

# Correlation between pathological staging, histological grading, ER/PR and Her2neu status in breast cancer

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## Abstract

**Introduction:** Breast cancer is the 2<sup>nd</sup> most common cause of cancer among women worldwide. Women in India it presents at a younger age who present themselves at an advanced stage with poorer prognosis compared to western counterparts. Estrogen and Progesterone play a key role in the growth kinetics of the breast. Tumors that are positive for both estrogen and progesterone receptors have a better possibility of remission following Hormonal therapy (70%).

**Objectives:** Hence this study was done to correlate the histological grading, tumor size and Nodal status with ER/PR and HER2neu status in women undergoing Modified Radical Mastectomy for breast cancer. **Results and Discussion:** 50 female patients who underwent Modified Radical Mastectomy for breast cancer proved by FNAC from Jan 2013 till September 2014 evaluated for correlation. Among 50 patients 25 had ER (+) receptor status, with tumor size of 2-5cm was seen in 19 patients. 9 patients with ER (+) status had zero lymph node status. 20 patients were SBR grade 2.16 patients had PR (+) status, among these patients 12 had a tumor size of 2-5 cm, 6 patients had 0 lymph nodes and 14 patients were SBR grade 2. 26 patients had HER2neu (+), 8 patients with HER2neu + status had a tumour size of more than 5 cm. 6 patients with HER2neu +receptor status had more than 10 lymph nodes, 21 patients were SBR grade 2.

**Conclusion:** Study concludes presence or absence of estrogen, progesterone and HER2 neu receptor status can help to decide on further plan of treatment and prognosis in breast cancer patients.

**Keywords:** Breast cancer, ER status, Her2neu status, PR status.

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## INTRODUCTION

Breast cancer is the 2<sup>nd</sup> most common cause of cancer among women worldwide and after lung cancer is the 2<sup>nd</sup> leading cause of cancer deaths and is the leading cause of cancer deaths among women.<sup>1,2,3</sup> Contrary to the west where it is more common in the elderly women in Indians it presents at a younger age who present themselves at an advanced stage of the disease with a poorer prognosis as

compared to their western counterparts.<sup>4</sup> Estrogen and Progesterone play a key role in the growth kinetics of the breast. Patients whose tumors are positive for both estrogen and progesterone receptors have a better possibility of remission following Hormonal therapy (70%), than those tumors who are positive for either receptor (30%) or who have very low levels of both receptors (10%). Tumors positive for estrogen and progesterone tend to be better differentiated and are low grade. Negative ER status has shown to be predictive of recurrence of low stage tumors. Negative PR status has shown to be predictive of lymph nodal metastasis.<sup>4</sup> HER2neu or erb-B2 is a epidermal growth factor and patients with metastatic disease with tumors which are HER2neu or erb-B2 positive are likely to benefit from anti HER2neu therapy Trastuzumab (Hercitin).<sup>2</sup> The excess risk of distant recurrence in triple-negative breast cancers[ER(-), PR(-) & HER2neu(-)] versus other forms of cancer, is attributable in large part to an excess of visceral metastases in the first five years following

diagnosis.<sup>4</sup> Triple negative subtype (ER/PR-,Her2neu) has the worst overall and disease-free survival compared to the other subtypes.<sup>5</sup> Nowadays IHC testing for ER and PR is mandatory for invasive cancers.<sup>6</sup>

**AIMS AND OBJECTIVES**

To correlate the Histological Grading, Tumor size and nodal status with ER- PR and Her 2 Neu status in women undergoing Modified Radical Mastectomy for breast cancer.

**MATERIALS AND METHODS**

Study is carried out on 50 female in patients who underwent Modified Radical Mastectomy for breast cancer proved by FNAC at Father Muller Medical College Hospital at Mangalore from Jan 2013 till September 2014. The study excluded patients who underwent lumpectomies, breast biopsies and neo-adjuvant chemotherapy for locally advanced breast cancers. The study was approved by the institutional ethical committee. Expression of estrogen receptors (ER), progesterone receptor (PR) and HER2neu receptors were analysed in the modified Radical mastectomy specimen. After formalin fixation, paraffin embedding and staining with hemotoxylin and eosin, histopathological features were determined, and histological grading was assessed using Scarff Bloom Richarson method modified by Elston and Ellis were determined prior to immunohisto chemical examination. ER or PR was considered positive, if more than 1% tumor cell nuclei are immunoreactive. Negative for ER or PR if less than 1% of tumor cell nuclei are immunoreactive. Her2neu status was assessed by a score that includes the intensity and percentage of positive tumor cells. HER2neu testing results fall into three categories positive, equivocal and negative. For the purpose of this study equivocal results were considered negative.

**Statistical Analysis**

The Fischer’ T test was used to compare the association of expression of ER, PR and Her2 neu and macroscopic and microscopic characteristics of the tumors.

**RESULTS**

50 patients were included in the study, 11 patients were in the age group of 30-40 years, 14 patients were in the age group of 40-50 years, 16 patients were in the age group of 50-60 years and 9 patients were above 60 years of age. Out of 50 patients 37 had SBR grade 2 tumors, 10 had SBR grade 1 tumors and 3 patients had SBR grade 3 tumors. Out of 50 patients 2 patients had a tumor size less than 2 cm, 37 patients had a tumor size between 2-5 cm and 11 patients had a tumor size more than 5 cm. Out of 50 patients, 23 patients had 0 lymph nodes, 11 patients

had less than 4 lymph nodes, 9 patients had 4-11 lymph nodes and 7 patients had more than 10 lymph nodes. Among 50 patients 25 patients had a positive estrogen receptor status and 25 patients had a negative estrogen receptor status 16 patients had a positive progesterone receptor status and 34 patients had a negative progesterone receptor status 26 patients had a Her2neu positive receptor status and 24 patients had a HER2neu negative receptor status. 14 patients were triple negative. 2 patients who were ER+ had tumor size less than 2 cm. 19 patients with ER +receptor status had a tumor size of 2-5cm and 21 patients with ER – receptor status had a tumor size of 2-5 cm.3 patients with ER + status had a tumor size of more than 5 cm .5 patients with ER –status had a tumor size of more than 5 cm. 1 patient who had a tumor size of less than 2 cm had a ER + receptor status

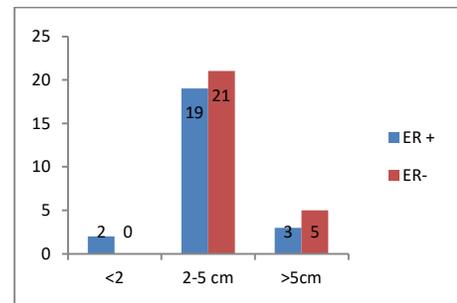


Figure 1: Correlation with tumour size and er status

2 patients who were PR (-) had tumour size less than 2 cm. 12 patients with PR (+) receptor status had a tumor size of 2-5cm and 27 patients with PR (-) receptor status had a tumour size of 2-5 cm.3 patients with PR (+)status had a tumour size of more than 5 cm .5 patients with PR(-) status had a tumor size of more than 5 cm. 2 patients who were HER2neu (-) had tumor size less than 2 cm. 18 patients with HER2neu (+) receptor status had a tumor size of 2-5cm and 22 patients with HER2neu – receptor status had a tumor size of 2-5 cm.8 patients with HER2neu (+)status had a tumor size of more than 5 cm . Triple negative 12 patients had a tumor size of 2-5 cm and 2 patients had a tumor size of less than 2 cm. 9 patients with ER(+ )receptor status had 0 lymph nodes 7 patients with ER (+)receptor status had less than 4 lymph nodes 7 patients with ER(+) receptor status had 4 to 10 lymph nodes 2 patients with ER (+)receptor status had more than 10 lymph nodes 14 patients with ER - receptor status had 0 lymph nodes 4 patients with ER -receptor status had less than 4 lymph nodes 2 patients with ER(-) receptor status had 4 to 10 lymph nodes 5 patients with ER(-) receptor status had more than 10 lymph nodes. 6 patients with PR (+) receptor status had 0 lymph nodes 5 patients with PR(+) receptor status had less than 4 lymph nodes 3 patients with PR (+)receptor status had 4 to 10

lymph nodes 2 patients with PR (+)receptor status had more than 10 lymph nodes 17 patients with PR - receptor status had 0 lymph nodes 6 patients with PR -receptor status had less than 4 lymph nodes 6 patients with PR( - )receptor status had 4 to 10 lymph nodes 5 patients with PR (-) receptor status had more than 10 lymph nodes.

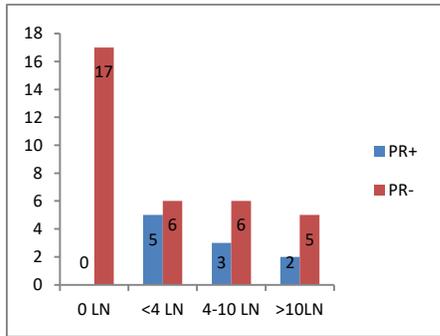


Figure 2: Correlation between lymph node status and pr

10 patients with HER2neu (+) receptor status had 0 lymph nodes 4 patients with HER2neu (+) receptor status had less than 4 lymph nodes 6 patients with HER2neu (+) receptor status had 4 to 10 lymph nodes 6 patients with HER2neu (+) receptor status had more than 10 lymph nodes 13 patients with HER2neu (-) receptor status had 0 lymph nodes 7 patients with HER2neu (-)receptor status had less than 4 lymph nodes 3patients with HER2neu -receptor status had 4 to 10 lymph nodes 1 patients with HER2neu - receptor status had more than 10 lymph nodes. Triple negative 10 patients had 0 lymph nodes, 2 patients had less than 4 lymph nodes, 1 patient had 4-10 lymph nodes, 1 patient had more than 10 nodes lymph node. ER (+) patients. 5 patients were SBR grade 1, 20 patients were SBR grade 2, ER - patients 5 patients were SBR grade 1, 17 patients were SBR grade 2, 3 patients were SBR grade 3. PR + patients 2 patients were SBR grade 1, 14 patients were SBR grade 2, PR - patients 8 patients were SBR grade 1, 23 patients were SBR grade 2,3 patients were SBR grade 3. HER2neu + patients 4 patients were SBR grade 1, 21 patients were SBR grade 2, 1 patients was SBR grade 3HER2neu - patients 6 patients were SBR grade 1, 16 patients were SBR grade 2,2 patients were SBR grade 3.

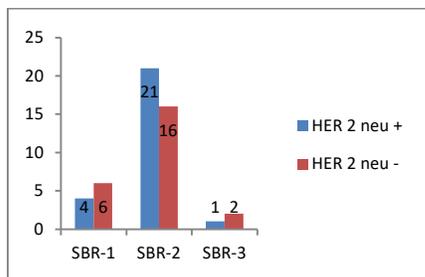


Figure 3: Correlation between tumour grade and her 2 NEU status

Triple negative 4 patients were SBR grade 1, 8 patients were SBR grade 2,2 patients were SBR grade 3.

**DISCUSSION**

Age group under study was 30-70 with majority of the patients in the age group of 51-60 years. Equal number of patients was estrogen receptor positive and negative. Majority of the patients were progesterone receptor negative and HER 2 neu receptor positive. Tumor size when compared with the estrogen receptor status in 50 women, most of them in the study had tumour size between 2 and 5 cm and majority of them were estrogen receptor negative and as the tumour size increased the negativity increased which was found to be stat statically significant. Tumor size when compared with the progesterone receptor status in 50 women, most of them in the study had tumor size between 2 and 5 cm and most of them were progesterone receptor negative and as the tumor size increased the negativity increased which was found to be statistically significant. Tumor size when compared with the HER2neu receptor status in 50 women, most of them in the study had tumor size between 2 and 5 cm and most of them were HER2neu receptor negative and as the tumour size increased the positivity increased which was found to be statistically significant. Most of triple negative patients had a tumour size of 2 to 5 cm. Lymph node status when compared with estrogen receptor status shows that when the lymph node number increases the estrogen receptor becomes negative which was found to be statistically significant. Lymph node status when compared with progesterone receptor status shows that when the lymph node number increases the progesterone receptor becomes negative which was found to be statistically significant. Lymph node status when compared with HER 2neu status shows that when the lymph node number increases the HER 2neu receptor becomes positive which was found to be statistically significant. Most of the triple negative patients had 0 lymph nodes. Tumor grade when compared to estrogen receptor status showed that out of 50 women most of the cases were grade 2 and majority were estrogen positive which was found to be statistically significant. Tumor grade when compared to progesterone receptor status showed that out of 50 women most of the cases were grade 2 and majority were progesterone negative which was found to be statistically significant. Tumour grade when compared to HER2 neu receptor status showed that out of 50 women most of the cases were grade 2 and majority were HER2neu positive which was found to be statistically significant. Majority of the triple negative patients had grade 2 tumours. Comparing the present study with other studies.

Studies	Mohala et al <sup>7</sup>	Eisenberg et al <sup>8</sup>	Almsari et al <sup>9</sup>	Present study
Number of patients	146	306	91	50
Duration of the study	3 years	1 year 6 months	4 years	1 year 6 months
Type of study	Prospective	Prospective	Retrospective	Retrospective
Tumour size and ER	Not considered	Smaller tumours were positive	Smaller tumours were positive	As tumour size increased positivity increased
Tumour size and PR	Not considered	No significant relation	Smaller tumours were positive	As tumour size increased negativity increased
Tumour size and HER2neu receptor	Not considered	Not considered	Her2 neu overexpression associated with larger tumour size	As tumour size increased positivity increased
Lymph node status and ER	Not considered	Not considered	Negative more lymph nodes	Negativity and lymph node status directly related
Lymph node status and PR	Not considered	Not considered	Negative more lymph nodes	Negativity and lymph node status directly related
Lymph node status and HER2neu status	Not considered	Not considered	HER2 neu overexpression associated with more than 3 lymph node metastasis	Positivity and lymph node status directly related
Tumour grade and ER	As grade increases more negative	As grade increases more negative	As grade increases more negative	As grade increases more negative
Tumour grade and PR	As grade increases more negative	As grade increases more negative	As grade increases more negative	As grade increases more negative
Tumour grade and Her 2 neu receptor	Not considered	Not considered	Not significant	As grade increases more positive

**CONCLUSION**

The present study observed, estrogen and progesterone receptor positive cases were well differentiated, less aggressive, and showed low lymph node metastasis. HER2neu receptor positive cases were poorly differentiated, more aggressive and showed high lymph node metastasis. So study concludes, presence or absence of estrogen, progesterone and HER2 neu receptor can help to decide on further plan of treatment and prognosis.

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