

SENTINEL LYMPH NODES DISSECTION VERSUS AXILLARY LYMPH NODES DISSECTION IN PATIENTS WITH EARLY BREAST CANCER AND SENTINEL NODES METASTASES

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ABSTRACT

Background: Sentinel lymph node biopsy (SLNB) has become the standard method for axillary staging of breast cancer with reliable accuracy and less morbidity compared with axillary lymph node dissection (ALND) aiming to minimize the rate of patients with negative axillary status who undergo ALND and restricted only to patients with positive axillary lymph node.

Objective: To compare the results of SLN dissection only and that of ALN dissection regarding the morbidity and locoregional recurrence.

Patients and methods: A hundred patients with histologically confirmed invasive breast cancer T1/T2N0M0 and SLN positive for metastases (≤ 3 SLNs) were entered the study and divided randomly into two groups. Group I: Fifty (50) patients underwent SLN dissection only. Group II: Fifty (50) patients underwent SLN dissection and ALN dissection.

Exclusion criteria: Patients with >3 positive SLNs, patients with matted nodes, patients with gross extranodal disease and patients received neoadjuvant hormonal therapy or chemotherapy.

Statistical analysis: SPSS version 15.

Results: Adverse surgical effects were reported in both groups. In SLND group (6%) had seroma while in ALND group (16%) had seroma, wound infection was (4%) in SLND and (8%) in ALND, postoperative paresthesia after 1 year was (16%) in SLND and (44%) in ALND, postoperative lymphoedema after 1 year was (4%) in SLND and (10%) in ALND and axillary recurrence was (2%) in SLND and no recurrence in ALND.

Conclusion: SLND mapping and excision is the standard of care for axillary staging for patients with early invasive breast cancer and clinically node-negative disease.

Keywords: Early breast cancer, clinically node-negative, SLND and ALND.

INTRODUCTION

Breast cancer is the most common invasive cancer in women. Breast cancer comprises 22.9% of invasive cancers in women. In 2012, it comprised 25.2% of cancers diagnosed in women, making it the most common female cancer.⁽¹⁾

Until the beginning of the last decade, axillary dissection was an established part of breast cancer surgery, alongside surgical removal of the primary tumor. Its main aim was to establish lymph node status as the most important parameter in prognosis, in order to select adjuvant therapy on a risk-adjusted basis.⁽²⁾

In the mid-1990s, sentinel lymph node biopsy (SLNB) was introduced for breast cancer as a method by which to identify the first lymph node in the nodal basin that could contain metastases in patients with clinically node-negative disease. SLNB allows completion axillary lymph node dissection (ALND) to be performed selectively in those patients with sentinel node metastases.⁽³⁾

Methylene blue is used as an identification agent due to its low risk profile, its low cost and wide availability.⁽⁴⁾

SLND has become the standard method for axillary staging of breast cancer with reliable accuracy and less morbidity compared to complete ALND.⁽⁵⁾

OBJECTIVE

To compare the results of SLN dissection only and that of ALN dissection regarding the morbidity and locoregional recurrence.

PATIENTS AND METHODS

This prospective study was represented randomly on 100 patients who had histologically confirmed invasive breast cancer T1/T2N0M0 and SLN positive for metastases (≤ 3 SLNs) who were selected from outpatient clinic of general surgery department of Zagazig University Hospitals in the period from April 2012 to July 2013.

Patients were divided randomly into 2 groups:

Group I: Fifty (50) patients will undergo SLN dissection only.

Group II: Fifty (50) patients will undergo SLN dissection and ALN dissection.

Exclusion criteria:

1. Patients with >3 positive SLNs
2. Patients with matted nodes
3. Patients with gross extranodal diseases
4. Patients received neoadjuvant hormonal therapy or chemotherapy.

Hundred cases of early cancer breast were thoroughly examined clinically after taking detailed history, routine laboratory, radiological (mammography-US) and pathological investigation (FNAC or core biopsy) all patients were subjected to SLNB using 3-5ml of 1% methylene blue in the peritumoral and subareolar region of the diseased breast.

Within 5 minutes 3-4cm axillary incision and dissection to the blue colored lymphatic channels and follow it to the blue sentinel lymph node. After excision mastectomy was done for group I and also mastectomy was done for group II after complete axillary dissection.

The SLNs were formaline fixed, paraffin embedded and sectioned for histological evaluation.

Follow up to all patients after 1,6,12 monthes to detect which group has more complication regarding seroma, infection, paresthesia, lymphoedema and recurrence.

Statistical analysis: Data were coded, entered and analysed using SPSS version 15.

RESULTS

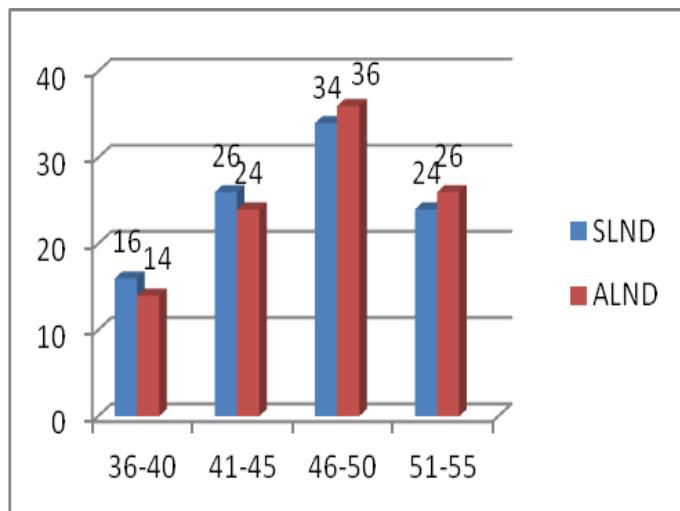


Figure (1): Age distribution of the patients involved.

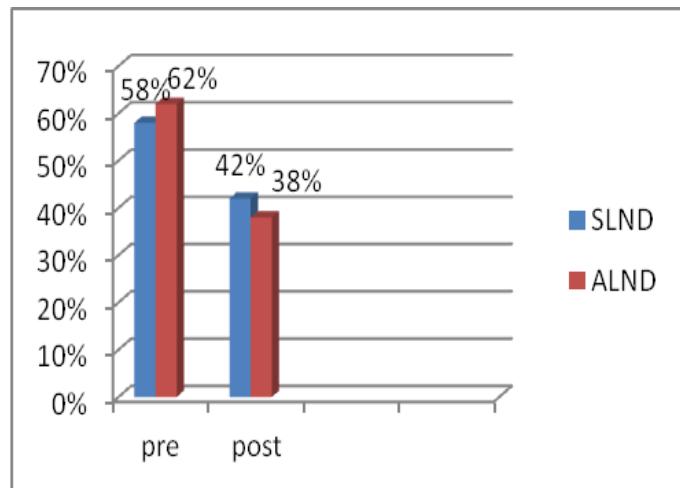


Figure (2): Menopausal status of the patients involved in the study.

Table (1): Clinical presentations of patients in both groups.

Complaint	SLND		ALND		P value
	N	%	N	%	
Painless lump	21	42%	23	46%	0.687
Painful lump	10	20%	11	22%	0.806
Painless lump +Nipple discharge	8	16%	7	14%	0.779
Painful lump +Nipple discharge	6	12%	4	8%	0.504
Nipple discharge	2	4%	3	6%	0.646
Pain and tenderness without lump or Nipple discharge	3	6%	2	4%	0.646
Total	50	100%	50	100%	

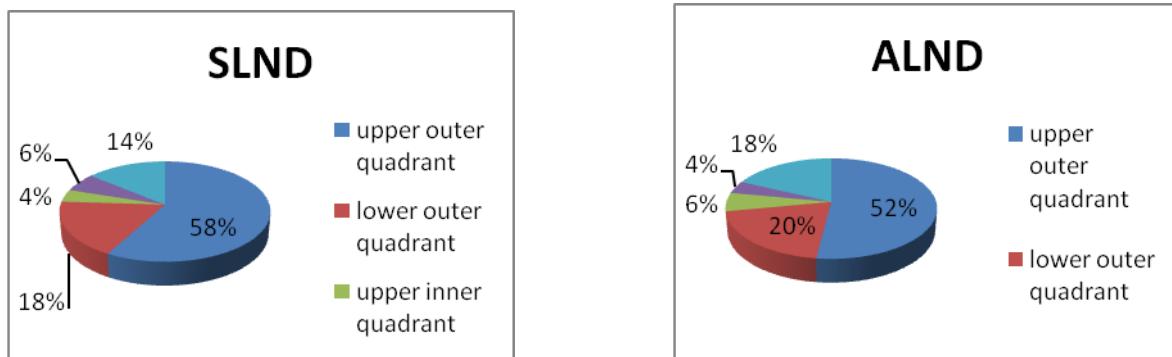
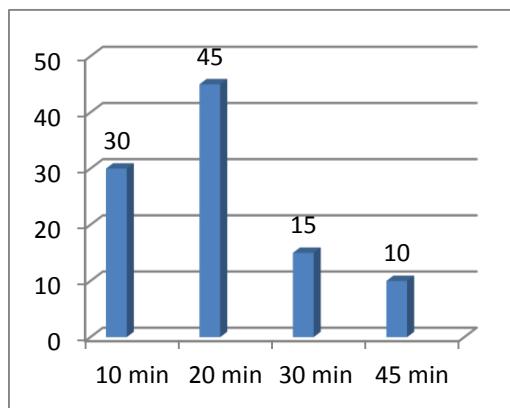
**Figure (3):** Site of breast mass in the both groups**Figure (4):** Time taken by the dye to reach the SLN.

Table (2): Histopathological types of the excised tumors.

Pathological type	SLND		ALND		P value
	N	%	N	%	
Invasive duct carcinoma(NOS)	32	64%	33	66%	0.833
Invasive duct carcinoma with intraductal component	14	28%	11	22%	0.488
Mixed Invasive ductal and lobular carcinoma	4	8%	6	12%	0.504
Total	50	100	50	100	

Table (3): Histopathological grade of the excised tumors.

Histopathological grade	SLND		ALND		P value
	N	%	N	%	
Grade I	22	44%	24	48%	0.688
Grade II	26	52%	23	46%	0.548
Grade III	2	4%	3	6%	0.646
Total	50	100	50	100	

SLN pathological results were:

- 1+ve in 40 patients.
- 2+ve in 50 patients.
- 3+ve in 10 patients.

Postoperative complications**Table (4):** Postoperative seroma.

Seroma	SLND		ALND		P value
	N	%	N	%	
After 1 month	3	6%	8	16%	0.11
After 6 months	-	-	-	-	-
After 12 months	-	-	-	-	-

Table (5): postoperative wound infection.

Wound infection	SLND		ALND		P value
	N	%	N	%	
After 1 month	2	4%	4	8%	0.393
After 6 months	-	-	-	-	-
After 12 months	-	-	-	-	-

Table (6): postoperative paresthesia.

paresthesia	SLND		ALND		P value
	N	%	N	%	
After 1 month	12	24%	27	54%	0.002
After 6 months	12	24%	24	48%	0.012
After 12 months	8	16%	22	44%	0.002

Table (7): postoperative lymphoedema.

Lymphoedema	SLND		ALND		P value
	N	%	N	%	
After 1 month	1	2	2	4	0.558
After 6 months	2	4	4	8	0.393
After 12 months	2	4	5	10	0.234

Table(7): axillary recurrence

Recurrence	SLND		ALND		P value
	N	%	N	%	
As first event	1	2	0	0	0.558
Concurrent with breast recurrence	0	0	0	0	0
Concurrent with distant metastasis	0	0	0	0	0
Total	1	2	0	0	0.558

DISCUSSION

This work was designed randomly on one hundred patients presented with early cancer breast, clinically negative axilla and had (1-3) +ve SLN to compare the results of SLN dissection only and that of ALN dissection regarding the morbidity and locoregional recurrence to ascertain if SLND alone was not inferior to axillary lymph node dissection for breast cancer patients who have a positive sentinel node. In our study, patients with clinically negative axilla were included as they are the most likely to benefit from axillary conservation even with positive sentinel lymph nodes.

In this study, the age ranges from 36 to 55 years with mean of age was 46.8 years and most of them were premenopausal, while in **Wang and his colleagues study (2014)**, out of 1269 patients (mean age of 60.5 year) and so most of them were postmenopausal.

Risk factors in both groups have no significant statistical difference. It was common in the patients with early menarche (68% in ALND group and 72% in SLND group) which is similar to **Bland and his colleagues, (2014)** and **Saunders and Baum, (2013)**. And it was more common in patients with breast feeding (74% in ALND group and 66% in SLND group), patients was no history of taking contraceptive pills (56% in ALND group and 54% in SLND group) and patients with negative family history of cancer breast(92% in ALND group and 88% in SLND group) which is against **Bland and his colleagues, (2014)** and **Saunders and Baum, (2013)**

In this study, upper outer quadrant is the commonest affected quadrant in both groups (52% in ALND group and 58% in SLND group) and this is similar to **Saunders and Baum, (2013)** and **Wang and his colleagues study in 2014**.

In this study, we injected Methylene blue in the deeper nondermal area of the peritumoral and subareolar area and as all the patients of the study underwent mastectomy we did not meet any case of inflammation, ulceration or skin necrosis. This is similar to results of **Varghese and his colleagues study (2008)** and **Mathelin and his colleagues study (2009)**. But against **Stradling and his colleagues study in 2002** that reported 5 necrotic skin lesions (21%) after the injection of 3 to 5 mL of Methylene blue (full strength 1%, 10 mg/mL) in a series of 24 patients. **Stradling et al, (2002)** and **Teknos and his colleagues study, (1984)** that reported a case of pulmonary oedema during a SLN

procedure using Methylene blue in a series of (30) patients (**Teknos et al, 1984**).

The small molecular weight of Methylene blue may also compromise its function as a mapping agent because of its capability for more rapid diffusion through the lymphatics, which will limit the time it spends within the sentinel lymph nodes before moving on to higher level lymph nodes. To overcome this problem, we harvested the sentinel lymph nodes within ten minutes after injection of methylene blue through an axillary incision which then extended to complete mastectomy as planned.

In this study the median number of removed lymph nodes in SLND group was 4 lymph nodes. The median number of removed lymph nodes in ALND group was not reported while in **Lucci and colleagues study, (2007)** a median of 2 lymph nodes in the SLND group and 16 in the ALND group was reported.

In this study, patients in SLND group who were found to have more than three positive lymph nodes were readmitted for completion axillary dissection and were excluded from our study and patients in the ALND group that found to have more than three positive lymph nodes were excluded too.

In this study, all patients were subjected to modified radical mastectomy to avoid bias due to comparison of complications of different procedures and as not all patients were candidate for conservative breast surgery

Histopathological evaluation was performed with hematoxylin and eosin for the breast specimen noticing that most of our cases (65%) were Invasive duct carcinoma which is similar to **Bland et al, (2014)**, **Saunders and Baum, (2013)**.

The SLNs were formalin fixed, paraffin embedded, and sectioned. Histologic evaluation was performed with hematoxylin and eosin. All non-SLNs were evaluated with standard hematoxylin and eosin stained sections because we wanted to avoid the fallacies in the frozen section histopathology.

After a median follow up period of 12 months postoperative complications were recorded in both groups at 30 day, 6 month and 12 month.

In this study, we had axillary seromas at 30 Days (3) patients in SLND group and (8) patients in (ALND) group while in **Lucci and his colleagues,(2007)** study, significant predictor of seroma formation ($P = .028$) in the ALND arm but not in the SLND-alone arm and in **Giuliano and his colleges study, (2011)** axillary seromas among

patients in the Z0011 trial was higher for the ALND group than for the SLND-alone group (70% vs 25%, $P < .001$) this may contribute to BMI, age and age/study group linkage and number of nodes removed were significant predictors of seroma.

In this study, we had wound infection at 30 Days (2) patients in SLND group and (4) patients in (ALND) group. This is similar to *Lucci and his colleges study, (2007)* on multivariate analysis, wound infection was higher for the ALND group than for the SLND-alone group. And in *Giuliano and his colleges study, (2011)* wound infection among patients in the Z0011 trial was higher for the ALND group than for the SLND-alone group (70% vs 25%, $P < .001$) this may contribute to BMI, but age and number of nodes removed were not significant predictors.

In our study, there was no significant difference between both groups in developing post-operative wound infection and seroma ($P = 0.399$ and 0.11, respectively). *Lucci et al,* showed a significant difference between both groups in Z0011 in developing post-operative wound infection and seroma.

In this study, axillary paraesthesia was the most common surgical effect at 30 days, 6 months and a year. It was highly presented in the ALND group throughout the follow up period, and statistically showed significant difference between both groups. The most commonly affected nerve was the intercostobrachial nerve and most of these cases had improved dramatically with conservative management. This is similar to *Giuliano and his colleges study, (2011)*. paresthesias among patients in the Z0011 trial was higher for the ALND group than for the SLND-alone group (70% vs 25%, $P < .001$) and in *wang and his colleges study, (2011)* Randomized controlled trials (RCTs) comparing SLNB with ALND in early breast cancer, SLNB results in a significant reduction of postoperative morbidity and improved quality of life (*Giuliano et al., 2011*) and (*Wang et al., 2011*). Our results for post-operative paraesthesia were similar to published literature (*Lucci et al., 2007*).

In this study, 2 patients had lymphedema after 6, 12 monthes in SLND group and 5 patients had lymphedema after 12 monthes in ALND group. This is similar to *Janni and his colleges study, (2014)*. a recent meta-analysis, the rate of complications (particularly lymphedema: 19.9% versus 5.6%) during long-term follow-up was four

times higher following axillary dissection than following sentinel node biopsy.

Post-operative lymphoedema was not significantly different in both groups throughout the post-operative period. Our results were different from published literature which showed significant difference between both groups (*Lucci et al., 2007*). The number of cases involved in our study was fewer and our assessment based on both subjective and objective analysis which could explain this difference.

However, our study agreed with others in that the incidence of post-operative lymphoedema is higher in the ALND group in comparison to the SLND group (*Fleissig et al., 2005 and Lucci et al, 2007*). There was a thought that clinicians overestimated the incidence of lymphoedema after ALND and underestimated it for SLND. Using arm measurements, lymphoedema occurred in 8, 7 and 7% of patients 6 months after SLND in Z0011, in ACOSOG Z0010 and in the ALMANAC trials, respectively (*Fleissig et al., 2005*).

On the other hand, post-ALND lymphoedema diagnosed by arm measurements occurred in 11 and 14% in Z0011 and in the ALMANAC trials, respectively (*Fleissig et al., 2005*).

In this study, there was no mortality recorded and this may be due to the short-term duration of the study in comparison to other studies that recorded mortality.

One case (2%) had a recurrence in the remaining axillary lymph nodes in the SLND group with no locoregional recurrence In the ALND group during our follow up period.

The low rates of locoregional recurrence at 5 years and the nearly identical overall and disease-free survival between treatment groups in Z0011 would suggest that differences in survival between study groups are unlikely to emerge with longer follow-up(*Ram et al.,2014*).

One of the difficulties in this study was recruiting patients for both groups as we have to send SLNs for histopathology and to confirm metastases for three or less lymph nodes before including the patient in any group. Patients without positive SLNs were excluded from enrollment.

The weakness of this study was in the limited follow up period for both patients' survival and recurrence of the disease. Continuous observation of those patients in the breast outpatient clinics is preferable to evaluate the long-term outcomes of these different techniques.

Our study supported the literature findings of the short-term outcomes of both ALND and SLND groups. It showed fewer post-operative surgical complications in the SLND group. However, our results were different from other published literature in the form of absence of any significant statistical differences between both groups in wound infection, seroma and lymphoedema. This may be explained by the number of cases involved in our study and the method we used to assess these complications both subjectively and objectively to consider patients quality of life.

Clinical guidelines recommend SLNB, by a team experienced in SLNB mapping and excision, as the standard of care for axillary staging for patients with clinically node-negative disease.

CONCLUSION

SLND mapping and excision is the standard of care for axillary staging for patients with early invasive breast cancer and clinically node-negative disease.

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