side involvement for carcinoma while 11 (35.48%) patients had carcinoma in the left breast. Of the affected breast the upper outer quadrant involvement is the most prevalent owing to 51.61%, followed by upper inner quadrant 22.58%, followed by lower outer quadrant of 16.12% and retro areolar (9.67%) and with no involvement of lower inner quadrant. Similar findings are reported in Parmar et al studies [5, 9, 11] and Hoar FJ et al [12]. The mean diameter of the breast lump was 4.2±1.54 cm, ranged from 1.6 cm to 7.3 cm which is comparable with the other studies [5, 8, 13]. Most of the patients had stage 2 tumour (64.51%) followed by stage 3 tumour (16.12%), which was followed by stage 4 (12.90%) and stage 1 tumour (6.45%). The average size of the tumour being 4.2 cms. These results are correlated with the earlier studies [5, 11, 12]. However, most of the patients (87.09%) had stage N0 tumour followed by stage N1 tumour (9.67%) and stage N2 tumour (3.22%). This N1 and N2 stage patients were given NACT and after that they were clinically N0 before procedure. In Parmar et al 2009, they have observed that, 212 patients have no axillary lymph node metastasis and 107 have axillary lymph node metastasis [11]. By clinical staging most of the patients belongs to stage II a (64.51%), followed by stage II a (16.12%), stage III b (13%) and stage Ia (6.45%). In the maximum cases (67.74%) 4 lymph nodes harvested in low axillary sample followed by 5 lymph nodes (22.58%) and 6 lymph nodes (9.67%). The median number of lymph nodes in the LAS was 3 and mean lymph nodes harvested in LAS was 4.5±0.91. Similar findings are reported in Parmar V et al studies [5, 11].

The sensitivity of LAS method to diagnose the metastasis was found to be 85.71%. The specificity was observed to be 87.5%, It was observed that, positive predictive value (PPV) of 66.66% and negative predictive value (NPV) of 95.45%. Hence overall diagnostic accuracy of LAS in the present study was observed to be 87.09%. These findings are correlated with the Parmar et al studies [9, 11] and Borkar MM et al [2]. Whereas sensitivity, specificity, PPV, NPV and diagnostic accuracy of 100%, 95%, 87.5%, 100% and 83.87% respectively for low axillary sampling of axilla, among operable breast cancer patients having node negative axilla. This result is in accordance with the study conducted by Borkar MM et al (N=29) [2]

The false-negative rate in women in present study with axillary sampling was 3.22% (1÷31) with low axillary sampling, which is better than the false-negative rate reported in the study done by Parmar V et al (2009) (8.8%) [11].

With the economic logistics of high price of the gamma probe and poor accessibility to nuclear medicine centres, there are difficulties in doing a radio guided targeted SNB in most peripheral centres in the developing world. Obviously, even if proven safe and effective in large, randomized trials, its acceptance and availability in developing countries may not be feasible. Also, due to delayed presentations, the tumours are relatively larger at detection as compared with those in countries with effective national breast cancer screening programs. Therefore, there is a need for a low-cost technology intervention with easy and uniform applicability across the developing world.

It is well known that the presence of involved lymph nodes can result in blocked lymphatics and in a non-sentinel lymph node being identified as the 'sentinel node' or in other words a 'false- negative sentinel node'. Chronologically, there isa direct correlation between increasing tumour size and higher axillary lymph nodal metastases. In patients with larger primary tumours, as seen in developing countries, in the absence of breast cancer screening, the chances of axillary lymph nodal metastases would be higher. The possibility of a false-negative rate with targeted SNB would effectively be higher as it relies upon the dynamics of lymphatic flow. In this setting, axillary sampling appears to be a more practical procedure especially since it involves a defined anatomical dissection of the axillary fat and lymph nodes in level III (including the distal axillary tail) of the axilla, ensuring completeness of the limited dissection with a lower risk of morbidity.

The result of the exploratory analysis further supports axillary sampling as a reliable procedure with a low false-negative rate with 4 nodes sampling. If and when SNB is considered as the standard of care, LAS can be considered as a reliable, alternative low-cost procedure for developing countries.

During this research work, for the initial few cases (around 15 cases) time required for harvesting low axillary sample was about 30 to 45

min. But gradually for further cases the time required for harvesting low axillary sample decreases to about 20 to 30 mins. Time taken for harvesting LAS on an average of 31 mins. It shows that this is less time-consuming procedure. We have not observed any complication of low axillary sampling during this research work.

CONCLUSION

Based on the findings of present study, low axillary sampling is easy, less-time-consuming procedure which is a reliable alternative to sentinel node biopsy for axillary nodal prediction in clinically node-negative primary breast cancer and LAS has no increased financial burden or skill requirement, so it is a reasonable option as an axillary staging procedure.

It would provide to be a good alternative for resource starved establishments, especially in developing and underdeveloped countries where expensive infrastructure is a luxury.

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