Original Research Paper

Radio-Diagnosis

AGREEMENT BETWEEN RADIOLOGICAL AXILLARY NODAL STAGING VERSUS HISTOPATHOLOGICAL STAGING IN PATIENTS UNDERGOING PRIMARY BREAST CANCER SURGERY.

Dr. Nupur Jha	Amrita School of Medicine, Amrita Vishwa Vidyapeetham
Dr. Janaki P Dharmarajan*	Amrita School of Medicine, Amrita Vishwa Vidyapeetham*Corresponding Author
Ms Sheejamol V S	Amrita School of Medicine, Amrita Vishwa Vidyapeetham

ABSTRACT **Background:** Breast cancer is the most common cause of death in women in india. For the correct staging of breast cancer and the implementation of appropriate treatment, knowing the status of axillary lymph nodes is mandatory. In determination of lymph node involvement physical examination alone is not sufficient. When AUS is positive, sentinel lymph node biopsy (SLNB) which is an invasive procedure and requires additional costs is passed and axillary lymph node dissection can be applied. Thus time and expenses can be saved .**Purpose:** For most of the patients it is imperative that the treating physician gets to know the total nodal burden so as to triage the patient from surgery and neo adjuvant chemotherapy.**Methods:** Data consists of 103 patients with breast cancer. Patients were taken for axillary ultrasonography for seeing axillary lymph node metastasis. AUS findings helped to assess the extent of involvement of axillary lymph nodes in Breast cancer. After AUS , the same patients did undergo surgery and specimen was sent for histopathology. Axillary ultrasound and histopathology findings were then compared and sensitivity, specificity and accuracy were calculated **Results** The overall sensitivity of the study was 81.2 %. and the specificity of the study was 67.3% which was similar to the specificity in the study done through MerveGursoy et al. Variability between examiners in the interpretation of ultrasound results may account for this difference. The PPV and NPV of the study were 68.4 % and 80.4 %. The overall accuracy of our study was 73.7 %. **Conclusion:** The study had an overall good sensitivity (81.2%) and specificity (67.3%). There was no numerically noteworthy difference between ultrasound and histopathology in axillary lymph node assessment in the setting of early invasive breast cancers.

INTRODUCTION

"As many people considered October a month for breast cancer awareness. But the one who survived breast cancer considered it as a just normal day".

It is seen that in the breast cancer the cells tend to grow in the breast and grow gradually which cannot be controlled. This may lead to mortality as well as morbidity in the women across the globe. It is seen that most of the women lose their life due to breast cancer.

Breast cancer is one such oldest cancers in the human kind. This cancer was discovered initially in Egyptian Papyrus in 1600 BC. This was mainly acquired in terms of inscriptions by Edwin Smith in the year 1862 this was during the time when Smith died and the inscriptions were mainly presented in the New York Historical society. That is also mentioned in Case 45, which was given the title "Instructions Concerning Tumors on the Breast." It is also chosen to be an aliment with no therapy.

Hippocrates (b. 460 BCE), known as the "Father of Medicine," invents the term "Carcinoma" to reflect his opinion that breast cancer is strongly linked to menopause. Heat, redness, pain, and swelling are some of the cardinal characteristics of inflammation recorded by Aurelius Celsus (b. 25 BCE). Later, around AD 30, Aurelius Celsus wrote De Medicina, which gives a description of the term "cancer." The term "cancer" is derived from the Latin word Crab, which meaning "woman's breast," which is one of the sites of cancer. Hippocrates was followed by the famous Greek physician Galen (b. AD 131), who was eventually acknowledged as the inventor of experimental physiology. Galen also described the term "Oncos," which means swelling in Greek, to describe the illness. However, despite hundreds of years of theoretical meanderings and heaps of systematic literature, cancer related to breasts remains the most feared of all human diseases. There has been some development in the technique of teaching individuals about this disease's early symptoms in order to reduce the fear of the disease among humans.

MATERIALS AND METHODS

This was a prospective study that was carried out after receiving consent from the Scientific and the Ethical Review Committee, Amrita Institute of Medical Sciences.

Inclusion Criteria:

For the purpose of determining the pre-operative axillary lymph node status of breast cancer with a positive biopsy, all patients are receiving axillary ultrasonography.

Exclusion Criteria:

1. Patients with extensive metastasis.
2. Patients not willing for surgery.
3. Patients deferred from surgery.

Study setting:

Amrita Institute of Medical Sciences' radiology division.

Duration of study:

Over a period of two years beginning on the day the thesis decorum review committee's (Ethical, Scientific, & Financial) approval was received at the Amrita Institute of Medical Sciences and Research Center in Kochi.

Study Design:
Prospective study.
Inclusion Criteria:

For the purpose of determining the pre-operative axillary lymph node status of breast cancer with a positive biopsy, all patients are receiving axillary ultrasonography.

Exclusion Criteria:

1. Patients with extensive metastasis.
2. Patients not willing for surgery.
3. Patients deferred from surgery.

Sample Size:

Based on the axillary ultrasound's (AUS) 78.9% accuracy rate as seen in the study of "Tumor as well as Histopathological and Characteristics" Related with adverse Negative Axillary Ultrasonography Outcomes in the Breast Cancer. With 95 percent confidence and 10 percent relative precision (MerveGursoy et al., MedUltrason.2019), the minimal sample size is 103.

Technical Information:

Primary Objective: Accuracy in the staging of abnormal axillary lymph nodes seen on ultrasound in early operable breast cancers with the metastatic lymph nodes seen on final histopathology.

Secondary Objective: To assess the relation of false negative result with tumour morphology and surrogate tumour markers.

Data consists of almost 100 patients having breast cancer. Patients were taken for axillary ultrasonography for seeing axillary lymph node Mets. Interpretation of data was done by a dedicated fellowship trained breast imaging radiologist with more than one decade of experience in breast imaging. Use of AUS findings was taken to assess the extent of involvement of axillary lymph nodes in Breast cancer. After AUS, the same patients then underwent surgery, and specimens were sent for histopathology. Axillary ultrasound and histopathology findings were then compared and sensitivity, specificity, and accuracy were calculated.

L12-5 transducer was used for the ultrasound. Ultrasound examinations and FNAC from axillary lymph nodes were done. The axillary lymph nodes were assessed with a 21 G needle for cytology Pathologic examination of lymph node specimens and immunohistochemistry was performed according to standard institutional protocols. 1 -3 lymph nodes were classified into N1 group. 4-9 lymph nodes were classified in to N2 and above that in N3 group.

Statistical Analysis:
The IBM SPSS Statistics 20 Windows program is seen to be used for the statistical analysis. For all incessant variables, the results are shown as mean SD, and for categorical variables, they are presented as frequency (%). A significant difference between the results of the ultrasound and the final histology in terms of the axillary lymph bump was determined with the help of McNemar chi-square test. Additionally, assessed were ultrasound's sensitivity, PPV, specificity, NPV , false negative rates and accuracy.

RESULTS
Overall out of 103 cases , 57 cases (55.34%) are positive by imaging and 48 cases (46.6%) are positive by histopathology , however there is no significant difference in the finding of lymph node between imaging and histopathology . There is moderate agreement between imaging lymph nodes in axilla and histopathology confirmed metastatic lymph nodes (k = 0.480 , P value = 0.001).

In Invasive ductal carcinoma category, out of 81 cases , 43 cases (53.1 %) are positive by imaging and 36 cases (44.4 %) are positive by histopathology , however there is no significant difference in the finding of lymph node between imaging and histopathology . P value is 0.189 .There is moderate agreement between imaging lymph nodes in axilla and histopathology confirmed metastatic lymph nodes (k = 0.485 , P value < 0.001)

In Invasive lobular carcinoma category, out of 9 cases , 7 cases (77.78 %) are positive by imaging and 6 cases (66.67 %) are positive by histopathology , however there is no significant difference in the finding of lymph node between imaging and histopathology . P value is 1.00 .There is good agreement between imaging lymph nodes in axilla and histopathology confirmed metastatic lymph nodes (k = 0.727 , P value = 0.023)

In others category, out of 9 cases , 3 cases (33.33%) are positive by imaging and 2 cases (22.22 %) are positive by histopathology , however there is significant difference in the finding of lymph node between imaging and histopathology . P value is 1.000 .There is no agreement between imaging lymph nodes in axilla and histopathology confirmed metastatic lymph nodes (k = - 0.364 , P value < 0. 257).

	Others	IMC	ILC	Overall
Sensitivity	0	80.6	100	81.2
Specificity	57.1	68.9	66.7	67.3
PPV	0	67.4	85.7	68.4
NPV	66.7	81.6	100	80.4
Accuracy	44.4	74.07	88.89	73.78
FNR	100	19.44	0	18.75

Table showing overall agreement between imaging metastatic axillary lymph nodes and pathological metastatic axillary lymph nodes in the study:

Lymph Nodes	Imaging LN	Pathological nodes
N0	46(44.7%)	55(53.4%)
N1	51(49.5%)	32(31.1%)
N2 and N3	6(5.8%)	16(15.5%)
Total	103(100%)	103(100%)

The above table shows that there is good agreement between imaging AUS and histopathology in N0 category . However in N1 category AUS is overestimating nodal burden and in N2 and N3 category AUS is underestimating nodal burden.

Discussion
In this study we prospectively did axillary ultrasound and compared the ultrasound results with final histopathological lymph nodes status after or post-surgery in patients undergoing primary breast cancer surgery. One of the benefits of preoperative axillary ultrasound lies in the fact that patients can go for upfront axillary dissection in same sitting of surgery as that of breast. Thus, the discomfort of patient might get reduced.

The overall sensitivity of the study was 81.2%. and the specificity of the study was 67.3% which was similar to the specificity in the study done through MerveGursoy et al.(2) where the overall specificity was 79%.Variability between examiners in the interpretation of ultrasound results may account for this difference

The PPV and NPV of the study were 68.43 % and 80.4 %. Premenopausal, peri-menopausal and post-menopausal women were included in the study. Maximum cases (78.6 %) belonged to the IMC category.

The overall accuracy of our study was 73.7 %. In this study, no statistically momentous variance between ultrasound & histopathology in axillary lymph node assessment in early operable breast carcinoma.

Accuracy varied with different receptor subtypes, so validity parameters were calculated for different tumour morphology subtypes. Clinical response evaluation, including the diagnostic precision of imaging techniques such as ultrasound, varied by tumour morphology. However the PPV and the NPV of our study group did not differ remarkably among different tumour morphology. The various tumour morpholgy showed no statistically significant difference between ultrasound and histopathology in axillary lymph nodes assessment. Strength Prospective study: It is a prospective study which gives indication based outcomes whereas most of the previously conducted studies were retrospective or non-randomized, which may have prejudiced results.

All the ultrasound examinations were performed by a senior dedicated fellowship trained breast imaging radiologist with more than one decade of experience in breast imaging radiologist. Thus further reducing bias between opinions.

Limitations
The major limitation is that due to the COVID-19 pandemic, as even though we could meet the desired sample size majority of patients presented with advanced disease and started on NACT and could not be included in the study.

CONCLUSION
- The study had an overall good sensitivity (81.2%) and specificity (67.3%).
- There was no numerically noteworthy difference between ultrasound and Histopathology in axillary lymph node assessment in the setting of early invasive breast cancers.
- Ultrasound is highly reliable for axillary lymph nodes assessment.
- Among the various tumour morphology subtypes, the highest accuracy for predicting the response assessment was for ILC category .

Tables And Figures
Bar diagram showing distribution of imaging lymph nodes according to number.
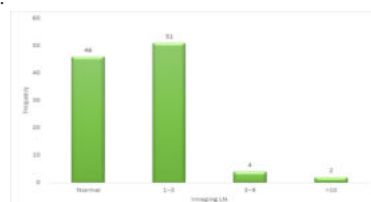
Bar chart showing distribution of pathological lymph nodes according to number.
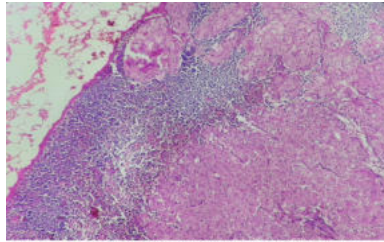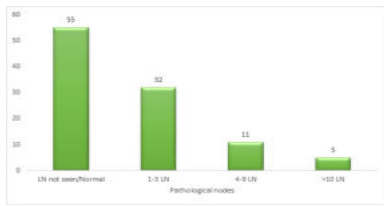

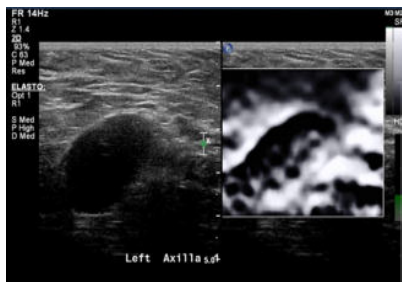Fig 4: Histopathological slide showing tumor cells involving lymph node

Fig 3: Suspicious lymph nodes on Axillary ultrasound

LN: lymph node.
AUS: axillary ultrasound
FNAC: Fine Needle Aspiration Cytology
USG: ultrasonography
ALN: axillary lymph node
IHC: Immunohistochemistry
SNB: sentinel node biopsy
NSABP: National Surgical Adjuvant Breast and Bowel" Problem Coordinating Committee
MRI: Magnetic Resonance Imaging
SLND: Sentinel Lymph Node Dissection
ALND: Axillary Lymph Node Dissection
IBCSG: International Breast Cancer Study Group
BCT: Breast Conservation Treatment
EBCTCG: Early Breast Cancer Trialists' Collaborative Group
DFS: Disease-Free Survival
DDFS: Distant Disease Free Survival
OS: Overall survival
BCT: Breast Conserving Therapy
WBI: Whole Breast Irradiation
NCCN: National Comprehensive Cancer Network
ASCO: American Society of Clinical Oncology
ACOSOG: American College of Surgeons Oncology Group
ITCs: Isolated Tumor Cells
H&E: Hematoxylin and Eosin Stain
USG: Ultrasound or Sonogram or Ultrasonogram
USGFNAC: Ultrasound Guided fine needle aspiration cytology
SLNB: Sentinel Lymph Node Biopsy
PE: Physical Examination
UNB: Ultrasound Guided needle biopsy
NPV: Negative predictive Value
DOR: Diagnostic Odds Ratio
PPV: Positive Predictive Value
FP: False Positive
ILC: Invasive Lobular Carcinoma

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