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Study of the Correlation between Tumor Size and Axillary Lymph Node Involvement in Females Breast Cancer

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ABSTRACT

Background: Axillary lymph node metastasis is the key on treatment and prognosis of breast cancer.

Objective: This study aimed to reduce the risk of unnecessary axillary lymph node dissection in female breast cancer finding the relation between size of tumor and axillary lymph node metastasis.

Patients and methods: This study included 41 female patients with operable breast cancer who were admitted to General Surgery Department, Zagazig University Hospitals. The patients were divided into two groups where group I included 17 patients with breast mass ≤ 2 cm and group II included 24 patients with breast mass > 2 cm.

Results: Breast lump was the major symptom complained by 41 patients (100%). Followed by axillary lump 22% and breast pain 22%. Left breast was the most commonly affected side with 21 patients (51.2%) and the upper outer quadrant was the most affected quadrant with 23 patients (56.1%). All patients had infiltrative duct carcinoma. 30 patients (73.2%) had infiltrative duct carcinoma grade II but only 11 patients (28.8%) had infiltrative duct carcinoma grade III. 39 patients (95.1%) underwent modified radical mastectomy and 2 patients (4.9%) underwent radical conservative breast surgery after fulfilling the criteria making them candidates for breast conservative surgery. There was no local recurrence in both groups during a follow up period up to six months.

Conclusion: There was no correlation between breast cancer mass size and axillary lymph nodes involvements. There was direct proportion between tumor size in cancer breast and number of axillary lymph nodes involvement when there is metastasis in axillary lymph nodes.

Keywords: Breast cancer, Tumor size, Axillary lymph node, Axillary lump.

INTRODUCTION

The most frequent malignant tumour in women is breast cancer. It is the biggest cause of cancer-related mortality in women worldwide. It is responsible for 15% of all cancer-related fatalities in women and around 30% of all female cancers [(1)].

The optimal methods for controlling this disease in communities must be determined because breast cancer is more common in women. This is dependent on a variety of factors, including cancer screening programs, early diagnosis, risk factors, cancer incidence in the general population, and the link between tumour features and invasive behaviour [(2)].

A useful strategy to lower breast cancer mortality and morbidity is early identification of the disease by mammographic and ultrasonographic programs. The most frequent locations for breast cancer metastasis outside of the main lesion are axillary lymph nodes (ALNs) [(3)]. For individuals with early breast cancer, axillary lymph node involvement (ALNI) is the most crucial prognostic factor. A higher risk of recurrence and death is associated with a greater involvement of axillary lymph nodes (ALNs) [(4)].

There seems to be a statistically significant correlation between initial tumour size and lymph node metastasis. Throughout the past century, axillary lymph node dissection (ALND) has been a successful surgical method in the early treatment of invasive breast cancer [(5)]. Although ALND has significant drawbacks, including discomfort, lymphedema, and shoulder stiffness, it is widely acknowledged that axillary staging is necessary to determine the best course of treatment for patients with invasive breast cancer [(4, 6)].

To prevent needless complete ALND, we can select individuals with a tolerable low risk of ALNI by predicting the condition of their axillary lymph nodes prior to surgery. It has long been debatable whether or not patients with tiny tumours should undergo total axillary dissection. Due to the minimal risk of ALNM in patients with tiny tumours (< 2 cm), some writers think we can spare these patients from complete ALND, while others think ALND should continue to be the standard of therapy for those with invasive breast cancer [(7)].

The fact that the initial tumor's size may be utilised as a trustworthy indicator of ALNI is reason for concern. Another obstacle is preventing any certain patient group from needless ALND because of the size of their underlying tumour [(3)].

Therefore, this study aimed to find the relation between size of tumor and axillary lymph node metastasis through assessment of breast mass size, evaluate axillary lymph node metastasis and correlate between breast mass size and positive axillary lymph nodes.

PATIENTS AND METHODS

This is a clinical prospective study that was carried out in the Department of General Surgery, Zagazig University Hospitals. The study included 41 female patients with operable breast cancer admitted with inclusion criteria.

Inclusion criteria: Female cases more than 18 years of age diagnosed as breast malignancy. Fine Needle

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Aspiration Cytology (FNAC), Tru-cut biopsy are diagnostic of breast cancer. Those who consented to participate in this study.

Exclusion criteria: Seriously ill patients in terminal stage of breast carcinoma requiring ventilator support, pregnant females, features suggestive of inoperability, distant metastasis, locally advanced breast carcinoma and patients who refused to participate in the study.

All patients were subjected to the following: Full history taking and physical examination including special concern looking for signs of metastases and examination of any breast mass assessing site, size, shape, surface, number, consistency, edge, tenderness and hotness, relation to underlying structures (fixation to pectoral muscles or chest wall), and relation to overlying skin. Also, examination of the axillary lymph nodes assessing number, size, shape, surface, consistency, fixation to each other and underlying structures.

Pre-operative investigations:

Routine laboratory investigations including complete blood picture (CBC), bleeding profile, liver function tests, kidney function tests, random blood sugar, and hepatitis markers. Mammography, breast ultrasonography, Tru-cut biopsy and excisional biopsy were performed. ECG and medical fitness for surgery was done for patients over 40 years.

After completing all investigations and confirming the stage of the disease and fitness of the patients for surgery; 41 patients were divided into two groups:

- **Group I:** included 17 patients (41%) who had breast mass less than 2 cm and underwent modified radical mastectomy or radical conservative breast surgery
- **Group II:** included the other 24 patients (59%) who had breast mass more than 2 cm and underwent modified radical mastectomy.

Patients who underwent conservative breast surgery showed the following criteria: Single clinical and mammographic lesion, the tumor size was up to 2 cm, no extensive axillary nodal involvement (N0 or N1), no distant metastases and patient wishes.

Surgical procedure:

For both group, with induction of anesthesia, 1 gm. of 3rd generation cephalosporin was given as prophylactic antibiotic. Breast surgery was done either modified radical mastectomy or radical conservative breast surgery whether lumpectomy or quadrantectomy. We began the axillary dissection with the identification of the classic landmarks and limits of axillary dissection were determined with the axillary vein superiorly, pectoralis minor medially and latissimus dorsi muscle laterally, taking care not to injure the important structures e.g., the axillary vein, the long thoracic nerve, the thoracodorsal neurovascular bundle. After that wound was closed after good haemostasis and suction drain was put. The resected specimen was sent for histopathological examination.

Post-operative care:

Monitoring of the vital signs of the patients every 6 hours, and the amount of the drain every 12 hours post-operatively. Patients were encouraged for early mobilization from bed after 6 hours and started oral intake and post-operative analgesia was given. Patients were encouraged for early mobilization of the upper limb from the 2nd post-operative day. Patients were discharged from the hospital in the next 24 hours.

Follow up:

Patients were followed up during their hospital stay. The sutures of the wound were removed from 10-12 days. Follow up of any post-operative complications such as wound infection, seroma, hematoma and numbness along the inner aspect of the arm. All patients were advised to visit outpatient clinic every week during the first 6 months postoperative. Careful examination of the scar of the breast and the axilla during the follow-up period up to six months for any possible recurrence. The patients were referred to the Oncology Department with the final pathology report to complete their treatment.

Ethical consideration: All participants provided their written informed permissions, and the research was authorised by the Zagazig University Faculty of Medicine's Research Ethics Council. The experiment was done in conformity with the Declaration of Helsinki, which is the World Medical Association's code of ethics for studies involving humans.

Statistical analysis

SPSS version 23.0 for Windows was used to analyse all the data (SPSS Inc., Chicago, IL, USA 2011). The mean ± standard deviation, and (range) were used to describe quantitative data, and absolute frequencies (number) & relative frequencies were used to convey qualitative data (percentage). When applicable, the Chi-square test or Fisher's exact test was used to compare the percentage of categorical variables. When calculating the Spearman rank correlation coefficient, values close to 1 indicate a high connection while values close to 0 indicate a weak correlation. $P \leq 0.05$ was regarded as significant.

RESULTS

The present study showed that all patients manifested by lump in breast, 22.0% of them had severe pain and axillary lump and 7 (17.1%) of patients had nipple discharge **(Table 1)**. About 20 patients (48.8%) had lump in right breast and 23 (56.1%) had lump at UOQ of breast also majority of patients 35 (85.4%) had single lump **(Table 2)**.

Table (1): Frequency and percentage distribution of breast cancer symptoms among studied patients (n=41)

Symptoms	Number of patients	%
Lump in breast	41.00	100.0
Nipple discharge	7.00	17.1
Pain	9.00	22.0
Axillary lump	9.00	22.0

Table (2): Frequency and percentage distribution of side, location and number of breast lump among studied patients (n=41).

	Number of patients	%
I. Breast side		
Rt breast	20	48.8
Left breast	21	51.2
II. Tumor location		
Central	3	7.3
Multicentric	6	14.6
UOQ	23	56.1
LOQ	4	9.8
UIQ	5	12.2
III. Number of lumps		
Single	35	85.4
Bifocal	5	12.2
Multifocal	1	2.4

Regarding tumor staging, 6 of patients had tumor stage I (14.6%), 17 of patients had tumor stage II (41.5%), and 18 of patients had tumor stage III (43.9%) **(Table 3)**.

The mean tumor size was 3.77 ± 2.9 ranged from 1 to15 cm. 41.5% of studied patients had tumor size equal or less than two centimeter and 58.5% of them had tumor size more than two centimeter **(Figure 1)**. Mean affected lymph node was 6.8 ± 6.6 with range from 1 to 22 LNs. About two thirds 65.9% of studied patients had affected lymph nodes and 34.1% of them had clear lymph nodes **(Figure 2)**.

Table (3): Frequency and percentage distribution of tumor Staging among studied patients (n=41)

Tumor Staging	Number	Percent
Stage I	6	14.63
Stage II	17	41.46
IIA	11	26.83
IIB	6	14.63
Stage III	18	43.9
IIIA	13	31.7
IIIC	5	12.2
Total	41	100.0

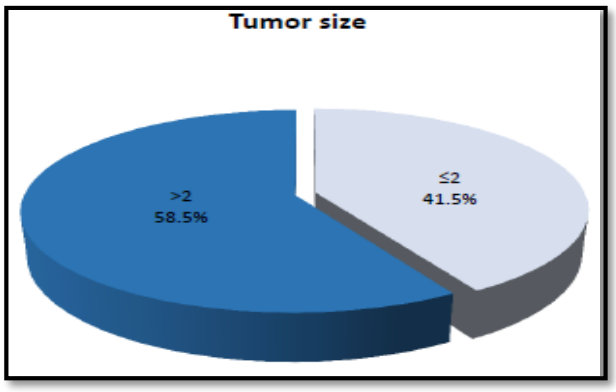

Figure (1): Tumor size of studied patients (n=41).

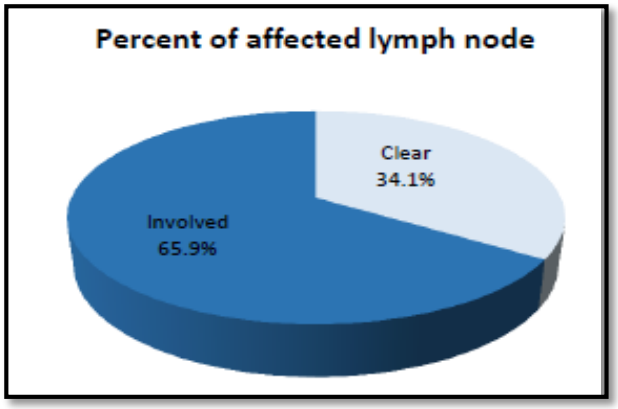

Figure (2): Percent of affected lymph nodes among studied patients defined (34.1%) of patients had clear lymph node and 65.9% their lymph node involved (n=41).

According to type of surgery, 39 (95.1%) of patients submitted to modified radical mastectomy with axillary clearance, and little percent of patients (2) 4.9% submitted to wide local excision with axillary clearance **(Table 4).**

Table (4): Type of surgery operation for removal of breast lump for studied Patients (n=41)

Type of surgery	Number of patients	%
MRM with axillary clearance	39	95.1
Wide Local excision with axillary clearance	2	4.9

There was statistically significant positive correlation between tumor size and number of lymph node affected p=0.017. While there was statistically significant negative correlation between tumor size and number of lymph node unaffected p=0.006. It's obvious that increased tumor size was associated with increased number of lymph nodes affected. Whereas decrease tumor size increased number of lymph node not affected **(Figures 3, 4).**There was statistically significant relation between ischemic heart disease and unaffected lymph node p=0.039. It is obvious that ischemic heart disease patients commonly had clear lymph node **(Table 5).** There was statistically insignificant relation between lump characteristics and lymph node affection among studied patients (p > 0.05) **(Table 6)**.

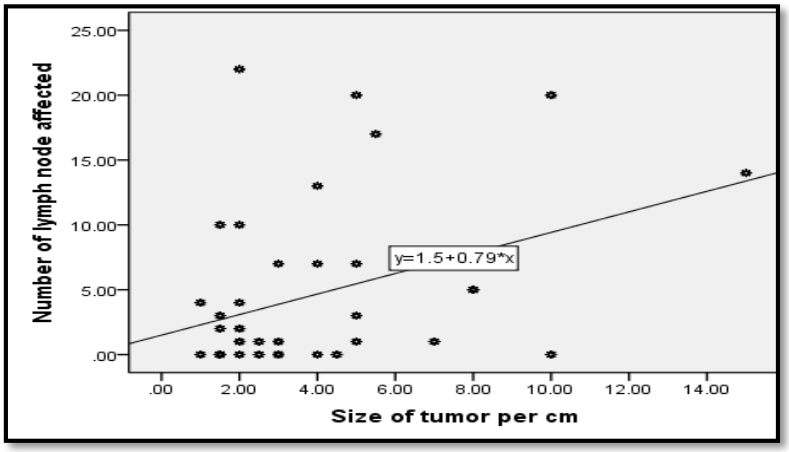

Figure (3): Scatter diagram showed correlation between tumor size per cm and number of lymph node affected

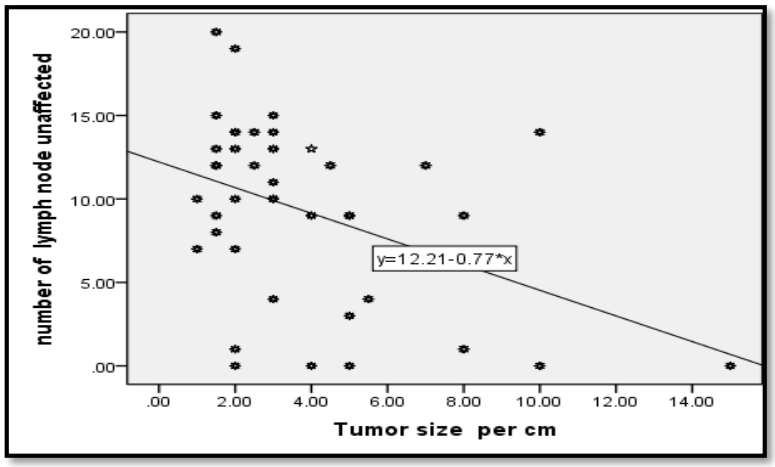

Figure (4): Scatter diagram showed correlation between tumor size per cm and number of lymph node unaffected

Table (5): Relation between patient's characteristics and their lymph node affection (n=41)

	Lymph node				n.	χ^2	p-value
	Unaffected		Affected				
	No.	%	No.	%			
Age per years							
≤50	**5**	**27.8**	**13**	**72.2**	**18**	**0.58**	**0.45**
>50	**9**	**39.1**	**14**	**60.9**	**23**		
HTN							
Present	**7**	**38.9**	**11**	**61.1**	**18**	**0.3**	**0.57**
Absent	**7**	**30.4**	**16**	**69.6**	**23**	**2**	
DM							
Present	**2**	**22.2**	**7**	**77.8**	**9**	**F**	**0.69**
Absent	**12**	**37.5**	**20**	**62.5**	**32**		
IHD							
Present	**4**	**80.0**	**1**	**20.0**	**5**	**F**	**0.039(S)**
Absent	**10**	**27.8**	**26**	**72.2**	**36**		
HCV							
Present	**1**	**33.3**	**2**	**66.7**	**3**		**0.99**
Absent	**13**	**34.2**	**25**	**65.8**	**38**		
Comorbidity							
Present	**10**	**37.0**	**17**	**63.0**	**27**		**0.73**
Absent	**4**	**28.6**	**10**	**71.4**	**14**		

χ^2 Chi square test f=Fisher exact test (S) significant p<0.05

Table (6): Relation between lump characteristics and lymph node affection among studied patients (n=41)

	Lymph node				n.	χ^2	p-value
	Unaffected		Affected				
	No.	%	No.	%			
Actual .size							
≤2	**6**	**35.3**	**11**	**64.7**	**17**	**0.02**	**0.89**
>2	**8**	**33.3**	**16**	**66.7**	**24**		
Site of lesion							
Rt breast	**8**	**40.0**	**12**	**60.0**	**20**	**0.49**	**0.55**
Lt breast	**6**	**28.6**	**15**	**71.4**	**21**		
Location of lesion							
Central	**0**	**.0**	**3**	**100.0**	**3**		**0.54**
LOQ	**1**	**25.0**	**3**	**75.0**	**4**		**0.99**
Multicentric	**2**	**33.3**	**4**	**66.7**	**6**	**F**	**0.99**
UIQ	**2**	**40.0**	**3**	**60.0**	**5**		**0.99**
UOQ	**9**	**39.1**	**14**	**60.9**	**23**		**0.67**
Grade of tumor							
Infiltrating duct carcinoma Grade II	**9**	**30.0**	**21**	**70.0**	**30**	**F**	**0.57**
Infiltrating duct carcinoma Grade III	**5**	**45.5**	**6**	**54.5**	**11**		
Number of lesion							
Single	**12**	**34.3**	**23**	**65.7**	**35**		
Bifocal	**2**	**40.0**	**3**	**60.0**	**5**	**0.59**	**0.74**
Multifocal	**0**	**0.0**	**1**	**100.0**	**1**		

$\chi 2$ Chi square test f=Fisher exact test non-significant p>0.05

DISCUSSION

Depending on whether breast cancer cells have spread to the axillary lymph node(s) or not, the main prognostic factor on which therapy decisions are based is the condition of the regional lymph node(s). The condition of the axillary nodes continues to be the most crucial prognostic factor and will have an immediate effect on treatment decisions [(8)]. An important long-term consequence of ALND is lymphedema, which impairs quality of life and causes a reduction in range of motion. Arm lymphedema following ALND was found to occur 7–20% of the time in earlier trials [(9)].

This study includes 41 cases divided into two groups according to tumour size. First group had 17 patients (41.5%) with tumour size ≤ 2 cm. while second group had 24 patients (58.5%) with breast mass > 2 cm. The mean age was 53 years (range from 37-74 years). This incidence is near to the report of **Orang *et al.*** [(3)], which estimated that the mean age was 51 years, and the study done by **Thompson *et al.*** [(8)] who mentioned that the mean age of patients was 49.7 years old (range 26-69 years).

The present study revealed that out of 41 cases, 27 (65.9%) suffered from chronic diseases, while 14 (34.1%) had no chronic diseases. Hypertension came first with 18 patients (43%) followed by DM that 9 patients (22%) then IHD was 5 patients (12.2%) and HCV +ve was 3 patients (7.3%). This finding matches with **Rao *et al.*** [(10)] who found that 32 (52.7%) had chronic diseases, while 28 (48.3%) had no chronic diseases.

In this study breast lump was the most common presenting symptom 41 (100%) that agrees with **Rao *et al.*** [(10)] who reported that 60 patients (100%) had breast lump.

Left breast was the most commonly affected side, 21 patients (51.2% incidence) and the upper outer quadrant was the most affected one (23 patients with 56.1% incidence). This matches with **Skandalakis *et al.*** [(11)] and **Bland *et al.*** [(12)] who reports that the upper outer quadrant contains the main bulk of breast tissue and thus it is the most usual site for both breast cancer and most benign breast pathologies.

The upper outer quadrant was affected in 56.1%, the upper inner quadrant was 12.2%, the lower outer quadrant was 9.8%, the lower inner quadrant was 0%, the central (subareolar) was 7.3% and multicentric was 14.6%. These are nearly the same results reported by **Leidenius *et al.*** [(13)] who stated that the upper outer quadrant was affected in 55.4%, the upper inner quadrant was 20.1%, the lower outer quadrant was 9.2%, the lower inner quadrant was 7.4% and the central (subareolar) area was 7.9% from a study carried on 363 patients with breast cancer.

In this study according to American Joint Committee in Cancer (AJCC) stage I included 6 patients (14.6%), stage IIA included 11 patients (26.8%), stage IIB included 6 patients (14.7%), 13 (31.7%) patients were in stage IIIA and only 5 patients (12.2%) had stag

IIIC breast cancer. This matches with what was reported by **Rao *et al.* [10]** who mentioned that 13.33% of patients had stage I disease and 26.65% of patients had stage IIA disease and 40% had stage IIIA tumors in their study on 45 patients.

In the studied group, 39 patients (95.1%) underwent modified radical mastectomy and 2 patients (4.9%) underwent radical conservative breast surgery (radical lumpectomy or radical quadrantectomy). This is near to the results of **Sandhu *et al.* [14]** whose results showed that 88.7% underwent modified radical mastectomy (MRM) and 11.3% underwent radical conservative breast surgery (CBS). Also, **Nos *et al.* [15]** showed that 71% underwent MRM and 29% underwent CBS. But, these results do not agree with **Rönkä *et al.*[16]** whose results reported that 70% underwent CBS and 30% underwent MRM and **Husen *et al.* [17]** who showed that 73% underwent CBS and 27% underwent MRM.

The patients selected for radical conservative breast surgery all had single lesion less than 4 cm, no palpable axillary lymph nodes or small mobile lymph nodes and the tumor size in relation to the breast size allowed good cosmetic results that were acceptable to both the surgeons and the patients. The idea of breast conservation was accepted by all patients who underwent the procedure. Also, this reflects the trend towards a more conservative breast surgery done in many centers for the cases with early breast cancer. This coincides with what is published by **Newman and Washington [18]**.

The postoperative histopathological examination of the resected specimens showed that invasive duct carcinoma grade II was the most common pathology diagnosed in 30 patients (73.2%) followed by invasive duct carcinoma grade III which was diagnosed in 11 patients (26.8%). This matches with **Cuschieri *et al.* [19]** and **Bland *et al.* [12]** who stated that invasive duct carcinoma represents the most frequently encountered histologic type of breast carcinoma, and both invasive duct carcinoma and invasive lobular carcinoma both represent about 85% of the diagnosed invasive carcinomas.

The number of excised lymph nodes ranged from 6-23 LNs with an average 13.8 LNs. This is the same result of **Wal *et al.* [20]** in their study where the median number of lymph nodes dissected was 14 (range 1-26) and **Casabona *et al.*[21]** who mentioned in their study that the mean number of lymph nodes excised in patients who underwent ALND was 16 (range, 9–24 nodes). **Veronesi *et al.*[22]** stated that there may be a difference in the number of excised lymph nodes between reports, this is either due to improper dissection of the specimen or may be due to incomplete axillary dissection. Also, re-examination of the surgical specimen taken from the axilla revealed that 19.5% of LNs removed during surgery, escaped examination by the pathologist. The escape of LNs may be due to improper preservation of the specimen, leading to confusion between the LNs and fatty tissue, due to the effect of formaldehyde. Also, lymph nodes may be tiny or not involved by metastasis and hence cannot be recognized or differentiated from the surrounding tissues.

From the excised LNs, 14 patients (34.1%) had negative LNs and 27 patients (65.9%) had positive axillary LNs. This matches with **Abdelhamid *et al.* [23]** study, which revealed that 9 patients (30%) had negative axillary LNs and 21 patients (70%) had positive axillary LNs.

This study showed that patients with tumour mass ≤ 2 cm were 7 patients (38.8%) with negative LNs involvement and 11 (61.2%) patients with positive LNs. Patient with tumour mass > 2 cm were 7 patients (30.4%) with unaffected LNs and 16 patients (69.6%) with metastatic LNs, which revealed that there is no relationship between axillary lymph node metastasis and size of tumor. This disagrees with the result of **Orang *et al.* [3]** who found that there is direct proportion between size of tumor and axillary lymph node metastasis.

CONCLUSION

There was no correlation between breast cancer mass size and axillary lymph nodes involvements. There was direct proportion between tumor size in cancer breast and number of axillary lymph nodes involvement when there was metastasis in axillary lymph nodes.

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REFERENCES

1. **Jemal A, Bray F, Center M *et al.* (2011):** Global cancer statistics. CA Cancer J Clin., 61 (2): 69-90.
2. **Wasserberg N, Morgenstern S, Schachter J *et al.* (2002):** Risk factors for lymph node metastases in breast ductal carcinoma in situ with minimal invasive component. Arch Surg., 137 (11): 1249-1252.
3. **Orang E, Marzony E, Afsharfard A (2013):** Predictive role of tumor size in breast cancer with axillary lymph node involvement - can size of primary tumor be used to omit an unnecessary axillary lymph node dissection? Asian Pac J Cancer Prev., 14 (2): 717-722.
4. **Lee J, Kim S, Suh Y *et al.* (2010):** Predictors of axillary lymph node metastases (ALNM) in a Korean population with T1-2 breast carcinoma: triple negative breast cancer has a high incidence of ALNM irrespective of the tumor size. Cancer Research and Treatment, 42 (1): 30-36.
5. **Takei H, Kurosumi M, Yoshida T *et al.* (2009):** Positive sentinel lymph node biopsy predicts the number of metastatic axillary nodes of breast cancer. Breast, 18 (4): 244-247.
6. **Giuliano A, Hunt K, Ballman K *et al.* (2011):** Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA., 305 (6): 569-575.

7. **Mincey B, Bammer T, Atkinson E *et al.* (2001):** Role of axillary node dissection in patients with T1a and T1b breast cancer: Mayo Clinic experience. Arch Surg., 136 (7): 779-782.
8. **Thompson M, Korourian S, Henry-Tillman R *et al.* (2007):** Axillary reverse mapping (ARM): a new concept to identify and enhance lymphatic preservation. Ann Surg Oncol., 14 (6): 1890-1895.
9. **Casabona F, Bogliolo S, Valenzano Menada M *et al.* (2009):** Feasibility of axillary reverse mapping during sentinel lymph node biopsy in breast cancer patients. Annals of Surgical Oncology, 16 (9): 2459-2463.
10. **Rao S, Patra R, Sonnathi Y (2017):** Clinical study of co-relation between positive axillary lymph node status and size of the tumor in breast malignancies. Archives of International Surgery, 7: 1. https://doi.org/10.4103/ais.ais_15_17
11. **Skandalakis J, Colborn G, Weidman T *et al.* (2006):** Breast. In: Skandalakis' surgical anatomy. 15th edition. McGraw-Hills, Pp: 151-205. https://herniaspecialists.com/curriculum-vitae-lee-j-skandalakis/
12. **Bland K, Beenken S, Copeland E (2010):** The breast. In: Schwartz's Principles of Surgery. Charles Brunicardi F, Andersen D, Billiar T, et al (editors): Eighth edition. McGraw-Hill Medical Publishing Division, Pp: 453. https://accesssurgery.mhmedical.com/content.aspx?sectionid=59610859&bookid=980
13. **Leidenius M, Krogerus L, Toivonen T *et al.* (2003):** The feasibility of intraoperative diagnosis of sentinel lymph node metastases in breast cancer. J Surg Oncol., 84 (2): 68-73.
14. **Sandhu D, Sandhu S, Karwasra R *et al.* (2010):** Profile of breast cancer patients at a tertiary care hospital in north India. Indian Journal of Cancer, 47 (1): 16-22.
15. **Nos C, Kaufmann G, Clough K *et al.* (2008):** Combined axillary reverse mapping (ARM) technique for breast cancer patients requiring axillary dissection. Ann Surg Oncol., 15 (9): 2550-2555.
16. **Rönkä R, von Smitten K, Tasmuth T *et al.* (2005):** One-year morbidity after sentinel node biopsy and breast surgery. The Breast, 14 (1): 28-36.
17. **Husen M, Paaschburg B, Flyger H (2006):** Two-step axillary operation increases risk of arm morbidity in breast cancer patients. The Breast, 15 (5): 620-628.
18. **Newman L, Washington T (2003):** New trends in breast conservation therapy. Surg Clin North Am., 83 (4): 841-883.
19. **Cuschieri A, Grace P, Darzi A *et al.* (2003):** Disorders of the breast. In: Clinical Surgery. 2nd edition. Blackwell Science, Pp: 428-440. https://www.academia.edu/5703036/Clinical_Surgery_by_Alfred_Cuscheri_2nd_Edition
20. **Wal B, Butzelaar R, Meij S *et al.* (2002):** Axillary lymph node ratio and total number of removed lymph nodes: Predictors of survival in stage I and II breast cancer. European Journal of Surgical Oncology, 28: 481-489.
21. **Casabona F, Bogliolo S, Valenzano Menada M *et al.* (2009):** Feasibility of axillary reverse mapping during sentinel lymph node biopsy in breast cancer patients. Annals of Surgical Oncology, 16 (9): 2459-2463.
22. **Veronesi U, Paganelli G, Viale G *et al.* (2003):** A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med., 349 (6): 546-553.
23. **Abdelhamid M, Bari A, Farid M *et al.* (2020):** Evaluation of axillary reverse mapping (ARM) in clinically axillary node negative breast cancer patients-Randomised controlled trial. International Journal of Surgery, 75: 174-178.